Geriatric Psychiatry Study Guide

Mastering the Competencies

Ana Hategan
James A. Bourgeois
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ISBN 978-3-319-77127-4 ISBN 978-3-319-77128-1 (eBook)
https://doi.org/10.1007/978-3-319-77128-1

Library of Congress Control Number: 2018938794

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Printed on acid-free paper

This Springer imprint is published by the registered company Springer International Publishing AG part of Springer Nature.
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Physician trainees in general psychiatry and the subspecialty of geriatric psychiatry need to master core competencies in geriatric psychiatry. Equally importantly, practicing psychiatrists confronting recertification examinations and/or desirous of a quick review of geriatric psychiatry can benefit from a concise, case-focused and question-based review of the current practice of geriatric psychiatry. This book is designed to provide short-answer question-based learning centered on the core curriculum topics in geriatric psychiatry. It features over 300 short-answer questions, each comprising the stem of a clinical scenario or concise question. The answers include succinct discussions, pertinent illustrations, and source references.

The format is practical and concise, designed to enhance the reader's clinical understanding and diagnostic skills, and the ability to critically manage an older adult presenting with psychiatric symptoms. This book is intended for physicians in training as well as for physicians who have previously mastered the clinical material and need something more concise on occasion. It will also be of use to professionals in other clinical disciplines. Medical students and graduate students in other disciplines may find the questions and answers a useful addition to their resources during their clinical placements involving the care of older adult patients.

This small-size book knits together evidence-based geriatric psychiatry principles and practice guidelines in a practical and problem-oriented guide for learners at all levels of experience. Unless otherwise specified in this text, "geriatric" and "older adults" refer to those aged 65 years or older. The material covered matches the common existing postgraduate curricula in geriatric psychiatry and helps prepare candidates for their specialty and subspecialty certification examinations. Because various national boards have different examination styles, the questions are written for knowledge and style commonality. Moreover, this book lists the questions by the specific topic rather than a random amalgamation of questions and case scenarios, making it an easy-to-reference text.

This study guide provides evidence-based information and contemporary clinical guidelines for diagnosis and management of geriatric psychiatric disorders. The advantages of this short-answer questions format are manifold: it is learner-focused, allows for active learning and self-directed learning skills, enhances content knowledge while simultaneously fostering critical thinking, and optimally positions readers to prepare for real-world examination experiences.

Written and edited by expert psychiatrists and educators, ***Geriatric Psychiatry Study Guide: Mastering the Competencies*** covers main topics within geriatric psychiatry, with some specific topics such as aging with neurodevelopmental disorders, substance use disorders, and sexuality and sexual dysfunctions in later life becoming even more relevant now that the Baby Boomers are aging. Since delirium so often presents in the context of other psychiatric illnesses, the authors have included delirium cases in many other chapters, where delirium is managed along with the other psychiatric comorbidities. The authors believe this approach presents patients with all of the complexities that they live with and illustrates the need for the psychiatrist to always actively manage all other psychiatric illnesses that co-present with delirium. We hope that this text becomes a valuable reference and teaching tool that provides an opportunity for learning across a rapidly growing field.

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Topic 1: Physiology and Pathology of Aging

Question 1.1

Mrs. A is 89 years old and has been a widow for the past 2 years. She lives alone in a two-story house, while her only family member, her 62-year-old son, lives overseas. She is a retired administrative assistant and has a reasonably good income. She has had varied interests throughout her life; most notably she likes reading and music. Mrs. A no longer drives and depends on a friend to drive her places, including to the medical appointments with her primary care physician, local bank, shopping, church, community library, and visiting another friend at a retirement home. Mrs. A has been having increasingly poor health over the past 5 years. She has a diagnosis of recurrent major depressive disorder, osteoporosis, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, peripheral neuropathy, and hearing and vision impairment for which she declined to wear hearing aids and corrected lenses, respectively. She quit smoking 40 years ago. Last year, she sustained compression fractures of the T12-L2 vertebrae and right hip fracture from a fall while getting out of bed. Her mobility has declined considerably since her hip repair so that she now uses a walker to ambulate outside and sometimes uses it in the house but more often relies on a cane and holding onto the furniture. She has complained of chronic muscle weakness. Her selective serotonin reuptake inhibitor (SSRI) antidepressant, citalopram, was switched to mirtazapine because of concerns of SSRI-related falls. Her memory has been deteriorating over the past 2 years, which concerns her primary care physician. She denies any problems about her memory and gets frustrated and annoyed with her physician who tries to assess her cognitive impairment to monitor for any illness progression. An occupational therapist has conducted a recent in-home functional assessment, which revealed evidence of burned pots, pile of unpaid bills left on the floor, the house unkempt, and little food in the refrigerator. She lost 10% of her body weight during the past year. Her physician has also

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_1

noticed that she has some difficulty finding words and is repetitive. She appears to be able to manage to dress herself, but her personal hygiene is questionable. To date she has refused any outside help. Her Montreal Cognitive Assessment (MoCA) score is 17/30 (a year prior this was 20/30). Her son has called her primary care physician asking for advice on what to do in order to help her remain at home. Her primary care physician has referred her to you, a psychiatrist at the outpatient geriatric psychiatry clinic, for assessment and intervention.

A. What Are the Main Components of Medical Assessment in This Case?

The key components of medical assessment to be reviewed in this case include the following:

- Evaluation of mobility in a patient with balance impairment and risk of falls.
- Identification of causes of falls to enable treatment and reduce morbidity (e.g., rule out cardiac disease, metabolic disorders, and medications as cause for falls including opioids and benzodiazepines). Based on fall risk, a 2012 update of the Beers Criteria classified SSRIs as potentially inappropriate medications in *all* older adults. Experts were of the opinion that the application of these recommendations, not only to frail seniors, but to all older adults, may impact clinical practice and health policy with negative consequences [1]. Subsequently, a 2015 systematic review found that there was no level 1 evidence that SSRIs cause falls [1].
- Provision of optimum osteoporosis management.
- Understanding the concept of blood pressure variability (e.g., supine hypertension with orthostatic hypotension) that can contribute to the risk of falls.
- Identification of the cause of peripheral neuropathy that can contribute to falls.
- Discussion of the differential diagnosis of cognitive decline: delirium, major neurocognitive disorder, and/or depressive disorder. For example, an acute versus more gradual decline suggests delirium, especially if there is evidence of infection on history or new medication is prescribed or increased. A change in cognition particularly in the context of a previously independent person, now limited functionally and socially isolated, may indicate depression. A low mood versus self-neglect due to memory difficulties needs to be explored.
- Provision of optimal management for comorbid depressive and neurocognitive disorder.
- Facilitation of education to family regarding management of neurocognitive disorder.
- Recommendation of non-pharmacological treatment (e.g., lifestyle measures like exercise, importance of smoking cessation) and addressing social isolation.
- Assessment of potentially reduced ability to access help due to communication, cognitive decline, and impaired judgment and insight.
- Assessment of capacity to make decisions and power of attorney.

Table 1.1 The five Fried's features of frailty [3]

Frailty: ≥ 3 features Pre-frailty: 1 or 2 features No frailty: 0 features	1. Unintentional weight loss (≥5% of body weight in the last year)
	2. Self-reported exhaustion (low energy)
	3. Muscle weakness (low grip strength)
	4. Slow walking speed (>6–7 s to walk 15 ft)
	5. Low physical activity (Kcal spent on activity scale—males <383 Kcal, females <270 Kcal)

B. Define Frailty Syndrome and Its Adverse Outcomes

Frailty is a common clinical syndrome in older adults, and it encompasses losses in physical, psychological, or social domains [2]. In the absence of a gold standard definition, frailty has been characterized by Fried et al. as meeting three or more of five clinical criteria (see Table 1.1) [3]. Therefore, this syndrome is marked by loss of physiological reserve, function, and strength. Alternatively, frailty has been defined as a risk index (or frailty index) by considering the number of deficits accumulated over time including disability, diseases, physical and cognitive impairments, psychosocial factors, and geriatric syndromes (e.g., falls, urinary incontinence, delirium) [3].

Frailty carries an increased risk for negative outcomes including falls, cognitive decline, infections, hospitalization, institutionalization, disability, and death [2, 3]. Frailty is associated with a significant financial cost to healthcare systems, particularly because frailty appears to have an incremental effect on ambulatory healthcare expenditures [4]. In this vein, developing cost-effective care for frail patients may result in improvement in long-term care and outcomes of frailty [2].

C. How Is Frailty Diagnosed?

Frailty is diagnosed with various instruments, which can be grouped into two operational types [3, 5]:

- Unidimensional level, based on the physical and biological dimension
- Multidimensional level, based on the interactions among physical, psychological, and social domains

On the unidimensional level, the best-known operational definition of frailty is that proposed by Fried et al. [3], which formed the basis for the Cardiovascular Health Study Index. As previously stated at Question B, frailty is defined by five features (see Table 1.1). The presence of three or more of these features indicates frailty, one or two indicates pre-frailty, and none denotes no frailty [3]. Age-related sarcopenia (i.e., age-related low muscle mass and low muscle strength or age-related physical performance) is not per se synonymous with frailty, but they may overlap in this type of operational definition [6, 7]. A majority of frail older adults present with sarcopenia, but not all older adults with sarcopenia are frail [2].

Nonetheless, a multidimensional approach to frailty reflects a wider context of a person's functioning based on interactions among physical, psychological, and social domains [5]. Within this framework, adults who present losses in one or more of these levels of functioning may be considered in a state of frailty [8]. This operational definition was used in various tools to assess frailty. One of those tools is the frailty index (also known as the deficit accumulation index), developed as an accumulation of deficits such as symptoms, physical and cognitive impairment, diseases, disabilities, psychosocial risk factors, and laboratory abnormalities, where more deficits identified in a given adult indicate a greater likelihood that an adult is frail [9]. The frailty index is a ratio of deficits identified in relation to the number of all deficits considered and is associated with adverse outcomes including risk of institutionalization and death [9].

Another multidimensional instrument is the Tilburg Frailty Indicator (TFI), which is a self-report questionnaire (see Fig. 1.1) [8]. The TFI has two parts: part A consists of ten questions on frailty determinants (e.g., age, sex, marital status, education level, lifestyle), whereas part B includes (1) physical domain (physical health, unintentional weight loss, difficulty walking, problems with balance, hearing, vision, hand strength, and physical tiredness), (2) psychological domain (cognition, depression, anxiety, and coping), and (3) social domain (living alone, social

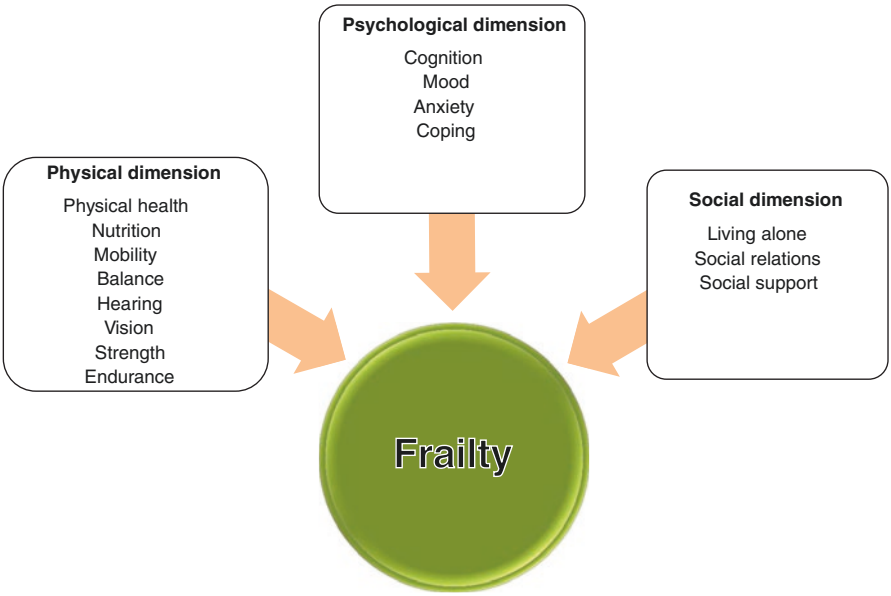


Fig. 1.1 Components of frailty using the Tilburg Frailty Indicator. Multidimensional concept of frailty integrating various domains of functioning that may interact and accelerate frailty development (the figure illustrates the structure of the Tilburg Frailty Indicator tool as defined by Gobbens et al. [8])

relations, and social support). The TFI tool's total score may rank from 0 to 15, where frailty is determined if the total TFI score is at least 5 [8].

D. According to the Tilburg Frailty Indicator (TFI), What Components of Frailty Do You Identify in Mrs. A's Case?

According to TFI tool described at the answer for Question C, a score of 5 or more indicates a state of frailty [8]. Mrs. A has a total score of 14. Based on Fig. 1.1, the components of frailty in this case include multiple physical health issues, unintentional weight loss, difficulty walking, problems with balance, sensory impairment with hearing and vision deficits, muscle weakness, low energy, cognitive impairment, depression, coping problems, living alone, and restricted social relations and social support.

E. What Is the Management of Frailty?

Exercise training appears to be the basis of effective management of pre-frailty and frailty, in addition to periodic monitoring of food intake and body weight. However, the most appropriate type of training requires further elucidation, and more high-quality trials are needed. Interventions such as nutritional supplements, vitamin D, androgen, antioxidants, and anti-inflammatory drugs require further investigation to determine the real effectiveness [2].

Question 1.2

What Cognitive Domains Tend to Be Preserved into Advanced Old Age?

In older adults, acute and chronic illnesses, including neurocognitive disorders, occur within the context of age-related alterations in physiology at the organ-system level, often influenced by patient behaviors (e.g., smoking, diet, physical activity) and the environment (e.g., toxins). These age-related changes affect virtually all organ systems, including the central nervous system, and increase the vulnerability of older adults to brain-system dysfunction, contributing to the burden of multiple comorbidities. In normal aging, episodic memory, rate of learning, memory retrieval, three-dimensional perception, problem-solving, processing speed, and many domains of executive functioning tend to decline. However, general skills and knowledge, implicit (automatic) memory, memory retention, procedural (motor) memory, vocabulary, fund of knowledge, attention, object perception, and the ability to perceive abstractions tend to be preserved into advanced old age (see Table 1.2) [10, 11].

Table 1.2 Cognitive changes in normal aging [10, 11]

Cognitive domain	Definition	Examples	Trajectory
Intelligence			
Crystallized intelligence	Skills, knowledge, and abilities that are well practiced and familiar Related to experience	Vocabulary, general knowledge	Stable or slight growth through the seventh decade
Fluid intelligence	Problem-solving and reasoning for new things	Executive function, judgment	Slow decline from third decade
Processing speed	Speed with which cognitive activities are performed	Slower performance on trails B test	Slow decline from third decade
Attention			
Selective attention	Ability to focus only on relevant information	Driving	Generally stable, with slight decline in late life
Divided attention	Ability to multitask	Drive and carry on a conversation	Generally stable, with slight decline in late life
Memory			
Semantic memory	Fund of knowledge	Recall of US presidents after WWII	Generally stable, with late-life decline
Episodic memory	Memory for personally experienced events	Recall of last year's summer vacation	Slow decline throughout life
Implicit memory	Automatic triggered recall Procedural memory (motor memory)	Recall of tune and lyrics to national anthem How to ride a bicycle, play piano, or type on a keyboard	Generally stable throughout life
Memory acquisition	Learning new things	Studying a foreign language	Rate of acquisition declines with aging
Memory retention	Successful learning		Preserved with aging
Memory retrieval	Recall	Recalling recently learned new words	Declines
Language			
Verbal fluency and vocabulary		Carrying on a conversation	Stable; vocabulary may improve with aging
Visual confrontation naming	Correctly naming a previously familiar object when presented with it	Seeing a pencil and calling it "pencil"	Stable with slow decline after age 70

Table 1.2 (continued)

Cognitive domain	Definition	Examples	Trajectory
Verbal fluency	Spontaneous word generation within a category	Naming as many words as possible beginning in "S" in 1 min	Declines
Visuospatial abilities			
	Understanding space in two and three dimensions	Assembling a furniture kit, drawing a complex shape	Declines
	Object perception	Spatial perception when driving, recognizing faces	Stable
Executive functioning			
	Organize, plan, problem-solve, self-monitor, mental flexibility	Planning and preparing a meal	Declines after age 70
	Response inhibition	Avoiding patterned responses inappropriate for situation, e.g., connecting 1-2-3 … when asked to connect the first number, first letter, and so on (1-A-2-B-3-C …)	Declines
	Reasoning	Solving math problems	Declines
	Abstractions	Appreciate similarities (train and bicycle are modes of transportation); meaning of proverbs ("People in glass houses…")	Stable

From: Hirsch CH, Hategan A: Physiology and Pathology of Aging. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; p. 7. 2018; used with permission

Question 1.3

What Are the Main Age-Associated Changes in the Central and Peripheral Nervous System That Increase Vulnerability to Falls?

Over one-third of adults aged 65 and older experience falls annually, resulting in 2.6 million nonfatal fall-related injuries in the USA in 2000 [12]. Age-related changes responsible in part for the high incidence of falls affect the central and peripheral nervous systems, which impact balance, coordination, and the speed and adequacy of motor response to avert a fall.

In older adults, the following physiological changes can contribute to loss of balance and falls [10, 13]:

- Muscle mass declines 20–35% between the ages 20 and 80, with a corresponding reduction in muscle strength (although this can be partially reversed with exercise).
- Peripheral vibration sense declines more rapidly than touch and pain.

- Sensitivity to light touch decreases.
- Myelinated nerve fibers conduct signals more slowly, resulting in delay of transmission of sensory information from the feet and joints to the spinal cord.
- Mechanoreceptors in the joints, including the knees, hips, and neck, may become damaged from osteoarthritic changes or lost because of joint replacement, resulting in loss of peripheral sensation and proprioception that may debilitate postural control in older adults [13].
- Motor signals are required to pass through the anterior horn cells of the spinal cord to the muscle in response of the brain to postural perturbations; however, the number of motor units (a unit represents a single motor neuron and all of its innervated muscle fibers) and the number and diameter of motor axons in the spinal cord decline with age, whereas the size of the motor unit increases, with the remaining motor neurons innervating relatively more muscle fibers, resulting in coarser movements.
- Motor deconditioning occurs more rapidly in older adults, with substantial decline of muscle strength and balance occurring from even a few days of bed rest due to both psychiatric and medical hospitalization.

Question 1.4

Describe the Key Age-Associated Changes in the Perception of Pain

Age-associated changes in the central and peripheral nervous systems include a reduced peripheral pain sensitivity but greater overall perceived pain once the threshold for pain is reached, which leads to central sensitization. This is explained by the myelinated A delta fibers that subserve the immediate sensation of pain, whereas the unmyelinated, slower-conducting C fibers mediate the sustained pain that may ensue. The numbers of both types of pain fiber decrease with aging, resulting in a reduced ability to detect pain. When pain is detected, there is often a decreased pain tolerance in older adults, which may result from central sensitization. This occurs in part from an increased activation of mast cells (mast cell activation syndrome) in the spinal cord and brain, especially in the thalamus, along with activation of microglia, resulting in the release of inflammatory cytokines and reduced central inhibition of pain sensitivity [14]. Certain psychotropic medications (e.g., serotonin-norepinephrine reuptake inhibitors, gabapentin, pregabalin) may help reduce central sensitization [15–17], despite their independent risk associated with falls [18].



Fig. 1.2 Rating scales for pain. From DeVido J, Hirsch CH, Sanger N, Rosic T, Samaan Z, Bourgeois JA. Substance use disorders in late life. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; p. 6. 2018; used with permission

Question 1.5

Clinicians working with older adults should include interviewing questions in their evaluation of pain interfering with daily functioning and recovery from comorbid psychiatric disorders, including depressive disorders.

A. Describe the Importance of Assessing Pain, and List Commonly Used Pain Rating Scales in Older Adults

In older adults, pain severity can interfere with daily functioning and recovery from depressive disorders [19]. Psychiatric clinicians should include questions about pain (e.g., location of pain, severity, aggravating factors, duration) in their routine evaluation of older patients. In older adults, pain is commonly rated by the visual analogue scale, numerical rating scale, and the verbal rating scale (see Fig. 1.2) [20]. The key descriptors of these scales are the following:

- With visual analogue scale, patients are asked to rate their pain experience along a line marked by verbal descriptors depicting pain intensity.

- With numerical rating scale, patients are asked to mark their pain on a numerical scale anchored by no pain at all at one end and worst pain imaginable at the other end.
- With verbal rating scale, patients are asked to choose from a list of adjectives that describe pain intensity.

B. Name Common Observable Signs or Behaviors That Indicate Pain in an Older Patient with Major Neurocognitive Disorder and Limited Ability to Communicate. Name Common Observational Validated Pain Scales in Those with Limited Ability to Communicate

Chronic pain is highly prevalent in the aging population. Patients with neurocognitive disorders are susceptible to pain which is frequently under-recognized and undertreated [21]. Evidence has shown that nearly half of cognitively intact long-term care residents had scheduled pain medication orders, but only 25% of residents with cognitive impairment had such orders [22]. Therefore, inability to successfully communicate pain in seniors with severe major neurocognitive disorders is a major barrier to effective treatment.

Research has focused on the identification of behaviors that may suggest pain in patients with major neurocognitive disorder, which have been incorporated in observational pain scales. Facial expression is an important nonverbal pain behavior. In addition to observing changes in patient's facial expression (e.g., grimacing, wincing), behavioral signs in other domains (e.g., vocalizations, body movements) have also been used in validated observational pain scales (e.g., Abbey Pain Scale, Pain Assessment in Advanced Dementia Scale (PAINAD), Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC)). The PAINAD and PACSLAC both have been recommended as among the best clinically useful instruments and psychometrically strongest instruments [21]. Figure 1.3 summarizes common signs or behaviors that can indicate pain in older adults with limited ability to communicate and which have been used in validated observational pain scales [21].

C. Describe the Key Principles of Pain Management in Older Adults with Comorbid Psychiatric Disorders

Given the strong association between chronic pain and depression and anxiety [23] and the potential adverse side effects of opioids and adjuvant drugs for pain management (e.g., antidepressants, anticonvulsants) on the management of comorbid psychiatric disorders, psychiatrists should be familiar with the basic principles of stepped analgesic regimens for chronic pain based on consensus guidelines in older adults [24, 25]. Mild pain should be treated with a non-opioid medication (e.g., acetaminophen) or nonsteroidal anti-inflammatory drugs (e.g., ibuprofen, naproxen). However, nonsteroidal anti-inflammatory drugs should be used cautiously because of potential

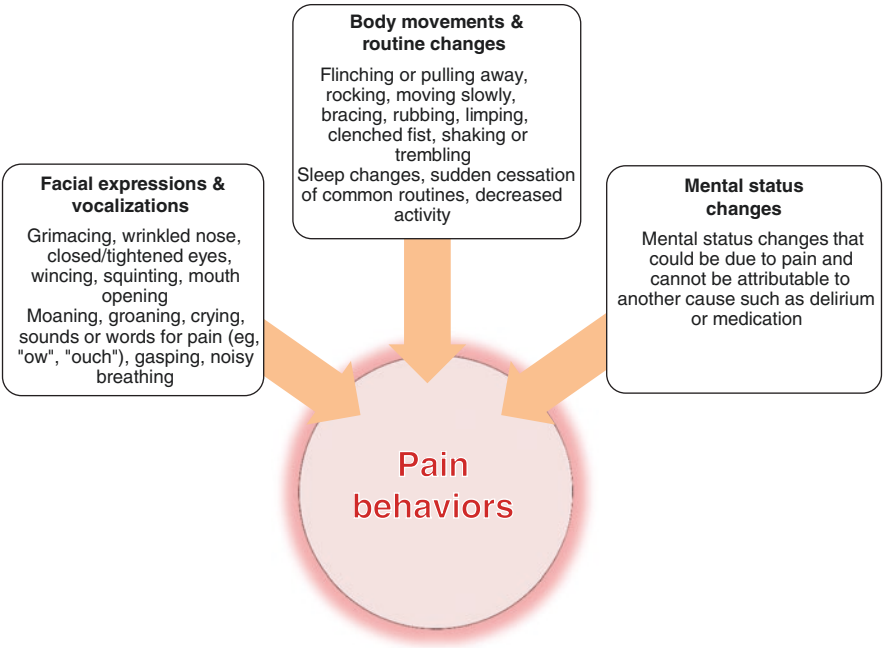


Fig. 1.3 Common signs or behaviors that can indicate pain in older adults

adverse effects on renal function, gastrointestinal bleeding, and sodium retention. Acetaminophen doses greater than 4000 mg within a 24-h period should be avoided due to the risk of hepatic injury. Acetaminophen should be continued whenever possible despite the addition of opioids, to provide a synergistic effect, with the goal of reducing opioid dosage. If opioid use becomes chronic, adding an adjuvant drug should be considered. Therefore, psychiatrists can recommend a selective norepinephrine reuptake inhibitor or another antidepressant class when depressive or anxiety disorders are comorbid with pain. Non-pharmacological approaches (e.g., cognitive behavioral therapy for pain, mindfulness, biofeedback, exercise) may reduce pain and improve function [24]. Escalating doses of opioids may be required in patients with chronic severe pain that is refractory to non-opioid and adjuvant analgesics, which can lead to physiological dependence (i.e., emergence of tolerance and/or withdrawal). These patients may benefit from referral to a pain specialist. Clinicians should be aware that a prior history of substance use is a risk factor for opioid misuse [26]. Drug-seeking behavior to achieve pain control can be difficult to distinguish from drug-seeking behavior resulting from addiction. Reported pain severity disproportionate to the patient's appearance and behavior (e.g., the patient jokes with the physician and looks physically comfortable, but when asked about pain, the patient states it is a "10 out of 10") and evidence of "doctor-shopping" for additional opioids are clues for addiction, which needs to be addressed by the clinician.

Question 1.6

Name the Clinically Relevant Age-Associated Changes in the Heart

In the absence of cardiovascular disease, aging is accompanied by [10]:

- Thickening of the left ventricle.
- Delayed diastolic relaxation (diastolic dysfunction).
- Reduced passive filling of the ventricles, with greater reliance on atrial contraction.
- Increased vulnerability to rate-related heart failure and decreased ability to tolerate supraventricular arrhythmias in general, and atrial fibrillation in particular, in those with diastolic dysfunction.
- Left ventricular ejection fraction at rest is usually preserved with aging. Notably, diastolic dysfunction is diagnosed when the contribution of early passive filling (E) drops below the atrial component (A), reported as an E/A ratio < 1 [27].

Question 1.7

What Is the Association Between Atrial Fibrillation and Cognitive Function?

The risk of developing atrial fibrillation increases with age and is an independent risk factor for major neurocognitive disorder, independent of history of clinical stroke [28].

In the Atherosclerosis Risk in Communities study (mean age, 76.9 years), persistent atrial fibrillation (100% of time in atrial fibrillation) was associated with significantly worse performance on multiple neurocognitive tests compared to participants with paroxysmal atrial fibrillation (1–6% of time in atrial fibrillation), after adjustment for history of clinical stroke [29]. Meta-analysis has shown that anticoagulation therapy in patients with atrial fibrillation has been superior to antiplatelet therapy in minimizing decline in scores on the Mini-Mental State Examination, but anticoagulation has shown neither benefit nor harm in preventing the development of major neurocognitive disorder [30].

Question 1.8

Provide Examples of Age-Related Autonomic Changes, and Outline How They Affect the Pathophysiology of Aging

The aging heart undergoes neurohumoral changes that contribute to autonomic changes and neurocardiovascular instability, including an alteration of baroreceptor reflex function that increases prevalence of orthostatic hypotension.

Age-related neurocardiovascular instability is more common in neurodegenerative disorders, such as Parkinson disease and Lewy body disease, with a synergistic effect. Neurocardiovascular instability is also more common in major neurocognitive disorder due to Alzheimer disease, vascular disease, as well as in mild neurocognitive disorder (also known as "mild cognitive impairment—no dementia"), compared to cognitively intact controls [31]. These age-related autonomic changes can affect heart rate, resulting in increased susceptibility to bradycardia and syncope in patients who take certain medications, such as cholinesterase inhibitors [32].

Question 1.9

Define Orthostatic Hypotension, Its Causes, and Associated Symptoms and Management

Orthostatic hypotension is defined as a drop in systolic blood pressure of ≥20 mmHg (or in diastolic blood pressure of ≥10 mmHg) within 3 min of standing when compared with blood pressure from the sitting or supine position. The prevalence of asymptomatic or symptomatic orthostatic hypotension in older adults is approximately 20% among those aged 65 and older, 30% among those aged 75 years and older, and over 50% among the frail seniors (e.g., those residing in skilled nursing facilities) [33]. The orthostatic hypotension is caused by a postural drop in blood pressure that occurs when α1-adrenergic vasoconstriction fails to counteract postural venous pooling, with an inadequate compensatory rise in heart rate, leading to a drop in cardiac output. Orthostatic hypotension can cause postural lightheadedness, syncope, loss of balance, falls, and fall-associated injuries. If severe enough, orthostatic hypotension can result in stroke or myocardial infarction.

Polypharmacy is prevalent among older patients. Medication classes, such as beta blockers, calcium channel blockers, and diuretics, independently and additively contribute to as well as exacerbate age-associated orthostatic hypotension. Many psychotropic medications, such as tricyclic antidepressants, trazodone, clozapine, quetiapine, olanzapine, and ziprasidone, have been implicated in causing or exacerbating orthostatic hypotension [34–36]. Lithium may cause impairment of the distal tubular response to vasopressin and result in diabetes insipidus, which can lead to volume depletion. In a clinical study of 342 older US veterans, the prevalence of orthostatic hypotension increased with the number of potentially causative medications, from 35 to 65% among those taking none to those taking three or more, respectively [37]. It is essential that psychiatrists review the current list of medications that could contribute to orthostatic blood pressure changes as well as check for orthostatic hypotension in their older patients before prescribing a new psychotropic medication that could cause or exacerbate orthostatic hypotension (see Table 1.3 for a list of select causative medications).

Table 1.3 Select medications that can cause orthostatic hypotension

Medication class	Examples
Antidepressants	Tricyclic antidepressants Trazodone Monoamine oxidase inhibitors
Antipsychotics	Third-generation antipsychotics (e.g., aripiprazole) Second-generation antipsychotics (e.g., clozapine, quetiapine, olanzapine) First-generation antipsychotics (e.g., chlorpromazine, loxapine, flupenthixol)
Antiparkinsonian drugs	Levodopa Selegiline Bromocriptine
Antihypertensives	Diuretics (e.g., thiazide, furosemide) Angiotensin-conversing enzyme inhibitors (e.g., enalapril, ramipril, lisinopril) Calcium channel blockers (e.g., diltiazem, nifedipine) Clonidine Reserpine
Vasodilators	Nitrates (e.g., nitroglycerin) Hydralazine
Alpha-blocking agents	Terazosin Prazosin
Miscellaneous	Barbiturates Narcotics Phosphodiesterase-5 inhibitors (e.g., sildenafil)

Question 1.10

A 69-year-old male with a diagnosis of schizophrenia has been taking olanzapine for several years, with a partial control of his psychiatric illness. He either did not respond to or was unable to tolerate first-generation or any other second-generation antipsychotics in the past. However, over the past 6 months, he has developed worsening parkinsonian symptoms and orthostatic hypotension. His olanzapine was last time optimized to 15 mg daily 2 months ago. More recently, he has complained of dizziness and intermittent chest pain. His other medications included carbidopa-levodopa (antiparkinsonian agent for parkinsonian symptoms) and ramipril (angiotensin-converting enzyme (ACE) inhibitor for hypertension).

In This Case, What Is the Management of Orthostatic Hypotension When Antipsychotic Therapy with Olanzapine Is Required to Continue?

Orthostatic hypotension is a common adverse effect of antipsychotics that may prevent titration to an optimal dose necessary to control psychotic symptoms. Complications of orthostatic hypotension include syncope, falls and fall-related

injuries, transient ischemic attack, stroke, and myocardial infarction [34]. It is imperative to assess the risk of antipsychotic-associated orthostatic hypotension, which is increased in patients with autonomic nervous system diseases (e.g., Parkinson disease) and fluid imbalance and those taking concomitant drugs that affect hemodynamic tone (e.g., ACE inhibitors).

Non-pharmacological strategies and patient education, including slowly rising from the supine position, are crucial first steps in the prophylaxis and management of both asymptomatic and symptomatic orthostatic hypotension. If symptomatic orthostatic hypotension persists despite implementation of non-pharmacological strategies, and there is an indication for continuation of antipsychotic treatment, pharmacological treatment is recommended. Fludrocortisone is a reasonable first choice for symptomatic orthostatic hypotension [34]. In those who do not respond to a trial of fludrocortisone, desmopressin and midodrine may be considered, but safety concerns and lack of evidence limit the utility of these medications [34].

Question 1.11

What Are the Age-Associated Changes of the Cardiac Conduction System?

Over 50% of patients aged 65 and older will have an abnormal electrocardiogram (ECG), and nearly 20% of their ECGs show ST-T changes. With aging, the QTc prolongs linearly between the ages 30 and 90, although the QTc is consistently higher in women but with a slightly higher slope of rise in men [38]. Antidepressants (e.g., citalopram, escitalopram), first-generation antipsychotics (e.g., haloperidol, droperidol), and second-generation antipsychotics (e.g., quetiapine, ziprasidone), which prolong the QTc interval to varying degrees, have the potential for precipitating *torsades de pointes* and ventricular tachycardia. With aging, the sinoatrial node loses pacemaker cells, and the PR interval and QRS duration lengthen [39]. In older adults without clinical cardiovascular disease, particularly the men, nearly 25% have a prolonged QRS duration of over 100 ms. Those with a QRS prolongation are more likely than those without prolongation to develop heart failure over time [40]. Tricyclic antidepressants block the cardiomyocyte sodium channels and should be used cautiously, if at all, in older adults. Although weaker sodium-channel blockers, selective serotonin reuptake inhibitors (e.g., fluoxetine, citalopram, escitalopram) can prolong the QRS duration and lead to cardiac arrest when doses are excessive [41]. Bupropion can also cause QRS prolongation but through a different mechanism than sodium-channel blockade [41].

Question 1.12

There are many non-pathological processes in the aging lung, including structural changes, changes in muscle function, and pulmonary immunologic function.

A. Describe the Clinically Relevant Changes in the Aging Lung

Without clinical lung disease, age-associated changes in pulmonary physiology and function can result in the following [42, 43]:

- Symptoms meeting the criteria for chronic obstructive lung disease stage 1.
- Emphysematous changes, with enlargement of alveoli without destruction of alveolar walls.
- Reduced elastic recoil leading to premature closure of the airways.
- Decreased forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC).
- Increased closing volume (CV), including in the supine position and during general anesthesia.
- Higher residual volume and functional residual capacity, as seen in chronic obstructive pulmonary disease (COPD).
- The chest wall stiffens, adding to the work of breathing by the respiratory muscles (principally the diaphragm and intercostals).
- Altered proportion of type IIa muscle fibers decreases the strength and endurance of the respiratory muscles.
- Altered oxygen transport.
- Greater susceptibility to respiratory failure (i.e., causing hypoxemia) particularly when there is comorbid acute or chronic pulmonary diseases, and medication use that interferes with respiratory drive (e.g., benzodiazepines, opioids).

B. What Are the General Principles of Management in Older Patients with Acute and Chronic Lung and Thoracic Disorders?

Use of sedating medications, especially those that can affect respiratory drive (e.g., benzodiazepines, opioids), in older patients with known lung disease may affect oxygenation and should be used judiciously [43]. A supine position should be avoided in patients with acute and chronic lung and thoracic disorders, including obesity, moderate-to-severe COPD or severe asthma, pneumonia, and kyphosis. For example, patients with COPD should be encouraged to sleep with their thorax elevated at more than 20° to maximize the function of their diaphragms [10]. Patients with kyphosis need to sleep more upright or on their sides. Older inpatients should be encouraged to minimize bed rest by encouraging ambulation (supervised if fall risk or needing oxygen) or sitting up on a chair as much as tolerated instead of lying in bed [10].

Table 1.4 Summary of age-related changes that affect the pharmacokinetics of drugs [44]

Physiologic change	Pharmacokinetic consequence
Decreased serum albumin	Increased free fraction in plasma for highly protein-bound acidic drugs
Increased 1-acid glycoprotein	Decreased free fraction of alkaline drugs
Decreased lean body mass Decreased total body water	Increased plasma concentrations of hydrophilic drugs
Increased body fat	Increased volume of distribution and $T_{1/2}$ of lipophilic drugs
Decreased hepatic blood flow	Potentially decreased first-pass metabolism
Decreased hepatic mass	Slightly decreased phase I metabolism (CYP oxidation, reduction, hydrolysis) *Preserved* phase II metabolism (glucuronidation, acetylation, sulfation)
Decreased renal blood flow and glomerular filtration rate	Decreased renal elimination

From Hirsch CH, Maharaj S, Bourgeois JA. The Chief Adverse Effects of Medications. In: Hategan A, Bourgeois JA, Hirsch CH, editors. On-Call Geriatric Psychiatry: Handbook of Principles and Practice: Springer International Publishing; 2016. p. 163; used with permission

Question 1.13

Describe the Pharmacokinetic Changes That Occur with Physiological Aging

Table 1.4 summarizes the age-related changes that affect the pharmacokinetics of drugs and their pharmacokinetic consequence [44]. There is an age-associated decline in lean body mass and a reduction in total body water, resulting in an increased plasma concentration of hydrophilic drugs. Moreover, there is an increase in total body fat (even in nonobese older adults), leading to an increased volume of distribution and half-life of lipophilic drugs.

Question 1.14

List Clinically Relevant Age-Associated Changes in Hepatic and Renal Function

The relevance of age-associated changes in the liver and kidney generally relates to alterations in drug metabolism (pharmacokinetics) (see Table 1.4). With aging, liver volume decreases between 20 and 40%; hepatic blood flow is reduced in adults aged

65 and older to approximately 35% of that in adults aged 40 and younger. Phase I metabolism, mediated by the cytochrome P450 system and consisting of oxidation, reduction, and hydrolysis reactions, undergoes age-related reduction in activity [45]. Phase II metabolism, consisting of glucuronidation, acetylation, and sulfation, is generally not affected by aging, although changes in protein binding of drugs may influence phase II activity, contributing to reduced clearance of certain drugs (e.g., valproic acid, acetaminophen, naproxen) [45].

Age-associated renal changes include a decline in renal mass, a decline in the glomerular filtration rate (GFR) starting at age 30–40 years at a rate of approximately 0.75 mL/min/year, and a decrease in the number of glomeruli of approximately 30% by age 75. Medications that are cleared by the kidney may necessitate a dose adjustment in older adults. This physiological decrease in renal function may be further accelerated by common conditions such as hypertension, atherosclerosis, and diabetes mellitus [46].

Question 1.15

With aging, there is a decline of skeletal muscle tissue, which is one of the most important causes of functional decline and loss of independence in older adults.

A. Define Sarcopenia of Aging and Its Common Etiological Factors

Sarcopenia, defined as the age-associated loss of muscle mass and function, with regional and age-related variations, has a prevalence of 1–29% in community-dwelling populations, 14–33% in long-term care populations, and 10% in acute care population [47]. Sarcopenia results from multiple pathophysiological mechanisms, including an imbalance between anabolic stimuli such as insulin-like growth factor-1 (IGF-1) and atrophy induced by activation of the ubiquitin proteasome and myostatin pathways, affecting primarily the fast-twitch (type II) motor fibers [48]. Common factors contributing to sarcopenia are summarized in Fig. 1.4.

B. What Are the Long-Term Outcomes of Sarcopenia?

The long-term consequences of sarcopenia include:

- Decreased mobility
- Decreased gait speed
- Difficulty standing from a low chair or toilet
- Difficulty climbing stairs
- Increased risk of falls, frailty, and fatigability

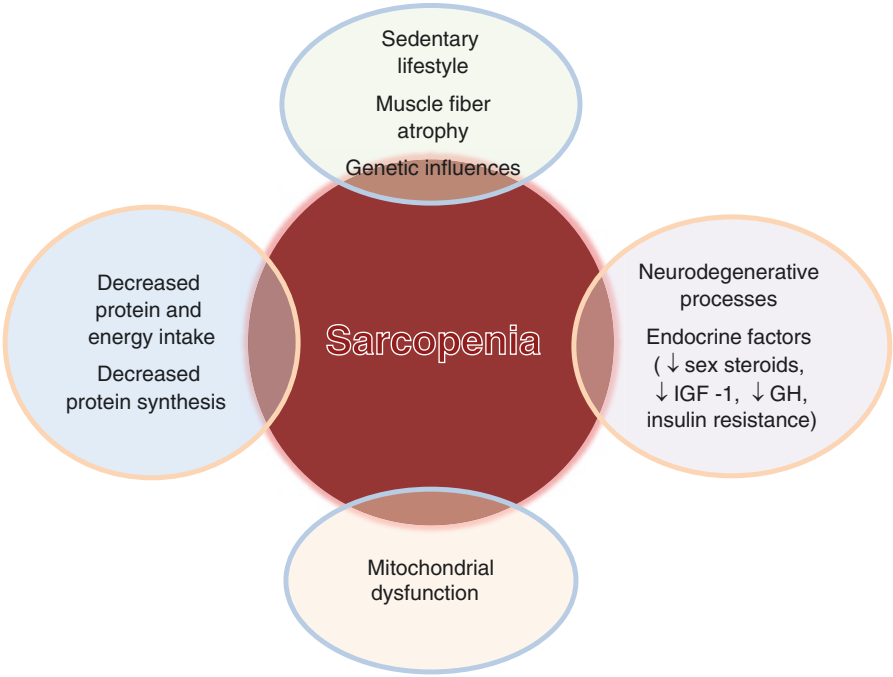


Fig. 1.4 Common factors contributing to sarcopenia. GH, growth hormone; IGF-1, insulin-like growth factor-1

These changes lead to dependence in physical instrumental activities of daily living and, eventually, basic self-care activities such as bathing and transferring. Frailty, a construct in which sarcopenia plays a major role, has been associated with a greater than fourfold risk of depressive and anxiety symptoms in community-dwelling Irish men and women aged 60 and older, after adjusting for age, sex, and history of major depressive or anxiety disorders [49].

C. What Are the Therapeutic Options in Sarcopenia?

Exercise and testosterone can slow or partially reverse sarcopenia, while a sedentary lifestyle, decreased testosterone, mitochondrial dysfunction, decreased protein synthesis, and reduced protein and energy intake promote it [48]. Therefore, therapeutic options can include exercise, nutritional therapy, androgens, and growth hormone [48]. Evidence suggests that exercise improves muscle strength and physical performance [47]. Evidence for nutritional interventions is equivocal due to the low number of studies and heterogeneous study designs. Essential amino acid supplements, including leucine and β-hydroxy-β-methylbutyric acid (HMB) supplements, may improve muscle outcomes [47]. However, protein supplements have not shown consistent benefits on muscle mass and function [47].

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Topic 2: Neuropsychology and Neuroimaging in Clinical Geriatric Psychiatry

Question 2.1

Over the years, there has been much research looking at brain structure and function and how it relates to behaviors. The idea of the brain controlling our thoughts, feelings, and behaviors has fascinated many scientists and physicians in the past. In attempting to understand this concept, Franz Joseph Gall and Johann Gaspar Spurzheim, both German physicians, developed the pseudomedical field of phrenology in the 1790s [1]. Phrenologists believed that by examining the shape and unevenness of the skull, one would be able to determine a person's intellectual aptitudes and character traits. Although phrenology was more or less discredited by 1860, the neuroanatomical studies by Gall and Spurzheim greatly advanced our knowledge of the brain and spinal cord [1]. In understanding brain pathology and psychiatric disorders in older adults, one must first understand the changes associated with normal aging.

A. What Are the Structural Brain Changes Seen in Normal Aging?

The structure of the brain is constantly changing throughout the lifetime. Magnetic resonance imaging (MRI) studies suggest that there is enlargement of the ventricles and that brain volume declines with age, with cortical thickness, and with subcortical volume decreasing by 0.5–1% annually [2] (see Table 2.1 for a list of structural changes seen in normal aging). The frontal cortex, temporal cortex, hippocampus, putamen, thalamus, and nucleus accumbens are the regions that are most strongly impacted by this volume change. The occipital cortex is the least affected [3]. While neuronal loss can occur, the reduction in grey matter is mostly due to shrinkage of neurons, reductions of synaptic spines, and lower numbers of synapses. The length of myelinated axons is reduced by up to almost 50% [2].

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_2

Table 2.1 Structural brain changes and cognitive changes seen in normal aging

Structural changes	Cognitive changes
Enlargement of ventricles Decrease in brain volume (most noted in the frontal cortex, temporal cortex, hippocampus, putamen, thalamus, and nucleus accumbens) Shrinkage of neurons Reduction of synaptic spines Decrease in number of synapses Reduction in length of myelinated axons	Decline in episodic memory Decline in semantic memory Decline in working memory Slower processing speed Increasing executive functioning impairments

B. What Are Some Cognitive Changes Seen in Normal Aging?

The most notable change seen in normal aging is that of memory, with episodic memory and semantic memory being more affected [3]. Episodic memory is a person's memory of autobiographical events (related to times, places, and associated emotions). An example of episodic memory would be of your 30th birthday or your high school graduation. Episodic memory declines from middle age onwards [3]. Semantic memory refers to memory of ideas and concepts that are not drawn from personal experience, such as information that is common knowledge, and are the facts of the world. Knowing the names of the colors, that France is a country in Europe, are examples of semantic memory. Semantic memory increases from middle age to the young old age but then declines in the very old age [3].

Processing speed also gradually declines as we age. Processing speed is the speed with which cognitive activities are performed and is considered a fluid cognitive ability [4]. This fluid ability peaks around the third decade of life and then starts to decline thereafter [4]. This slowing in processing speed can have a negative impact on other cognitive domains. Evidence suggests that the decline in processing speed in normal aging is associated with changes in white matter integrity [5].

There is also much literature suggesting that executive function impairments increase as we age, negatively impacting on daily living activities in older adults [6]. The cognitive abilities of concept formation, abstraction, inductive reasoning, and mental flexibility decline with age, while the abilities of appreciating similarities, reasoning about familiar material, and describing the meaning of proverbs tend to remain stable throughout life [4].

Question 2.2

Briefly Describe the Three Primary Processes in Memory

The three main processes involved in memory are:

- *Encoding*—this is the first step to creating a new memory, beginning with perception through the senses, and is affected by attention and emotion (as emotion tends to increase attention). The four main ways that memory can be encoded are visual (picture), acoustic (sound), tactile (touch), and semantic (meaning).

- *Storage*—this is the passive process of retaining information in the brain, whether in sensory memory, short-term memory, or long-term memory. The more the information is repeated or used, the more likely it is to be retained in long-term memory (process of consolidation).
- *Retrieval*—recall or retrieval is the reaccessing of events or information from the past. In simple terms, this is the process of remembering. Retrieval can only occur if information was encoded and stored. During the recall process, information from long-term memory is moved to short-term memory or working memory, where it can be accessed.

Question 2.3

Over the years, there have been numerous screening tools developed to assess cognition in an older adult. These tools are not meant to be a substitute for a full neuropsychological assessment but are meant to obtain information of key cognitive domains in a brief assessment. The two most commonly used cognitive screening tests are the Mini Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA).

What Is the Sensitivity and Specificity of the MMSE and MoCA in the Diagnosis of Major Neurocognitive Disorder?

The MMSE or the Folstein test is a 30-point questionnaire developed in the 1970s, looking at areas of orientation, registration, attention and calculation, recall, and language. It is a test that has been well validated. The cutoff score for normal cognitive function is generally set at ≥24–26. In a recent meta-analysis of 48 studies, using a cutoff score of 24 in the community population, the sensitivity was 0.85 and specificity was 0.90 for the MMSE in diagnosing major neurocognitive disorder [7]. Using a cutoff score of 25 increases the sensitivity to 0.87 but decreases specificity to 0.82. A study looking at using the MMSE in the "oldest old" suggested that the cutoff score may need to be adjusted depending on age [8]. In the study, using a cutoff score of ≥25 in those between the ages of 90 and 93, with a college degree or higher level of education, the sensitivity is 0.82 and specificity is 0.80. For those between 94 and 96 years, a cutoff score of ≥24 has a sensitivity of 0.85 and a specificity of 0.80. Thus, while the MMSE has good sensitivity and specificity across all ages and educational groups, the authors proposed that cutoff scores may need to be adjusted depending on age to preserve specificity [8].

The MoCA is also a 30-point test that is well validated in various languages. The domains tested include visuospatial/executive functioning, naming, memory, attention, language, abstraction, delayed recall, and orientation. A cutoff score of ≥26 is recommended [9]. Sensitivity for the MoCA with this cutoff at detecting Alzheimer disease is 1.0, with a specificity of 0.87 [10]. The MMSE and MoCA are comparable simple office screening tests used for major neurocognitive disorders. However, studies seem to suggest that the MoCA is better than the MMSE in detecting patients with mild neurocognitive disorder [11, 12].

Question 2.4

Neuropsychological assessment provides information about a person's cognitive, motor, behavioral, linguistic, and executive functioning. This information can then be used to develop a differential diagnosis, to confirm a diagnosis, or to help generate individualized treatment recommendations for the patient. A comprehensive neuropsychological assessment in an older adult includes an interview (with the patient and with collateral informant if available), cognitive screening (to provide information whether lengthier cognitive testing is required), and the neuropsychological testing that is required depending on the referral question.

Name the Major Domains of Cognition That Are Assessed by Basic Neuropsychological Testing

- *Intellectual ability*—this is an estimation of a person's premorbid general ability and his/her current objective ability. Premorbid intellectual functioning can be measured using a word reading test such as the Test of Premorbid Function or North American Adult Reading Test. The most commonly used test to assess current intellectual ability is the Wechsler Adult Intelligence Scale (WAIS). Please see Table 2.2 for some other common neuropsychological tests.
- *Attention/concentration*—this domain deals with a person's ability to focus awareness on a given task and to concentrate on the task long enough to accomplish a goal. This is typically assessed by using both auditory verbal and visual stimuli. Auditory attention span is commonly assessed using the digit span test, where a series of digits are read aloud and the patient repeats them back. A normal span is 7 digits, plus or minus 2 digits.
- *Memory*—memory can be tested based on either visual, verbal, or motor content. It can involve immediate, short-term, or delayed/long-term recall. As mentioned in Question 2.2, memory involves encoding, storage, and retrieval. It is important that formal memory assessment involves all three processes.
- *Language*—language skills are typically associated with the left (dominant) cerebral hemisphere. Language assessment consists of looking at one's ability to comprehend, repeat, and express in both oral and written formats.
- *Visual spatial skills*—this involves testing a person's abilities to make sense of the visual world (shapes, angles, gestalts vs. details). Problems noted in this domain can affect a person's ability to conceptualize complex ideas and relationships.
- *Motor skills*—gross manual or fine-motor abilities are assessed within this domain. Motor praxis is the neurological process by which cognition directs motor action—planning what to do and how to do it. The neuropsychological tests in this domain assess how effectively a person is able to coordinate hand-eye movements, finger dexterity, balance, and motor speed. Deficits in this area may have an implication on how one performs the many tasks of daily living.

Table 2.2 Examples of commonly used neuropsychological tests

Domain	Neuropsychological test
Intellectual ability	Test of Premorbid Function (TOPF) North American Adult Reading Test (NAART) Cambridge Contextual Reading Test (CCRT) Wechsler Adult Intelligence Scale-IV (WAIS-IV) Stanford-Binet Intelligence Scale-5 (SB-5)
Attention/concentration	Digit span forward and backward Trail making tests Vanderbilt Assessment Scale Serial sevens subtraction
Memory	California Verbal Learning Test-2 (CVLT-2) Rey Auditory Verbal Learning Test (RAVLT) Wechsler Memory Scale-IV (WMS-IV) Brief Visuospatial Memory Test-Revised (BVMT-R) Rey-Osterrieth Complex Figure (Rey-O)
Language	Boston Naming Test (BNT) Multilingual Aphasia Examination Token test
Visual spatial skills	Clock drawing Block design subtest from WAIS Copy of complex design Hooper Visual Organization Test (VOT) Judgment of Line Orientation (JLO) Test
Motor skills	Index finger tapping Fist-edge-palm test Reciprocal Motor Programme Test
Executive functioning	Wisconsin Card Sorting Test Trail Making Test-B Stroop Test Category Test

- *Executive functioning*—the aspects of executive functioning that are assessed by neuropsychological testing include problem-solving, planning and organization, working memory, and cognitive flexibility. This domain is generally related to the functions of the frontal lobes.

Question 2.5

Describe the Wisconsin Card Sorting Test (WCST). What Is the Implication of Impaired Performance on This Test?

The WCST is a test to assess abstract reasoning ability and the ability to shift cognitive strategies in response to changing situational demands. During the test, the subject is instructed to sort and match a number of cards but is not told how to match them. They receive feedback as to whether a particular match is correct or wrong.

The WCST is a test for executive functioning and assessing a person's planning and cognitive flexibility, visual spatial working memory, deductive reasoning, and problem-solving [13].

Poor results on this test can suggest brain dysfunction in the frontal lobes. Patients with frontal lobe damage have been found to perform more poorly on the WCST than patients with damage to other lobes [14]. Patients with schizophrenia, especially in those with negative symptoms, have also been found to perform poorer on the WCST compared to controls [13]. One positron emission tomography (PET) study suggested that performance on the WCST produces activation of the frontal cortex, as well as the dorsolateral prefrontal cortex, inferior parietal lobe, inferior temporal cortices, and portions of the cerebellum [15]. As it is believed that the frontal lobes are largely involved in executive functioning, it stands to reason that damage in this area of the brain would affect performance on the WCST.

Question 2.6

You are seeing Mrs. G, a 69-year-old married female, for follow-up of her major depressive disorder in your clinic today. In the past 6 months, Mrs. G's mood has remained mildly depressed despite trying a few different pharmacological options. She has also been endorsing significant short-term memory concerns in the last few months. She tells you today that she is worried that she is going to develop Alzheimer disease. She has a friend who has similar depressive and memory symptoms that recently underwent neuropsychological testing. Based on the results of the testing, her friend has been told that it is only going to be a matter of time before she develops a major neurocognitive disorder. Mrs. G wants to know if you could refer her for testing so she can know whether she will have Alzheimer disease in a few years.

Are There Neuropsychological Predictors of Conversion from Mild Neurocognitive Disorder to Major Neurocognitive Disorder?

Patients presenting with memory concerns are often worried that their memory impairment implies an eventual diagnosis of major neurocognitive disorder. There has been much research looking into possible neuropsychological predictors of major neurocognitive disorder. Evidence from a number of studies suggests that deficits noted in verbal memory, visual spatial abilities, and psychomotor speed-executive function abilities may predict conversion from mild neurocognitive disorder to major neurocognitive disorder [16, 17]. There was also a study suggesting that impaired autobiographical and semantic forms of personal memory may be useful in predicting conversion [18]. Literature also suggests that depressed older adults with deficits in memory and executive functions are at higher risk for developing major neurocognitive disorder [19].

For Mrs. G, she needs to be aware that while neuropsychological assessment may provide us with some information pertaining to her risk of developing major neurocognitive disorder given her current symptoms (poor short-term memory and low mood), it is not an absolute prediction.

Question 2.7

Mr. W, a 68-year-old married male, is being seen for assessment of his cognitive difficulties. Mr. W tells you that there is nothing wrong with him, that the only issues he has are physical. He reports that he seems to be having more trouble with his balance lately as he has had a number of falls. He also has noticed a tremor in his right hand, which is starting to be an issue as he is right-handed. He does not feel that he is forgetful at all.

His wife tells you that he has been more forgetful in the past year, but not dramatically so. Her concern is that he constantly talks about seeing bugs on the wall where none exist. Despite her trying to tell him that there are no bugs, he cannot appreciate this and will try to smack these nonexistent bugs with his shoe, leaving shoe prints on their walls at home.

You wonder about a possible diagnosis of major neurocognitive disorder with Lewy bodies and referred Mr. W to your neuropsychology colleagues for testing to confirm your suspicions.

What Cognitive Domains Do You Expect to See Impairments in Someone with Lewy Body Disease?

Major neurocognitive disorder with Lewy bodies is a gradually progressive disorder characterized by not only cognitive symptoms but also psychiatric and motor symptoms. In patients with Lewy body disease, they typically have the core features of (see Table 2.3 for a list of core and supportive features) [20]:

- Fluctuating cognition or alertness
- Recurrent visual hallucinations
- Spontaneous features of parkinsonism

Table 2.3 Features of major neurocognitive disorder with Lewy bodies [20]

Core features	Fluctuating cognition or alertness Recurrent visual hallucinations Spontaneous features of parkinsonism
Supportive features	Rapid eye movement sleep behavior disorder Severe antipsychotic sensitivity Repeated falls Transient loss of consciousness Syncope Autonomic dysfunction (e.g., orthostatic hypotension, urinary incontinence) Auditory, tactile, or olfactory hallucinations Depressive disorder

However, there are times when diagnosis remains uncertain and information is sought from neuropsychology assessments to help confirm the diagnosis. In a patient with major neurocognitive disorder with Lewy bodies, attention and concentration seem to be significantly impaired, even more so than a patient with Alzheimer disease [21]. Difficulties with visual spatial and constructional skills indicating subcortical features are also expected. Impairments may be seen on such tests as copy of complex figure, clock drawing, or block design subtest from WASI-II or WAIS-IV. Memory is also impaired in patients with Lewy body disease, with more difficulties in visual memory tasks noted [21].

Question 2.8

Major neurocognitive disorder due to Alzheimer disease is the most common type of major neurocognitive disorder, accounting for 60–80% of all major neurocognitive disorders [22]. Patients with this disorder usually struggle with short-term memory loss initially and gradually progress to withdrawal from family and society, eventually requiring significant dependence on others in daily living activities.

What Is the Neuropsychological Profile for a Person with Major Neurocognitive Disorder Due to Alzheimer Disease?

Patients with major neurocognitive disorder due to Alzheimer disease typically have changes in the medial temporal lobe structures during early disease, leading to significant episodic memory impairment with deficits in language, semantic knowledge, abstract reasoning, executive functions, attention, and visual spatial abilities [23]. As the disease progresses into other brain regions, such as the association cortices of temporal, frontal, and parietal lobes, impairments can be seen in loss of general knowledge and language abilities [24]. This language impairment is reflected in difficulties in confrontational naming, verbal fluency, and semantic categorization.

Impairments in executive functions also tend to occur early on in the disease process. Patients in early stages of disease are noted to have set-shifting or sequencing problems [23]. They may be expected to do poorly on tests such as the Tower of London Test, WCST, Part B of the Trail-Making Test, and the Raven Progressive Matrices Task.

Deficits in attention and visual spatial abilities can also be seen during the progression of the neurocognitive disorder. These deficits are usually less pronounced compared to the impairment seen in memory and executive functioning [23]. Deficits can be seen in tasks that require the shifting of attention or tests of visual spatial skills such as the block design test, the clock drawing test, and complex figure copying.

Question 2.9

Mrs. P is a 76-year-old female who comes to your office for assessment of her depressive symptoms. She came to the appointment today with her very supportive daughter. Both Mrs. P and her daughter describe a history of depressive symptoms that started after Mrs. P's spouse passed away suddenly from a myocardial infarction 2 years ago. Mrs. P was started on the antidepressant sertraline about 6 months ago by her primary care physician, and she has had some improvement since its initiation. Mrs. P believes she is approximately 75% back to her normal self. She still has lack of motivation and initial insomnia but feels much better overall.

In addition to her depressive symptoms, Mrs. P and her daughter have noticed some changes with Mrs. P's memory that started about 1 year ago. She finds that she has been more forgetful and now has to write everything down. She also has trouble multitasking where this was never a concern before. Navigating the Internet on her computer has been more challenging for her. She has never been a technologically inclined person, but now, she seems to be calling her daughter more often with questions. When she would try to do her on-line banking, she would have trouble figuring out what she had to do. Mrs. P is concerned that she is getting Alzheimer disease as her older brother was diagnosed with this a few years ago. However, her primary care physician had previously told her that her memory deficits were likely due to her depressive disorder. She wants to know if her primary care physician is right.

What Are the Changes/Deficits in the Various Cognitive Domains That You Would Expect to See in Someone with Major Depressive Disorder? What Do You Tell Mrs. P About Her Memory Concerns?

Literature supports that about 40–60% of non-demented older adults with major depressive disorder would be classified as cognitively impaired by neuropsychological assessment [25]. Studies have shown in older adults with depression that deficits can be seen in attention and inhibition, working memory, episodic memory, semantic memory, expressive language, visual spatial skills, processing speeds, and executive functions [25]. The decline in processing speed and executive functioning has been noted to be fairly prominent. Even when the slower information processing speed is controlled for in studies, results still suggest a stronger degree of executive deficits in depressed vs. non-depressed older adults, with the Tower of London Test and the Trail Making Test part B being fairly sensitive at detecting the deficits [25].

Unfortunately, even after successful treatment of the depressive symptoms, the cognitive impairment may persist. One study found that 94% of patients, whose depression did remit, continue to remain cognitively impaired 1 year later [26]. In that same study, 23% of patients who were cognitively intact while depressed developed cognitive impairment 1 year later. There is increasing evidence to suggest that depression itself is a risk factor for the development of major neurocognitive disorders.

In Mrs. P's scenario, it is possible that her cognitive impairment (deficits in memory and executive functioning) is related to her depressive disorder. However, the fact that she has experienced some improvement in her depressive symptoms without an improvement in her cognition suggests that she may be in the subset of people where cognitive impairment remains despite resolution of depressive symptoms. The appropriate course of action would be to further optimize her antidepressant to achieve full remission and continue to monitor her cognition over time, as she may be at an increased risk for development of a major neurocognitive disorder.

Question 2.10

Neuroimaging or brain imaging is the use of various techniques to image brain structure and brain function. These imaging techniques fall into two broad categories:

- *Structural imaging*—this is used to detect changes in brain morphology, volume, and overall integrity. Computed tomography (CT) and magnetic resonance imaging (MRI) are two common structural imaging modalities.
- *Functional imaging*—this is used to measure an aspect of brain function, to help further understand the relationship between activity in certain brain areas and specific mental functions. Common functional neuroimaging techniques include positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and single-photon emission computed tomography (SPECT).

What Are Some Contraindications for MRI?

As strong static magnetic fields are induced in MRI, one potential concern is that ferromagnetic devices may be moved, rotated, dislodged, or accelerated toward the magnet [27]. An absolute contraindication for MRI is the presence of cardiac pacemakers, penile implants, or cochlear implants. Relative contraindications include metallic implants (e.g., vascular clips, coronary stents, prosthetic heart valves, pacing devices). The concern for metallic implants stems from the ability for these devices to concentrate radiofrequency energy, which then leads to local heating [27]. Radiofrequency energy can also induce electrical currents in the wires from a pacing device, which may then induce arrhythmias. Tattoos may also contain iron oxides or other metals and, if these particles interact with the magnetic field, may cause burns, swelling, or local irritation. Claustrophobia is another relative contraindication, but this concern may be circumvented by the use of sedation. Impaired renal function or allergies to contrast dyes may prevent the use of contrast during the MRI procedure (contrast dyes are used in 40–50% of MRI examinations [27]).

Question 2.11

You just saw an 82-year-old male in the emergency department. The patient had presented with worsening confusion for the past 4 days. The patient endorses both visual hallucinations and paranoid delusions. There are no appreciable depressive or cognitive symptoms. He was noted to have had a significant fall at home where he did hit his head prior to the onset of his symptoms. At the time of the fall, he had complained of a mild headache, which resolved after a few hours, so he never sought medical help. All laboratory investigations, including urinalysis, thus far have not revealed any significant abnormalities. As part of your workup for this patient, you are arranging for brain imaging to rule out any brain pathology. Your medical student wants to know if you will be ordering a CT scan or an MRI.

When Would One Use CT Vs. MRI for Brain Imaging?

Brain CT scans are basically multiple X-ray images acquired around the head at multiple angles. As a result, despite the fact that scans have become quicker over the years, a patient is still exposed to some amount of radiation. CT scanning has no absolute contraindications [28]. MRI scans, on the other hand, use powerful magnetic fields and radio frequency pulses to produce detail pictures of the brain—there is no radiation involved in MRI. This makes MRI the preferred imaging technique in children and patients requiring multiple imaging examinations. CT is generally less costly than MRI and can be performed on patients with implantable medical devices. It is also less sensitive to patient motion as imaging can be performed much more rapidly than MRI. Because CT imaging is usually quicker, it may be a better choice for a claustrophobic patient.

CTs are better at visualization of bone structures, whereas MRIs offer a greater range of soft tissue contrast and, thus, are more sensitive for abnormalities within the brain itself [29]. Table 2.4 lists some conditions for which one may order a brain CT vs. an MRI. However, as specific techniques of imaging may vary in different centers, it may be best to discuss with the neuroradiologist which technique would be preferred for a specific indication.

Table 2.4 Indications for brain CT vs. MRI [27, 28]

Computed tomography (CT)	Magnetic resonance imaging (MRI)
Headaches	Seizures
Trauma	Memory loss/neurodegenerative disorders
Suspected intracranial hemorrhage	Infection
Acute stroke/transient ischemic attack	Tumors/masses
Initial evaluation for space-occupying lesions	Inflammatory conditions
Initial evaluation for psychiatric disorders	Cranial neuropathies
	Congenital abnormalities

In this patient scenario, confusion and psychosis are the presenting symptoms. These symptoms emerged after the patient had a significant fall with injury to the head. It is possible that the patient has an intracranial hemorrhage and/or delirium. A brain CT is the preferred imaging technique as bleeding is better visualized on a CT scan.

Question 2.12

Neuroimaging has played an increasing role in the research of various psychiatric disorders including bipolar disorders.

What Are Some Structural Brain Abnormalities Seen in Bipolar Disorders?

Data from a meta-analysis of 98 structural imaging studies found enlarged lateral ventricles in patients with bipolar disorder compared to control subjects [30]. This enlargement is present at the beginning of the bipolar illness—the enlargement does not progress with illness duration. In the same review study, patients with bipolar disorder were found to have increased rates of deep white matter hyperintensities. This increase in white matter hyperintensities is higher in those with a late-onset bipolar disorder compared to early-onset patients [31]. Some studies have also found higher rates of white matter abnormalities in tracts connecting to the frontal cortex; these are the regions that are thought to be involved in visual spatial ability, information processing, and executive function [32]. For abnormalities in other brain regions, such as the amygdala, hippocampus, and thalamus, study findings seem to be conflicting [32].

Question 2.13

What Are Some Structural Neuroimaging Changes Seen in Late-Life Depression?

Many imaging studies have shown an increased rate and greater severity of signal hyperintensities in deep white matter on T2-weighted MRI in older adults with late-onset depression compared with normal controls [33, 34]. Evidence also suggests that depressed older adults with MRI hyperintensities show greater cognitive impairment and are associated with a poorer response to treatment [34]. From these observations, the hypothesis of vascular depression was born—the notion that cerebrovascular disease, such as small-vessel disease, causes structural damage to the corticostriatal circuits. This damage, in turn, creates a subtype of late-onset depression that is treatment resistant and is characterized by the presence of deficits in executive functioning [34].

Late-life depressive disorder (which includes both late-onset depressive disorder and recurrent depressive disorder with later-in-life episodes) also seems to be associated with reduced volumes in multiple areas of the brain including the orbitofrontal and medial regions, as well as the temporal lobe, the anterior cingulate cortex, the hippocampus, and the parahippocampal area [35, 36].

There is also evidence from SPECT studies suggesting a decrease in regional cerebral blood flow in the frontal and prefrontal cortical regions in late-life depression [37]. Some studies also note a decrease in whole brain glucose metabolism [38] but an increase in glucose metabolism in the anterior cingulate and insula, the areas implicated in mood symptoms [39].

Question 2.14

Only one-third of patients with major depressive disorder benefit from the first antidepressant they try [40]. There has been much research in determining predictors of clinical outcomes in treatment of major depressive disorder. The goal in all the research in this area is to be able to personalize treatment for our patients in the near future.

Can Functional Neuroimaging Predict Response to Antidepressant Treatment in Major Depressive Disorder?

There is some evidence for biomarkers that may predict response to pharmacological intervention in major depression. Suggested predictors of antidepressant response include [41]:

- PET studies found that metabolism in the subgenual anterior cingulate cortex may serve as a biomarker for treatment response.
- Decrease in glucose metabolism in the insular cortex is associated with greater treatment response.
- Decrease in glucose metabolism in ventral regions of the prefrontal cortex is related to positive treatment response to selective serotonin reuptake inhibitors.
- Greater activation in the dorsomedial prefrontal cortex, posterior cingulate cortex, and superior frontal gyrus when viewing negative emotional pictures compared to resting condition is associated with positive antidepressant response.

The results of the neuroimaging studies have shown promise that clinicians may be better able to choose a treatment strategy that will better help our depressed patients.

Question 2.15

You are reviewing a SPECT perfusion imaging report of a patient you had recently seen for cognitive impairment. You had sent the patient for neuroimaging as you were not certain in your diagnosis after your initial assessment. You were considering a major neurocognitive disorder associated with either Alzheimer disease or Lewy body disease. The report notes hypoperfusion in the temporoparietal regions bilaterally.

Which Diagnosis Does the SPECT Scan Support?

Major neurocognitive disorder with Lewy bodies is generally associated with perfusion deficits in the parietal and occipital regions, with relative sparing of the temporal areas [42], whereas in Alzheimer disease, hypoperfusion is seen in the bilateral temporoparietal areas [43].

In cases where the diagnosis may be unclear, functional imaging may help in confirming a diagnosis. In one study, patients with a clinical diagnosis of "probable" Alzheimer disease were found to be associated with an 84% likelihood of pathologic Alzheimer disease on autopsy. A positive SPECT scan increases this likelihood to 92% [43]. The same study also found that in those whom the diagnosis was only "possible" Alzheimer disease, the likelihood of pathologic Alzheimer disease increased from 67% to 84% with a positive SPECT.

In the case scenario, as the SPECT report noted hypoperfusion in the temporoparietal areas, it helped in confirming a diagnosis of major neurocognitive disorder due to Alzheimer disease.

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Topic 3: Pharmacotherapy, Somatic Therapies, and Psychotherapy in Late Life

Question 3.1

As our population ages, polypharmacy in older adults becomes an increasing concern. Polypharmacy is conventionally defined as a medication count of five or more concurrently administered medications. Not only does polypharmacy lead to increased healthcare burden, but it can also be associated with increased health risks because of adverse drug events, drug-drug interactions, falls, functional decline, cognitive impairment, urinary incontinence, and malnourishment [1].

What Is the Prevalence of Polypharmacy in Older Adults?

In the outpatient setting, the prevalence of polypharmacy in older adults is between 35 and 45% [1, 2]. In hospitalized patients, this number increases to 40–76% depending on the study [1, 3]. The prevalence of polypharmacy increases with age and the number of comorbid chronic medical conditions [4]. Cardiovascular, endocrine, gastrointestinal, renal, and psychiatric disorders were among the more common medical conditions in patients taking multiple medications [2]. Table 3.1 shows some of the more commonly reported medications in polypharmacy studies. Dietary supplement use plays a significant contributory role in polypharmacy [2]. This is concerning, as patients often do not disclose supplement use, as they do not think of supplements as "medications," yet, there can be potential drug-drug interactions between some supplements and prescribed medications. Observational studies also show that over 50% of older adults are taking at least one or more unnecessary medications [1]. Research clearly shows a relationship between polypharmacy and negative health consequences—this is an important point to keep in mind whenever medications are prescribed to an older adult.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_3

Table 3.1 Common medication classes reported in polypharmacy of older adults [1]

Medications in polypharmacy	Beta blockers
	ACE inhibitors
	Diuretics
	Statins
	Genitourinary antispasmodics
	Antidepressants
	Benzodiazepines
	Antipsychotics
	Opioids
	Nonnarcotic pain relievers
	Laxatives
	Vitamins

Question 3.2

Undoubtedly, with aging, the body and how it functions change. These changes can greatly affect how we process medications and how these medications affect us.

A. What Are the Pharmacokinetic Changes Associated with Aging?

Pharmacokinetics is defined as "what the body does to the drug." This includes:

- *Absorption*. With aging, there is an age-related decrease in small bowel surface area, slowed gastric emptying, and increase in gastric pH, all of which can affect absorption. However, these changes do not appear to have much of a clinical effect [5].
- *Distribution*. Body fat increases and total body water decreases with age. The increase in body fat increases the volume of distribution for highly lipophilic drugs such as diazepam and midazolam and increases elimination half-lives. Serum albumin also decreases with age, which then may increase the free serum levels of drugs such as phenytoin and warfarin.
- *Metabolism*. Overall hepatic metabolism through the cytochrome P450 enzyme system decreases with age, typically decreasing clearance by 30% [6]. Medications affected by this include diazepam, nortriptyline, and trazodone. First-past metabolism also decreases due to changes in liver mass and perfusion. This can lead to a higher bioavailability of some drugs.
- *Excretion*. Renal elimination of drugs significantly decreases with aging. Creatinine clearance starts to decrease, and thus, doses of drugs that rely heavily on renal excretion, such as risperidone, furosemide, and metformin, need to be lowered.

B. What Are the Pharmacodynamic Changes Associated with Aging?

Pharmacodynamics is defined as "what the drug does to the body," i.e., the response of the body to the drug. Similar drug concentrations at the site of action can lead to a greater or lesser response in older adults, depending on the drug, when compared to the younger population. This can be due to drug sensitivity (due to changes of the drug response at receptor site of post-receptor events) or changes in homeostasis. It has been noted that older adults tend to have a more exaggerated response to central nervous system-active medications (e.g., benzodiazepines, anesthetics, opioids) due to increased sensitivity [7], while β[beta]-adrenoreceptors are less responsive, affecting the response to beta blockers [8]. Changes in homeostasis can impair processes such as temperature regulation, blood pressure regulation, bladder function, and fluid and electrolyte balance. In older adults, this can increase susceptibility to drug-induced side effects such as hypothermia, postural hypotension, urinary incontinence, hyponatremia, and confusional states.

Question 3.3

The Beers Criteria for potentially inappropriate medication (PIM) use in older adults are a set of guidelines developed to help improve the prescribing safety in older adults. It is an explicit list of PIMs that is best avoided in older adults, prescribed at reduced dosage, or should be monitored closely.

List Some Common Psychotropic Medications That Are Under the "Avoid" Category According to the Beers Criteria

Many of the psychotropic medications that are used to treat a variety of psychiatric disorders are, in fact, listed as "avoid." A number of antidepressants, benzodiazepines, and antipsychotics are identified as "avoid" with a "strong" strength of recommendation (see Table 3.2) [9]. However, the Beers Criteria should serve only as a guide, with care tailored to each patient's needs, and should not solely dictate prescribing for specific patients.

Table 3.2 Psychotropic medications that are best avoided according to the Beers Criteria

Medication class	Examples
Antidepressants	Amitriptyline, clomipramine, doxepin (>6 mg/day), imipramine, desipramine, nortriptyline, paroxetine
Antipsychotics (first, second, and third generation)	Haloperidol, perphenazine, olanzapine, quetiapine, risperidone, aripiprazole
Benzodiazepines	Alprazolam, clonazepam, diazepam, lorazepam, oxazepam, temazepam
Non-benzodiazepines	Eszopiclone, zaleplon, zolpidem

Question 3.4

The old saying "red as a beet, dry as a bone, blind as a bat, hot as a hare, mad as a hatter" has been used to describe the side effects of anticholinergic medications. Older adults can be particularly sensitive to the anticholinergic action of drugs because of the physiological changes that accompany aging.

A. List Some Common Side Effects of Anticholinergic Medications

Common side effects include:

- Dry mouth
- Blurred vision
- Dry eye
- Constipation
- Urinary retention
- Sedation
- Heat intolerance
- Postural hypotension
- Memory impairment/confusion/delirium
- Heart rhythm disturbance

B. List Some Common Anticholinergic Psychotropic Medications

Some common psychotropic medications with significant anticholinergic properties include:

- Benztropine
- Trihexyphenidyl
- Amitriptyline
- Clomipramine
- Desipramine
- Doxepin
- Nortriptyline
- Loxapine
- Chlorpromazine
- Clozapine
- Trifluoperazine
- Perphenazine
- Olanzapine

Question 3.5

Mr. N is a 74-year-old widowed male who lives alone in a one-story home. He has been struggling with depressive symptoms over the past 2 years since the death of his wife. Mr. N has been referred to you for assessment of his mood and for management recommendations. He comes to your office with his son today for assessment. Mr. N tells you that he no longer cares about anything. He cannot recall the last time when he felt excited or happy about anything. Even visits with his grandchildren seem pointless to him these days. He tells you that he would not care if a car hit him and killed him tomorrow; he cannot think of a single reason to stay alive. His son tells you that Mr. N has been complaining about feeling very lonely ever since his wife (the son's mother) passed away 2 years ago and that he just has not been the same man since. You diagnose Mr. N with a major depressive disorder and discuss treatment with Mr. N and his son—in particular, a trial of escitalopram. His son mentioned that he saw a documentary special on television a few days ago that looked at the number of falls in older adults and that the documentary suggested that antidepressants could lead to an increased risk of falls and fractures. He wants to know if that is true.

What Is the Risk of Falls with Selective Serotonin Reuptake Inhibitor (SSRI) Use?

While there have been studies that suggest SSRIs are associated with an increased risk of falls in older adults [10], a recent systematic review of 26 studies looking at the association between SSRIs and falls in older adults did not support the notion of SSRIs causing falls [11]. The authors reported that the majority of past studies were observational (only one was a randomized controlled trial) and that the studies suggested an association between falls and SSRIs, but not the direction of the relationship—causation or effect. Depression itself has also been linked to disability [12], thereby increasing the risk of falls, possibly having nothing to do with the pharmacological intervention at all.

Given that untreated depression can have detrimental effects, it is important that Mr. N's symptoms are treated. Psychotherapy for depression is always a reasonable treatment option. However, in Mr. N's case, he may be too disinterested to be fully engaged in psychotherapy; thus, the use of antidepressants may be unavoidable. If antidepressants are used, then SSRIs would still be a relatively safe option compared with some of the other classes of antidepressants given their side effects profile.

Question 3.6

Despite the increasing use of antipsychotics for the treatment of both bipolar depressive and manic episodes, lithium remains the first-line treatment for bipolar disorder and is an augmentation strategy in treatment of major depressive disorder. However,

even with supportive evidence for its use, many clinicians are hesitant to initiate lithium as a treatment option because of the potential complications and toxicity burden, especially in older adults.

What Are the Side Effects and Risks of Treatment with Lithium? What Is Their Management?

Lithium has a number of potential side effects, common ones including dry mouth, drowsiness, tremor, nausea, diarrhea, cognitive impairment, decrease in libido, weight gain/anorexia, alopecia, polydipsia, polyuria, acne, and psoriasis. Between 67 and 90% of patients treated with lithium will report at least one side effect [12]. The key to managing milder side effects is to "wait, wait, and wait." Some side effects will resolve with time but not others. Nausea, seen in about 10–20% of patients taking lithium [12], tends to improve with time but not the adverse effect of weight gain. Sometimes, altering the time that the lithium is taken can be helpful; e.g., if drowsiness is an issue, then taking it closer to bedtime may be helpful. Changing the brand/preparation may also resolve gastrointestinal side effects. Lowering the dose is another strategy in managing side effects. Tremor, primarily noticed in the hands, can occur in up to 25% of lithium-treated patients [12]. As the risk of tremor tends to increase with dosage of lithium, lowering the dose may help in those who are particularly sensitive to this side effect.

Lithium can also potentially directly affect various body organs. Lithium-induced renal impairment has been reported since the 1970s [13]. The most common renal side effect is a urine-concentrating defect despite normal or elevated concentrations of the antidiuretic hormone vasopressin—leading to nephrogenic diabetes insipidus. This has been reported to occur in 20–87% of patients on lithium [13]. Chronic renal impairment has also been linked to the use of lithium; however, there are contradictory studies on whether lithium causes reduction in the glomerular filtration rate and, if it does, whether that is significant enough to contribute to renal disease [13]. The general recommendation is to use low-dose lithium to lower renal risk and to monitor serum creatinine and estimated glomerular filtration rate regularly.

Treatment with lithium has also been associated with both overt hypothyroidism (symptoms of hypothyroidism, high thyroid-stimulating hormone [TSH], and low thyroxine) and subclinical hypothyroidism (asymptomatic with high TSH but normal thyroxine). The prevalence rates of overt hypothyroidism are reported to be between 8 and 19% and that of subclinical hypothyroidism to be up to 23% [12]. Symptoms of hypothyroidism, including lethargy, mental slowing, and weight gain, can overlap with those of depression, making diagnosis difficult if regular thyroid function tests are not performed. It is recommended that thyroid parameters be checked prior to lithium initiation, after every dose adjustment, and also monitored regularly every 6–12 months once established on a stable dose.

Lithium has been found to increase blood calcium by 10% in a meta-analysis of 385 studies [14]. This seems to occur via increasing renal calcium reabsorption and by independently stimulating parathyroid hormone release [12]. Common symptoms of hypercalcemia are listed in Table 3.3. Clinicians should monitor serum calcium levels prior to lithium initiation and annually for monitoring purposes.

Perhaps the most concerning risk of all is the risk of acute lithium toxicity. Table 3.4 lists some of the symptoms of lithium toxicity. Lithium has a narrow therapeutic index, with toxicity generally defined as concentrations of ≥1.2 mmol/L (mEq/L). In a young adult, therapeutic serum lithium level is typically targeted at 0.7–1.2 mmol/L (mEq/L). In an older patient, lithium seems to be more effective at lower doses [15], generally aiming for a serum level of 0.4–0.7 mmol/L (mEq/L). While lithium is considered a useful option in the treatment of mania or as an augmentation strategy in unipolar depression in older patients, lower doses and careful monitoring are required as older adults tend to have more side effects. Patients starting on lithium should be warned on the effect of dehydration on serum lithium concentration—that vomiting from a gastrointestinal illness or excessive sweating on a hot summer day can potentially lead to lithium toxicity and, subsequently, a medical emergency if one is not careful.

Table 3.3 Symptoms and signs of hypercalcemia

Clinical presentation	Loss of appetite
	Weakness
	Fatigue
	Confusion
	Nausea/vomiting
	Polydipsia/polyuria
	Renal stones
	Renal insufficiency
	Osteoporosis
	Heart palpitations/fainting
	Depression

Table 3.4 Symptoms and signs of acute lithium toxicity

Clinical presentation	Vomiting or severe nausea
	Coarse hand tremor
	Myoclonus
	Dystonia
	Hyperreflexia
	Blurred vision
	Ataxia
	Dysarthria
	Cardiac dysrhythmias

Question 3.7

Neuroleptic malignant syndrome (NMS) is a life-threatening idiosyncratic reaction to dopamine-blocking medications. NMS has been associated with first-, second-, and third-generation antipsychotic medications and other medications that affect central dopaminergic neurotransmission. It is a rare condition, occurring at around 0.01–0.02% of patients treated with antipsychotics [16].

What Are the Features of NMS?

Features of NMS usually develop within 72 h of exposure, though it is possible that symptoms may not occur for up to 1 month [17]. It is classically characterized by a triad of:

- Hyperthermia (>100.4 °F or >38.0 °C)
- Generalized rigidity
- Changes in mental status/delirium

Other symptoms observed may include neurological signs such as tremor, sialorrhea, akinesia, dystonia, trismus, myoclonus, dysarthria, dysphagia, and rhabdomyolysis or signs of autonomic nervous system instability such as tachycardia, diaphoresis, labile blood pressure, tachypnea, urinary incontinence, and skin pallor [18].

No single laboratory abnormality is specific to the diagnosis of NMS, but creatine phosphokinase can often be elevated due to rhabdomyolysis. Metabolic acidosis, leukocytosis, and low serum iron concentrations may also be seen [18]. Cerebrospinal fluid analysis and neuroimaging studies are usually normal, but electroencephalography may show generalized slowing consistent with delirium [17].

Question 3.8

Mr. D is an 83-year-old widowed gentleman who presents to the emergency department with his daughter. His daughter is quite concerned as Mr. D has not been feeling well for the past 2 days, initially with symptoms of chills, headaches, and diaphoresis, which they thought was a flu-like illness. However, when she came over to visit him today, she found him to be extremely confused and restless, so she decided to take him to the hospital. During assessment, he is found to have a temperature of 105.8 °F (41 °C). However, the emergency physician was not able to find a locus of infection (urinalysis and chest X-ray were both normal). After further discussion with the daughter, the emergency physician found out that Mr. D has

been on duloxetine 120 mg daily for the past 3 years, prescribed for treatment of his depressive symptoms and fibromyalgia. He recently developed an exacerbation of an old knee injury 4 days ago, which led to worsening pain and limited mobility, so his primary care physician gave him a prescription for 15 tablets of tramadol 100 mg. There are five tablets left in the bottle. The emergency physician suspects a possible serotonin syndrome as the culprit of his symptoms.

What Is the Treatment for Serotonin Syndrome?

Serotonin syndrome is a constellation of symptoms that may occur when there is a high serotonergic burden in the body. These symptoms may range from mild to severe, with severe symptoms being fatal if not properly treated. The mortality of severe serotonin syndrome is estimated to be 2–12% [19].

In mild serotonin syndrome, stopping the medications that are determined to be contributory would be the treatment, as most cases are self-limiting. In more severe cases, as in this case, the treatment is directed at the symptoms. If hyperthermia is present, it should be aggressively treated with external cooling, hydration, or intubation with induced muscle paralysis if the temperature is high (>105.8 °F or >41 °C), as seizures and irreversible brain damage may result. Dantrolene or benzodiazepines can be used if muscle rigidity caused by tonic muscle contraction occurs, to prevent rhabdomyolysis, which may result in acute renal failure. In severe serotonin syndrome, the use of the antihistamine cyproheptadine, which is also a 5-HT_{2A} inhibitor, is recommended. Antipsychotic medications with 5-HT_{2A} antagonist effects such as olanzapine and chlorpromazine may also be options [19]; however, as NMS is sometimes misdiagnosed as serotonin syndrome, caution is required when using antipsychotics.

As Mr. D has a significant hyperthermia along with his other symptoms, he should be admitted to the hospital under the care of the medical team and monitored medically so that he can be treated aggressively with external cooling and hydration. His duloxetine and tramadol should both be stopped (a taper is not advised given the severity of his symptoms). He should be closely monitored for emergence of any other symptoms that may require treatment. If he does not improve with the above measures, then the use of cyproheptadine can be considered.

Question 3.9

Many of the psychotropics that we use can increase the risk of QT prolongation. Some of these medications are listed in Table 3.5. As the corrected QT interval (QTc) actually lengthens with age, this risk becomes even more of a concern in the older population.

Table 3.5 Common psychotropic medications that can increase risk of QT prolongation

Medication class	Examples
First-generation antipsychotics	Thioridazine, haloperidol, chlorpromazine
Second-generation antipsychotics	Ziprasidone, quetiapine, risperidone
Selective serotonin reuptake inhibitors	Citalopram, escitalopram, fluoxetine
Tricyclic antidepressants	Amitriptyline, nortriptyline, imipramine, clomipramine
SNRIs	Venlafaxine, duloxetine
Other antidepressants	Mirtazapine, trazodone

What Is the Consequence of a Prolonged QT Interval?

In most cases, a prolonged QT does not cause problems. However, physical or emotional stress may trigger an irregular heart rhythm known as *torsades de pointes* (TdP) in those with a prolonged QT interval. TdP is a polymorphic ventricular tachycardia characterized by rapid, irregular QRS complexes, which appear to be "twisting" around the ECG baseline. This arrhythmia can lead to dizziness or loss of consciousness if the episode is short. However, if this rhythm is prolonged and is not corrected, ventricular fibrillation can occur, resulting in brain damage and sudden cardiac death.

Question 3.10

Mrs. C is a widowed 90-year-old female who lives alone in an apartment. She was diagnosed with a major neurocognitive disorder a few years ago but still seems to be managing at home with extra supports from her family and community agencies. Her family accompanied her to her follow-up appointment with you today. They are concerned that Mrs. C has not been taking her medications appropriately. They recently found half-full bottles of medications that were dispensed 3 months ago, including her metformin, ramipril, and donepezil. When they ask her about it, her reply would be either that she no longer needs the medication or that she has forgotten to take it for a day or two, but she is taking it most days and to stop bothering her about it. Her family is frustrated as Mrs. C refuses to acknowledge this as a problem. Her recent blood test shows her HbA1c to be higher than her baseline at 9.2% (she normally ranges between 7 and 8%) and that her blood pressure is just mildly elevated at 135/90 mmHg. Her family is worried that Mrs. C would have to move to either a retirement home or nursing home so that her medications can be monitored.

What Are Some Practical Suggestions You Can Give to the Family to Improve Medication Compliance?

It is often frustrating from a clinician's point of view when a patient does not comply with the prescribed treatment plan. There are a variety of reasons why patients may not be compliant. These barriers may be due to patient factors, prescriber factors, or healthcare system factors (see Table 3.6).

As discussed in Question 3.1, many older adults are on multiple medications. The regimen for these medications may be too difficult for the patient to follow (i.e., if the patient has to take multiple medications divided up to four times a day). If possible, simplifying their regimen by adjusting the frequency and timing of the medications may help improve compliance. Detailed instructions of the timing of the medication should be given—tell patient to "take this pill at 9 AM and 9 PM" rather than "take it twice a day." The use of adherence aids (e.g., medication alarms or calls from family members at time of medication administration) may also help, especially if memory is a concern. The use of a dosette or blister pack would also make it easier to track compliance and, as well, would allow the patient to see whether a medication has been taken for the day. Medications should be placed in an obvious place and not hidden in a cupboard to provide a visual cue. As well, they should be in a container that the patient is able to access (some patients may have difficulty with child-safe containers due to pain/dexterity).

The physician prescribing the medication should also provide effective education by using simple everyday language when explaining the diagnosis/medical condition and describing the treatment plan—50% of patients leave the physician's office without understanding what they were told [20]. In patients whose memory is impaired, written instructions would be helpful. Family members/caregivers can also be involved to improve compliance as they can help with medication monitoring and reinforcing need for the medication.

Table 3.6 Factors contributing to medication non-compliance

Patient-related factors	Prescriber-related factors	Other factors
• Poor memory/cognition • Personal health beliefs—not a "pill person" • Did not understand reason/need for medication • Patient has psychiatric disorder that affects self-care/motivation	• Poor communication • Poor patient-prescriber relationship • Lack of patient involvement in treatment planning • Lack of follow-up	• Medication not covered by government funded/insurance plan • Difficulty opening containers • Complex dosing regimen • Adverse drug reactions

For Mrs. C, her medication compliance issues are likely secondary to her cognitive deficits—that she either forgets to take her medications or that she needs medications. Suggesting to the family that she switches over to a dosette or blister pack would help make monitoring easier. Mrs. C would also be able to tell at a glance whether she has taken her medications for the day. If the pharmacy prepares the dosette or blister pack, then usually, they would also look after refills for the medications, so Mrs. C would not inadvertently stop taking a medication because she has run out. It may also be helpful to write down a list of all her medications and the medical condition that she is taking it for. If Mrs. C still is noted to be forgetting her medications after these changes, her family can consider using an alarm as a reminder or to call her or visit when it is medication time so that Mrs. C actually takes the pills while she is on the phone with them or while family is physically present. Attempts at simplifying her regimen would also likely improve compliance—if she is currently prescribed medications three or four times a day, this could be condensed to twice-daily dosing instead. If these changes are still not successful at improving her compliance, then supportive housing may need to be considered as safety becomes an issue if her diabetes mellitus or hypertension goes untreated.

Question 3.11

In addition to pharmacotherapy, other biological treatments such as electroconvulsive therapy (ECT) have been used in a variety of psychiatric disorders. Some of the earlier treatment modalities used in the past include pyrotherapy, insulin coma therapy, and frontal lobotomy. Of these earlier therapies, ECT is the only one that is still commonly used today, although psychosurgeries can play a limited role in some disorders (e.g., cingulotomy in refractory obsessive-compulsive disorder) [21]. ECT, is a procedure in which the goal is to induce a generalized tonic-clonic seizure by applying an electrical stimulus to the head. Over the years, there have been many studies looking into the use of ECT in psychiatric disorders.

A. What Are Some Contraindications of ECT?

ECT has no absolute contraindications, but there are many medical conditions that can increase the risk of complications. It is important to consider the risk relative to the potential of benefits with ECT in making the decision of whether or not to administer ECT. Medical conditions that are associated with substantial increase in risk include increased intracranial pressure, which is generally not an issue unless there is a mass effect. Brain tumors can be of concern, but again, only if there is a mass effect. Other considerations include having had a recent stroke or myocardial infarction, hypertension, cardiovascular conduction defects, aortic and cerebral aneurysms, asthma/chronic obstructive pulmonary disease, and cervical spine instability.

B. What Are the Risks of ECT?

The risks of ECT include the risks of anesthesia itself. Other ECT risks include acute confusion that can occur immediately after the treatment, generally lasting a few minutes to a few hours, rarely a few days. One may also experience memory loss of events that occurred before the treatment (retrograde amnesia) or difficulty remembering new events posttreatment (anterograde amnesia). Physical side effects such as nausea, headache, muscle ache/stiffness, fatigue, and jaw pain may be experienced. Fractures, although rare, can occur with severe osteoporosis.

Question 3.12

There is substantial evidence for the use of ECT in treatment of unipolar depression, bipolar depression, and severe mania [22, 23], with response rates of up to 80% in major depressive disorder [24, 25].

What Are Some Other Psychiatric Disorders Where ECT May Be Indicated?

There are several studies that support the use of ECT in combination with pharmacotherapy for patients with schizophrenia—in particular, those with catatonia, aggression, or suicidal behavior [26]. There have also been case reports where ECT, in combination with benzodiazepines, appears to be efficacious as treatment for neuroleptic malignant syndrome (NMS) and catatonia [27]. ECT is used in older patients with Parkinson disease for treatment of comorbid depression or for the motor symptoms of Parkinson disease [28, 29]. There is also evidence supporting the use of ECT in depressed older adults with major neurocognitive disorders and in older patients with poststroke depression [30, 31].

Question 3.13

What Is the Mechanism of Action of ECT?

The exact antidepressant and antipsychotic effects of ECT have not been clearly elucidated. Both anticonvulsant effects and neurotrophic effects have been suggested as being related to the mechanism of action of ECT. The anticonvulsant effects are related to the decrease in blood flow and metabolism in the frontal lobes, whereas the neurotrophic effects are related to the increase in perfusion and metabolism in the medial temporal lobes [32]. Some neuroimaging studies have shown an increased in the volume of the hippocampus with ECT [33], which is thought to be a key component of the neural circuitry involved in mood. It has also been hypothesized that ECT increases the availability of neurotransmitters including serotonin,

norepinephrine, and dopamine via changes in receptors and post-receptor mechanisms [34]. ECT also seems to normalize hypothalamic-pituitary-adrenal axis dysfunction, which is known to be associated with depression, as it restores dexamethasone suppression of cortisol [34].

Question 3.14

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive procedure that was developed in the 1980s used to study and better understand the brain-behavior relationship. It has also been used as a therapeutic tool in various psychiatric disorders because of its ability to modulate very specific brain areas. rTMS works on the principle of electromagnetic induction by using an electrical wire coil to induce a brief dynamic pulsed magnetic field. Electrical current flow is induced in the brain as neural tissue is conductive, with the skull and scalp being transparent to the magnetic field. The current flow in turn leads to the immediate stimulation or inhibition of the cortex depending on the frequency of the current.

There is robust evidence for the use of rTMS in depressive disorders in the adult population [35]. Positive predictors for response seem to be associated with patients who are younger and nonpsychotic and have a shorter duration of depressive episode, low degree of treatment resistance, and a history of positive response to ECT and/or rTMS [35]. Age seems to be inversely related to response to rTMS in depression. However, it is thought that perhaps higher rTMS stimulation intensity and more treatments may be needed in older adults for optimum results [36].

While the primary indication for rTMS is major depressive disorder, there is also some evidence for its use in bipolar depression [37], although there are relatively few controlled trials specific to bipolar depression. Other psychiatric conditions that show promise but require further studies include depressive episode with psychotic features, vascular depressive disorder, depressive disorder in context of mild or major neurocognitive disorder, depressive disorder in Parkinson disease, and anxiety disorders.

How Does rTMS Compare to ECT in the Treatment of Depressive Disorders?

Several meta-analyses have consistently found that rTMS is less effective than ECT for depressive disorders [24]. In patients where ECT has failed, they are less likely to respond to rTMS [24]. However, rTMS is generally better tolerated (see Table 3.7) and is a modality that is more acceptable to patients than ECT. rTMS also does not require anesthesia and, thus, has a safer profile than ECT. However, with its well-established efficacy, ECT still remains the gold standard in treatment for severe major depressive disorder.

Table 3.7 Adverse effects for repetitive transcranial magnetic stimulation [24]

Adverse effects	Prevalence (%)
Scalp pain	40
Headache	30
Seizure induction	0.01–0.1

Question 3.15

You have been approached by a very keen medical student in your ECT clinic. The medical student recently saw a male patient on the inpatient unit who was diagnosed with a severe unipolar depression. The patient was tried on a number of medications but had difficulty tolerating most of them. The only one he was able to tolerate was sertraline, which he has been taking for the past 4 weeks at 75 mg daily. He has had a minimal response to the medication thus far, so the attending physician is considering a referral for the patient to start ECT. The student wants to know if the patient should continue on the sertraline if he does start ECT and whether he would need to remain on medications after the course of ECT is completed.

A. Should ECT Be Combined with Pharmacological Treatment?

Although ECT is a highly effective treatment for major depression, there have also been high rates of relapse, especially early relapse, noted by various studies [38]. Lower relapse rates have been reported in studies where antidepressants were used concurrently with the course of ECT compared to studies where maintenance pharmacotherapy started after the course of ECT, 29.2% vs 41.6%, respectively [38]. It would be reasonable, unless there were significant side effects or health concerns, for patients to continue on their antidepressants during ECT treatment.

B. Should Antidepressants Be Continued After ECT?

The highest rate of relapse after ECT treatment is within the first 6 months of treatment. In one meta-analysis study, those who were maintained on continuation pharmacotherapy have a relapse rate of 27.1% within 3 months, 34% within 6 months, and 51.1% by 1 year. In patients who did not receive pharmacotherapy after ECT, the relapse rates were 62.7% at 3 months and 65.5% at 6 months [38]. The authors of the meta-analysis noted that most of the published literature is from trials with older antidepressants such as imipramine and amitriptyline and that published evidence for the newer antidepressants (including SSRIs) was lacking. However, given the high rate of relapse without continual treatment, it would stand to reason to continue antidepressant therapy after ECT treatment, even when using the newer antidepressants.

Question 3.16

Deep brain stimulation (DBS) is a neurosurgical procedure where unilateral or bilateral electrodes are implanted. These electrodes are connected to a neurostimulator that electrically stimulates specific brain regions. DBS is most commonly used in movement disorders such as essential tremor and Parkinson disease. There have also been studies looking at its use in treatment-resistant depression. However, most studies looking at its effectiveness in acute treatment refractory depression have been open-label trials, and the two sham-controlled randomized trials to date were discontinued early due to lack of efficacy (24). Currently, DBS is still considered experimental treatment for depression.

What Are Potential Adverse Effects of DBS?

DBS can have potential psychiatric side effects including apathy, hallucinations, hypersexuality, hypomania, depression, and cognitive dysfunction [39]. These side effects are felt to be related to placement of the electrodes and calibration of the stimulator and, thus, are potentially reversible. Some studies have also reported blurred vision and strabismus in higher amplitude settings [40]. There are also risks associated with the surgical procedure itself, including intracranial hemorrhage (occurring in 0.2–5% of patients) and post-op infection (ranging from 1.8 to 15.2% of patients) [40]. Another serious concern is the reports of increased rate of attempted and completed suicide following DBS, making careful preoperative screening and postoperative monitoring very important [40].

Question 3.17

Treatment of psychiatric disorders is important to improve quality of life and to prevent further disability. However, as we have seen, there is a multitude of risks and adverse events that are associated with pharmacological interventions. In patients who have difficulty tolerating medications, or if they have failed a few antidepressant trials, psychotherapy is a reasonable alternative. Cognitive behavioral therapy (CBT) appears to be effective for mild-to-moderate depression, generalized anxiety disorder, and insomnia in older adults [41]. Interpersonal therapy (IPT) has also been found to be effective for the treatment of depression in older adults [42].

When Initiating Psychotherapy in an Older Patient, What Are Some Modifications to the Procedure of Therapy That Can Be Made to Improve Its Success?

Given some of the specific challenges that come with aging (e.g., impaired vision/hearing, sensitivity to cold), certain adaptations should be made to ensure the comfort of the patient. The therapist should ensure that the room being used

for the therapy is set to a comfortable temperature. The room should also be well lit. Any written material that is given should be in a larger font. If hearing is impaired, make sure that the patient is wearing their hearing aids or has access to a sound amplifier during the sessions. Handouts of important key concepts and/or audio/video taping the sessions can also improve in retaining the information. The number of sessions may be increased to allow for repetition, summary, and review. By paying attention to these issues, psychotherapy in an older adult can be an effective intervention.

Question 3.18

What Are Some Factors That May Make CBT Difficult to Carry Out Effectively in Older Adults?

While there are no absolute contraindications to CBT, there are some factors that may limit the benefits of CBT. The greater the cognitive impairment, the less likely the patient will grasp the more abstract concepts of CBT. In a patient with severe depression or severe anxiety, the severity of the symptoms may interfere with the patient's ability to participate meaningfully in psychotherapy; e.g., profound apathy may make it difficult for the patient to complete the "homework." In a person with significant comorbid medical illness, their illness may affect regular attendance in the therapy or affect the physical stamina necessary to attend a full therapy session. Visual and hearing impairments may also make delivery/comprehension of the CBT concepts difficult. It is important for a clinician to consider these factors prior to therapy and strategize whether these difficulties could be overcome before engaging in therapy.

Question 3.19

Apart from Cognitive Behavioral Therapy (CBT) and Interpersonal Psychotherapy (IPT), Name and Briefly Describe Three Other Common Psychotherapies Used in the Treatment of Depression

Problem-solving therapy, brief dynamic therapy, and reminiscence therapy have all been shown to be effective interventions for depressed older adults [43].

- Problem-solving therapy (PST) is based on the notion that negative stress and poor coping can lead to breakdown of problem-solving abilities and subsequently lead to depression. The goal of PST is to better understand how stress may lead to emotions and develop adaptive problem-solving skills in order to resolve or better cope with these stressful problems. The steps of PST include identifying and analyzing a problem, developing solutions to the problem, weighing out the pros and cons of each solution, and assessing the effectiveness of the solution in context of the patient's life.

- Brief dynamic therapy (BDT) is an intensive short-term psychodynamic therapy concentrating on one major focus for the therapy rather than allowing the patient to associate freely and discuss a number of unrelated issues, which are seen in long-term psychodynamic therapy. Using a psychodynamic approach, BDT helps the patient overcome internal resistance to experiencing true feelings about the present and past. These true feelings have been suppressed because they are either too frightening or too painful. It is believed that unconscious conflict of these feelings is what leads to depressive and anxiety symptoms. Once these feelings are better understood, the patient can then learn to cope better with them and be better able to regulate their emotions.
- Reminiscence therapy is based on the patient re-experiencing personal memories and significant life experiences. Through the exploration of past events and feelings, pleasure, a better sense of continuity of one's life is obtained, which can then better help with emotions that stem from transitions (e.g., sadness from having to move to a nursing home).

Question 3.20

Ms. K is a single 69-year-old female who lives alone in her home. She has a long history of alcohol use disorder that she never sought treatment for. Ms. K is currently in the hospital as she presented to the emergency department 10 days ago with confusion. She was admitted to the hospital after she was found to have hepatic encephalopathy (delirium) immediately due to liver cirrhosis. A psychiatric consultation has been requested to assess her alcohol use disorder. During your assessment, you found out that Ms. K has been drinking significant amounts of alcohol since her 30s. She was in a relationship at the time whereby her partner was also a heavy drinker, and even though the relationship ended many years ago, Ms. K continued her drinking. While she has never missed work because of her drinking, she feels she has alienated herself from friends and family over the years as she did not want them to find out about her alcohol use. Her recent issue with hepatic encephalopathy has given her a "wake-up call." She now recognizes the extent of her drinking problem but is not sure how to go about stopping it—she is just so used to drinking alcohol that it has almost become second nature. Ms. K is wondering whether therapy can help her alcohol addiction.

Are There Any Psychotherapies That Would Be of Benefit in an Older Adult with Substance Use Disorders?

There is a common misconception that older adults do not abuse alcohol or other substances. In fact, there is evidence to suggest that substance use disorders have been under-identified in older populations for many years [44]. As our population of baby boomers ages, the need to identify and treat substance use disorders becomes more critical given the ongoing burden of increasing healthcare costs.

Motivational interviewing is a client-centered, nonjudgmental approach that tries to engage the patient in making positive, healthy changes to the individual life; e.g., discontinue maladaptive substance use behaviors. While motivational interviewing and its use in substance use disorders have been studied in the younger population, there is little evidence supporting its use in older adults and substance use [44]. There have been some studies for its use in older adults targeting other behaviors such as smoking cessation or increasing physical activity [45].

PST has also been used in substance use disorders with some success [46], targeting around problem-solving for the "addiction problem." Unfortunately, there is a lack of studies looking at the efficacy of PST for substance abuse specifically in older adults. Generally, evidence for the use of psychotherapies for substance use in older adults is extrapolated from that of studies with the younger population.

There has also been an interest looking at brief interventions—brief advice or counseling—for substance use disorders as there is evidence for reducing heavy alcohol consumption in the general adult population [47, 48]. Evidence also seem to support the use of brief interventions in older adults as they also show comparable reduction in alcohol consumption when compared to younger adults given the same brief interventions [49].

For Ms. K, motivational interviewing or other brief interventions may help her progress along in her decision making to be committed to stopping her alcohol use. PST may also be helpful in determining the best plan of action for Ms. K to achieve her goal of alcohol abstinence (e.g., Should she go to Alcoholics Anonymous or inpatient rehab program?).

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Topic 4: Ethics and Law

Question 4.1

The United Nations' 2015 *Ageing Report* estimates that between 2015 and 2030, the number of people in the world over 60 years old will grow by 56% from 901 million to an estimated 1.4 billion [1]. Furthermore, the number of people who are aged 80 years or over, the "oldest-old," is growing faster than the number of older persons overall [1]. The United Nations anticipates that the higher proportion of older individuals will become "… one of the most significant social transformations of the twenty-first century." Consequently, providers of health services will increasingly face complex ethical dilemmas that are uniquely raised by an aging population. An ignorance of the laws and policies, particularly in the area of psychiatric illness and interventions, will no longer suffice [2].

What Is Ethics?

Ethics is a set of moral standards for behavior to guide how individuals *ought* to act [3]. Ethics deals with questions of what is right or wrong. Some ethical issues are more relevant to clinicians working in geriatric psychiatry by virtue of the population of older adults with whom they work [4]. For example, end of life, surrogate decision making, and the presence of progressive neurocognitive disorders (NCD) are issues that are commonly encountered in an older population.

Question 4.2

List and Describe Four Core Ethical Principles in Medicine

Table 4.1 presents four core ethical principles in medicine, definitions, trends, and consequences [2, 5].

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_4

Table 4.1 Four core ethical principles in medicine, definitions, trends, and consequences

Ethical principles	Definition	Trends	Examples of potential consequences
Respect for autonomy	Respecting individual's abilities to make reasoned informed choices	1970s to current	Fundamental to assessing decisional capacity in older adults with psychiatric illness
Beneficence	Moral obligation to act for the benefit of the individual, helping them to further their important and legitimate interests by preventing or removing possible harms	Dominated in the first half of the twentieth century	Physicians taking a paternalistic approach toward their patients
Nonmaleficence	Avoiding causing harm to patients	Ongoing	Focus on risk/benefit ratio for interventions
Justice	Distributing the benefits, risks, and costs of fairly and equitably treating similar patients alike in similar circumstances	Dominated in the first half of the twentieth century	Was previously cited as justification for sterilization of developmentally disabled people; used to justify distribution of access to medical resources

Data extracted from references [2, 5]

Question 4.3

What Factors Affect the Application of the Principle of Respect for Autonomy?

Respect for autonomy is considered to be a fundamental principle that needs to be considered when treating older adults with psychiatric illness [2]. The extent to which patient autonomy is applied can be greatly affected by patients' cultural background. For example, in some cultures, the norm is for older adults to play a passive role in clinical encounters about their medical care. In these situations, clinical staff may routinely consult with predominant family members (e.g., the oldest son) before consulting with their older patients. This could include even withholding pertinent medical information—such as the diagnosis of a terminal illness—from the older patient. Clinicians need to understand that they have cultural biases that may run counter to that of their patients. Rather than assuming that an individual highly values their personal autonomy regarding medical care, direct inquiry about their degree of autonomous participation in medical decision making versus that of their family members is important. Thus, patients must "autonomously decide not to exercise their full autonomy" in cases where they (despite having intact decisional capacity) cede authority to others.

Question 4.4

What Is Narrative-Based Ethics?

Narrative-based ethics may be relevant for psychiatrically ill individuals who lack the capacity to make medical decisions and for older adults who by virtue of their age have a life history to share [6]. Narrative ethics refers to the clinical story itself and the process of telling such a story. A patient's narrative includes values or opinions they have expressed over a lifetime. For example, a patient may have expressed disdain for becoming indefinitely ventilator dependent or to living in a skilled nursing facility for an extended period of time. These expressions of values could inform decisions about aggressiveness of care in the absence of an advance directive.

Question 4.5

What Are Some Important Legal Issues in Elder Law to Consider?

The field of elder law has emerged as a relatively new area to deal with the impact of laws affecting seniors. In the USA, the *Older Americans Act*, passed in 1965, was intended to help older citizens by providing grants to US states for community-based social and health-related services [7, 8]. Elder law is rooted in the *Older Americans Act* and evolved as a specialty of law directing services to the needs of older people [9]. In 2003, the *Elder Justice Act* was passed in the USA as comprehensive legislation to "prevent, detect, treat, intervene in, and prosecute elder abuse, neglect, and exploitation" [10]. In Canada, amendments have been made to federal legislation to protect seniors. For example, in 2012, the *Protecting Canada's Seniors Act* amended section 718.2(a) of the *Criminal Code* to allow judges to consider vulnerability due to age as an aggravating circumstance for sentencing purposes [11].

Question 4.6

What Are the Four "Cs" That Attorneys Practicing in the Area of Elder Law Tend to Focus on?

The four "Cs" are client, confidentiality, conflicts of interest, and capacity [9, 12] (See Table 4.2).

Table 4.2 Four main legal areas of focus in elder law [9, 12]

Areas of focus	Description
Know your *client*	The client's social, medical, psychiatric, legal history; values, beliefs; important relationships
Understand the importance of *confidentiality*	Family members whom clients have been estranged with for years—and do not wish to have informed of their medical/legal circumstances—may demand information that they should not be privy to
Be alert to potential *conflicts of interest*	The client's needs—not that of family members, clinical staff, or even legal representative—are the attorney's top priority
Inquire into the *capacity* of the client	The client's decisional capacity is important to determine (see Question 4.7)

Question 4.7

What Is Informed Consent?

Grounded in both ethics and law, the doctrine of informed consent was developed to redress some of the inequality of information that had previously characterized the doctor-patient relationship. Informed consent represents respect for the person as a human being and as a moral agent with fundamental rights in society [13]. Informed consent allows individuals to determine their own course of action regarding their healthcare.

Informed consent must:

- Relate to the treatment
- Be informed (knowledgeable)
- Be given voluntarily (free of coercion or duress)
- *Not* be obtained through misrepresentation or fraud
- Be disclosed (whether implied or expressed)

When obtaining informed consent, relevant questions include [2]:

- What is the *nature* of the consent given?
- What *effect* will the consent have?
- Is the consent *valid*?
- How does one *manifest* informed consent (e.g., written, verbal, video)?
- What are the reasonable *consequences* of each treatment option?

Question 4.8

What Is Decisional Capacity?

The ability to consent to treatment, or decisional capacity, is the foundation of informed consent. Capacity to consent has been defined as "the ability to understand significant benefits, risks, and alternatives to proposed healthcare and to make and

Table 4.3 Comparison between capacity and competence [16]

Features	Capacity	Competence
Category	Medical	Legal
Who determines	Physician or other clinician	Court of law (judge, magistrate, or arbitrator, depending on the state/territory)
Parameter	Regarding a particular treatment decision at a specific point in time	May be global determination regarding ability to make decisions regarding financial, property, and other matters
Impact on legal status	Does *not* affect legal status directly, although clinician evaluation can be used as evidence in competency proceeding	*Does* affect legal status

communicate a health-care decision" [14]. Consent to treatment is the most common type of capacity assessment requested by psychiatric consultants.

Decision-making capacities include four major components related to the abilities to [15]:

1. *Understand* relevant information as it relates to the choice, such as the nature, purpose, and the potential risks and benefits of the proposed treatment as well as alternatives.
2. *Appreciate* the relevance of treatment methods and their consequences for one's condition or situation.
3. *Reason* about the different treatment options (i.e., to consider and compare potential consequences of various options).
4. *Communicate* a consistent choice.

Question 4.9

What Is the Difference Between a *Capacity* and a *Competence* Evaluation?

The terms *capacity* and *competence* are often used interchangeably, but there are subtle differences between them. Table 4.3 shows the key features between capacity and competence [16].

Question 4.10

List Common Medical or Neuropsychiatric Conditions Among the Geriatric Population That Could Impair Decisional Capacity

Table 4.4 lists some common systemic medical and neuropsychiatric conditions that can occur among the geriatric population that could impair decisional capacity [17].

Table 4.4 Common systemic medical and neuropsychiatric conditions among the geriatric population that could impair decisional capacity [17]

Clinical context	Examples
Intensive care, hospitalization	Severe cognitive impairment (comatose, obtunded, medical emergencies)
Intensive care, hospitalization	Delirium
Psychiatry or neurology clinic	Severe neurocognitive disorder (formerly dementia)
Psychiatry unit	Mania
Psychiatry clinic or unit	Severely depressed mood with suicidal ideation, and/or psychotic features
Psychiatry unit	Schizophrenia (e.g., paranoid or somatic delusions regarding the medical condition and/or treatment team, severely disorganized thought process)

Question 4.11

What Are Major Steps in Completing a Decisional Capacity Assessment?

A clinical assessment of mental capacity of an older adult often includes the following five steps [18, 19]:

1. Determination of the specific type of decisional capacity to be assessed
2. Collection of collateral information about the older adult from significant others and healthcare professionals
3. General assessment of psychiatric state, including formal cognitive assessment
4. Specific assessment of decisional capacity
5. Professional judgment of decisional capacity that integrates these components

Confirm that the primary treatment team requesting a capacity assessment has provided (or attempted to provide) information about the recommended treatment, including what medical condition the treatment is for, basic description of the treatment, and potential risks and benefits of undergoing the treatment *and* of not undergoing the treatment. The primary treatment team may be held legally liable if consent was not provided, if the treatment deviates significantly from what the patient consented to, and/or if the consent was obtained through misrepresentation [20, 21].

Clarify the referral question. A consult stating simply, "capacity evaluation" does not suffice due to lack of specificity. Why does the primary treatment team need a capacity assessment? For example, is the patient refusing a specific treatment? Is the patient consenting to the treatment but appears confused by the information?

Sometimes, the treatment team believes the patient has decisional capacity to consent to undergo or refuse a treatment, but family members disagree with the patient's decision and are requesting a "second opinion." Specify what specific treatment you are evaluating and for what specific condition.

Some principles to consider when completing a decisional capacity assessment of geriatric patients are described in Table 4.5 [22, 23].

Table 4.5 Principles to consider when completing a decisional capacity assessment of geriatric patients [22, 23]

Principles	Rationale and examples
Decisional capacity should be considered in all encounters with geriatric patients	The geriatric patient is at higher risk of lacking decisional capacity
Ineffective or inconsistent communication between the primary clinical team and patients may lead to a finding of incapacity	Potential barriers to communication: impaired hearing, cultural and linguistic differences, inaccurate assumptions made by the clinical team regarding geriatric patients
	The presence and input of multiple family members
Decisional capacity is *not* "all or nothing"	A patient may have decisional capacity in one area, but not another
	Medical decision-making capacity is limited to a *particular* medical decision at a particular time. A determination of global lack of capacity is ill-advised other than in cases with severe cognitive impairment. Otherwise, a patient may not be allowed to make some that he/she is actually capable of making
	Decision-making capacity impairment may be transient. For example, a patient may recover decisional capacity once delirium resolves
How information is presented varies based on clinicians' knowledge, biases, and time constraints	Geriatric patients may require more time to think through their treatment options and to consult with family members and friends
Completing a decisional capacity assessment may bring up important existential issues. Understanding your own biases and perspectives will help you to keep the patient's interests (including their legal rights) foremost in your mind as you complete an assessment	Due to the nature of a capacity assessment, a patient's worldview—including values, the purpose of life, and what happens after one dies—will often come up
	Interpersonal dynamics among the patient, loved ones, and treatment team members may be further heightened by the results of your evaluation
Decision-making capacity is required for informed consent to undergo a treatment *or* to refuse a treatment	Refusal of recommended treatments often triggers a psychiatric consult to ensure that the patient understands a potentially dire outcome
	Family members who want "everything" done to prolong life may request a decision-making capacity assessment be completed

(continued)

Table 4.5 (continued)

Principles	Rationale and examples
Your job is *not* to convince a patient in the decision one way or another. If the patient has decisional capacity, the patient has the right to undergo or refuse a recommended treatment, even if you, the treatment team, and the patient's family disagree	You may have a unique opportunity to help the patient and their loved ones discuss difficult end-of-life and other important topics that were previously avoided. Psychiatrists are specifically trained to help patients—as well as clinical team members—emotionally and mentally process a patient's decision
	A patient's decision to forgo a potentially lifesaving treatment is not a "failure" on your part, or that of the treatment team, or family members
Attempt to maximize a patient's functioning during a capacity assessment	For example, written instructions, sensory aids such as reading glasses or hearing aids, assistance of trained medical interpreter
If your findings are equivocal, a reassessment or second opinion may be warranted	The results of your evaluation may significantly impact a patient's health and may have legal implications. Consider contacting your risk management office if you are not sure what to do. If available, consider recommending a formal involvement by your facility's ethics committee

Question 4.12

What Standardized Assessment Tools Can You Use as Part of Your Decisional Capacity Assessment? What Is Their Role?

Standardized tools cannot solely determine a patient's decisional capacity and should only be used as part of a comprehensive assessment. Valid clinical tools that may be of use are listed in Table 4.6 [2].

Question 4.13

What Are Advance Directives?

Advance directives are legal documents in which individuals express their prior capable wishes in the event they become mentally incapacitated at some point in the future [24, 25]. Advance directives have many different terms. Refer to Table 4.7 for different types of documents that can be used [2]. If an individual is found to be incapable, medical decisions can be made according to their previously expressed values, wishes, and beliefs. Some advance directives are *instructional* in nature in that individuals can include detailed instructions about what to do in a given situation, whereas others are *proxy* in nature whereby someone else is named as an agent to make decisions for the incapable person.

Table 4.6 Common capacity instruments [2]

Test	Abbreviation	Time to complete (min)	Comments
Aid to Capacity Evaluation	ACE	10–20	Freely available; uses the patient's own medical situation and diagnosis or treatment decision; an eight-question tool that assesses understanding of the problem, proposed treatment/alternatives, option to refuse treatment, foreseeable consequences of the decision, and the effect of an underlying psychiatric disorder on decision; it provides objective criteria for scoring responses
Hopkins Competency Assessment Tool	HCAT	10	Freely available; a four-paragraph essay tool written at three reading levels of 6th grade, 8th grade, and 13th grade (completed high school); the examiner reads aloud while the patient reads the same material, starting with the 13th grade example, followed by six questions; if score <3 on higher-level essay, the 8th grade and then 6th grade level essays are used. Scores <3 suggest incapacity
MacArthur Competency Assessment Tool for Treatment	MacCAT-T	20–25	Available from Professional Resource Press
Understanding Treatment Disclosure	UTD	<30	The tool provides three subscale scores; the tool has a scoring manual that provides objective criteria for scoring responses

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Table 4.7 Types of advance care planning documents

Name	Description
Advance agreement	Term used by the *English Mental Health Act* Legislation Committee to describe plan of care between patient and treatment provider
Advance directive	General term for document with statutory authority for capable person to state wishes of what should happen to them if becomes incapable
Advance healthcare directive	Term used in Newfoundland and Labrador and Prince Edward Island
Advance refusal	A stronger version of advance directive that highlights refusal rather than "directed"
Advance statement	A weaker version of advance directive in that person's wishes are stated rather than "directed"
Authorization	Term used in Nova Scotia
Healthcare directive	Term used in Manitoba and Saskatchewan
Joint crisis plan	Currently a research intervention in the UK where facilitator negotiates with the person and comes to some agreement

(continued)

Table 4.7 (continued)

Name	Description
Living will	Term used to highlight that the document can only be used while the person is alive. In wider use in the USA than Canada
Mandate in case of incapacity	Term used in Quebec
Mill's will	Term used to refer to John Stuart Mill's philosophy which highlights self-determination and the right to refuse and accept treatment
Nexum contract	Advance agreement that follows a contractual model in that it is inherently bilateral
Odysseus contract, pact, or transfer	Greek term for Ulysses emphasizing different aspects of the document
Personal directive	Term used in Alberta and northwest territories
Physician's order for life-sustaining treatment (POLST)	A legally binding advance directive signed by patient (or surrogate) and physician as an order through enactment of a California, USA statute. Original kept by patient and placed in a conspicuous location (e.g., on refrigerator door) to prevent emergency medical services from inappropriately initiating or not initiating resuscitation and transport
Power of attorney (continuing, durable, enduring, springing)	Terms used in New Brunswick and Ontario
Pre-commitment contract	Used to highlight that individuals with recurrent and treatable conditions could make a wish before becoming ill
Psychiatric advance directive	Widely used term in the USA stressing the importance of autonomy
Psychiatric will	Original term proposed by Thomas Szasz in 1982 to protect patients from coercion or psychiatric neglect
Representation agreement	Term used in British Columbia
Ulysses commitment contract	Term used to reflect a commitment to follow through on the self-binding contract
Ulysses contract	Roman term used to highlight different issues around self-binding wishes
Ulysses clause	Proposed in this article to reflect that a legal provision can be included into the advance directive making the document irrevocable
Ulysses directive	Term avoids reference to any contractual relationship as through a Ulysses contract
Ulysses statement	Less strong than a Ulysses directive or contract
Voluntary commitment contract	Term highlights that document is not entered into under undue influence or coercion

From Ambrosini DL, Hirsch CH, Hategan A. Ethics, Mental Health Law, and Aging. In: Ethics, Mental Health Law, and Aging. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018; used with permission from Springer

Question 4.14

What Are Three General Legal Criteria That Must Be Met to Impose Involuntary Psychiatric Commitment on a Patient?

Involuntary commitment refers to detaining an individual in a designated psychiatric facility against their will. Since patient autonomy is a fundamental ethical principle of healthcare, involuntary commitment should be used when specific legal criteria are met. The exact wording of involuntary commitment criteria varies by state and province but generally refers to a high risk of imminent self- or other harm or inability to reasonably meet one's need for self-care due to a psychiatric and/or medical condition. The duration of an involuntary commitment before requiring a legal hearing varies from 72 h to 7 days.

Question 4.15

The patient is a 70-year-old female with stage IV adenocarcinoma of the colon, having not responded to multiple surgical and chemotherapy interventions. She has no history of psychiatric illness. She is regressing physically rapidly over the last 3 months, with profound weight loss with wasting, poor sleep, little energy, and intermittently refusing to eat or drink adequate amounts of food and water. She also experiences constant abdominal pain and nausea. She lives at home with her spouse; she also has three adult children nearby with their families. While she prefers to live at home, her spouse is not sure he can continue to manage her care as she is more regressed and needing assistance. They have some in-home caregivers, but her spouse is concerned that "it isn't enough."

She is seen for palliative care by her long-term oncologist and has also received a palliative care consultation that has focused on pain relief and other mostly supportive measures. Her medications include morphine, acetaminophen, and zolpidem. You are consulted because the oncologist is concerned that "her symptoms look like depression" and wants your input to the case. She is briefly admitted to the hospital for fluid, nutritional, and pain management. When you call the oncologist for greater clarity, she also tells you that "it really is end stage now, we need to discuss goals of care. Also I want to know if her cognitive status is intact for goals of care discussions. Are there any psychiatric medications we should be trying? How about an SSRI (selective serotonin reuptake inhibitor) or a TCA (tricyclic antidepressant)?"

A. What Are the Broad Diagnostic Possibilities You Need to Think About in This Case?

As with any other seriously ill patient, the first item in the differential diagnosis must be delirium, which is present in 75% or more of terminally ill cancer patients. Due to the low energy state of terminal cancer, the motor subtype of delirium is typically hypoactive, which is both a poor prognostic sign and a syndrome (because of the psychomotor retardation) that can appear similar to depressive disorder. She has at least the population baseline risk of major neurocognitive disorder, plus metastatic disease to the brain leading to neurocognitive disorder on the bases of brain metastasis plus surrounding edema, even if she does not meet full diagnostic criteria for delirium per se. Depressive disorder is common in cancer, and her neurovegetative signs are consistent with major depressive episode; however, the same physical symptoms can also be due to the effects of the cancer itself, a distinction that is rarely one that can be made with absolute certitude.

B. What About the Oncologist's Question Regarding Decisional Capacity?

While severe depressive disorder (if validly diagnosed) can affect cognitive function, and thus decisional capacity, most patients with depressive disorders have *intact* decisional capacity. Neurocognitive disorders (delirium, major neurocognitive disorder, or both) far more commonly impact decisional capacity. As the decision being considered is not consent for medical intervention per se, the usual informed consent-based decisional capacity paradigm is not as directly applicable, so the assessment of her decisional capacity is about withdrawal of care/accepting natural death.

Case continued: You go to see her in the hospital. She is cachectic and mildly somnolent (Richmond Agitation-Sedation Scale (RASS) -1), with psychomotor retardation and minimal spontaneous speech. Her attentive husband and daughter are nearby, and they both agree that she is more regressed lately and that the poor sleep and profoundly poor appetite were not present 2 months ago. There was some depressed mood when initially diagnosed with cancer, which resolved without intervention when she was in active cancer treatment ("She is a real fighter, when she is committed to something, she is *all in*"). With her recent progression, her family members think she is "maybe accepting the inevitable, maybe giving up, it is hard to say." There is no evidence of psychotic symptoms nor suicidal ideation. Her affect is blunted, dysphoric, non-tearful, and near melancholic. MoCA is 20/30 with poor recall and concentration and with poor persistence at some of the testing items.

C. What Is Your Clinical Impression at This Point?

A MoCA score of 20 in this context is consistent with cognitive impairment, which could be attributable to depressive disorder, delirium, and/or other neurocognitive disorder, but this level of function is not so impaired as to a priori result in a finding

of decisional incapacity. The illness narrative is consistent with depressive disorder in the context of cancer.

D. How Do You Handle the Decisional Capacity Element of the Consultation?

Given only mild cognitive impairment on formal assessment, you would proceed to assess the goals of care discussion separately. As no active new treatment is being offered, this is not about informed consent in the usual sense, although it could be argued that withdrawal of active care is somewhat analogous to informed consent but in the "negative sense" in that the patient must well understand and accept the natural course of illness as expected.

She understands that she has metastatic disease and that no more active disease modifying interventions are being offered. She understands that palliative management focused on symptom control is the focus of care. She understands that her estimated survival is 3 months or less.

E. Does She Have Decisional Capacity?

Cleary the answer is yes. She understands the essential elements of the goals of care discussion. Her reasoning is intact and consistent with a patient with only mild cognitive impairment.

F. How Would You Intervene at This Point?

Given the ambiguous presentation on examination, it is reasonable to try a course of an antidepressant to see if the manifest symptoms improve; such an intervention may improve her quality of life/illness experience.

G. What Antidepressant Is to Be Considered?

This case is the prototype case of "not all antidepressants are created equal." There are significant physical risks with the SSRIs and TCAs that the internist queried about. SSRIs increase nausea especially in a patient with premorbid gastrointestinal (GI) distress and carry a significant risk of syndrome of inappropriate antidiuretic hormone secretion (SIADH). TCAs also have a significant SIADH risk and, owing to their anticholinergic effects, can provoke delirium, so both of these medication classes are best avoided. A better choice is mirtazapine 15 mg at bedtime, in part to improve sleep and appetite and to decrease nausea. It may also have an adjunctive effect on pain, decreasing the need for opioids. This patient is highly delirium-prone, and the improved sleep-wake pattern with mirtazapine could help to slightly decrease the delirium risk. Zolpidem and similar medications are contraindicated in any cognitively impaired or otherwise delirium-prone patient.

H. How Would You Manage Follow-Up?

You would tell the oncologist to consider her to be "permanently delirium-prone." You would want to reassess her in 2–4 weeks to reexamine her and recheck a MoCA; any improvement in mood and/or cognitive status is indirect, but persuasive, evidence that a depressive episode (responsive to mirtazapine) was putatively culpable for her initial presentation. With a robust response such as this, treatment with mirtazapine would be considered indefinitely.

Question 4.16

The patient is a 65-year-old white male with a long-standing history of paranoid schizophrenia. He first became psychiatrically ill in his late 20s, with subacute onset of command auditory hallucinations directing his behavior and elaborate paranoid delusions including his having assumed the identity of many historical figures, including "Jesus Christ 125 times, but I got tired of the crucifixions"; later "Marcus Aurelius, Nero, and of course Julius Caesar" many times each; and finally the identity of Oscar Wilde "because we are both very intellectual. Many people don't know that I actually wrote all of his best stuff."

He was hospitalized many times over the years; after multiple failed antipsychotic trials, he was finally managed on clozapine (current dose 600 mg per day) over many years. When medication compliant and without undue external stressors, he was able to manage his own small apartment and volunteered helping other chronic mentally ill patients. However, he remains very psychically fragile in the interpersonal space, with a proneness for acute decompensation. This is especially true when he interacts with his elderly mother, who has borderline personality disorder and a tendency to become excessively emotional and critical of him.

He was brought to the emergency department (ED) by the police, who report that he "was talking nonsense, wandering about the community, and was unable to tell us where he lives or how he cares for himself." Your consultation team is covering the ED at your hospital. The ED physician calls you: "This guy is really out there, thinking he is all these famous people. Right now he can't think straight. You need to see him right away."

A. What Initial Workup Do You Direct the ED Physician to Initiate Before You See Him?

While the narrative is classic for chronic, relapsing schizophrenia, with acute mental status changes, especially in a geriatric patient, delirium needs to be ruled out first. Ergo, he needs a metabolic panel, liver-associated enzymes, complete blood count

(CBC), thyroid stimulating hormone (TSH), B_{12}, urinalysis and urine toxicology, and blood alcohol level. Since he is on clozapine, an electrocardiogram (ECG) to check the QRS and QTc is needed. If a STAT clozapine level is available, it should be ordered. Brain CT scan is recommended but not urgent unless there is evidence of traumatic brain injury (TBI) or lateralizing neurologic signs. Due to clozapine therapy, surveillance for opportunistic infections associated with neutropenia is needed. Clozapine-associated myocarditis, if suspected on exam, needs an echocardiogram. While exceedingly rare, there have been cases of clozapine-associated neuroleptic malignant syndrome (NMS) reported, so any physical findings consistent with NMS obligate checking a creatine phosphokinase (CPK); it would be reasonable to order a CPK initially.

Case continued: You see him in the ED. He is alert and a bit restless (fidgeting on the bed) consistent with a RASS of +1. He is fearful and suspicious, saying that "they will get me, they will get me" perseveratively without elaboration, and he identifies himself as "Oscar Wilde the Second"; the place as "London, of course"; and the year as "1900 in the reign of her Majesty Queen Victoria." He denies suicidal or homicidal ideation per se but cannot describe how he would care for self, other than "putting my full trust in the Queen and the good graces of my literary colleagues." He struggles with understanding the MoCA items instructions and only can manage a 10/30, with notable perseveration.

B. How Would You Interpret These Exam Findings?

The RASS of +1 is nonspecific, as it could represent mildly agitated delirium or the agitation consistent with acute psychotic decompensation. He is clearly unable to care for himself, given his responses to interview queries and exam findings. A MoCA score of 10/30 is severe impairment, but clearly the score is affected by his disorganization, so a diagnosis of major neurocognitive disorder is not likely and could not be validated until his psychotic symptoms are improved.

Case continued: His laboratory studies return. Metabolic and liver-associated enzyme panels are normal. White blood cell count (WBC) is in the normal range. Clozapine level is sent but will not be available for several days. ECG is nonspecific, with normal QTc and QRS.

C. What Would You Do Next?

A CT of the head is reasonable to request to rule out structural lesions. He could have chronic delirium and/or onset of major neurocognitive disorder fueled by the anticholinergic effects of clozapine. It seems prudent to restart his clozapine at current doses as an initial intervention. Additional antipsychotic PRN (e.g., PO or IM olanzapine) to contain acute psychotic symptoms is needed.

D. What Do You Do About His Delusions? Do You "Go Along" to Placate Him or Confront Him Regarding Their Inaccuracy?

Two approaches to consider in tandem are "don't confront delusions but don't validate them either" and to ask the patient to describe the *distress* he is experiencing *as a result of* the psychotic symptoms. Reinforcement of the "bigger reality" is helpful (e.g., "You are in the ED because we are concerned about your psychiatric status. We want you to describe your experiences and how they may change over time as we treat you").

E. And Finally, What About His Legal Status?

In most jurisdictions, a psychiatric commitment order requires the clinician to demonstrate danger to self (suicidality), danger to others (threat of violence, including murder), or grave disability (with either intrusive hallucinations or delusions that distract the patient from the ability to self-care, or extreme cognitive disorganization leading to the same condition). He is a classic example of grave disability, owing both to the presence of profound delusions and evidence of a grossly disorganized thought process.

F. What Is Your Disposition in This Case?

He needs a transfer to a psychiatric unit under cover of a commitment order. Contact with his outpatient psychiatrist needs to be attempted, to validate clozapine dosing and other relevant recent experiences with outpatient care. He needs delirium precautions, as clozapine is notable at inducing delirium (rare among antipsychotics in this regard, likely due in substantial part to its alpha-one blockade and anticholinergic effects).

Question 4.17

The patient is a 66-year-old homeless male with a history of chronic alcoholism and multiple (poorly documented) strokes. He was admitted for "failure to thrive" (rejecting placement, poor self-care, not taking advantage of social supports when offered) and is a high utilizer of the ED. After admission, he was detoxified without incident from alcohol intoxication. On the internal medicine unit, he was marginally cooperative, irritable, demanding, and prone to irritable outbursts. He refuses to be placed in a supervised setting and wants to be allowed to leave. The internal medicine resident calls your consultation team: "My attending needs psych to see this patient before he is discharged. He needs a psychiatric commitment order."

A. What Are Your Initial Thoughts at This Time?

In most jurisdictions, a patient must be found to be an imminent danger to self and/or others or be gravely disabled (i.e., disorganized) to meet the legal criteria for an involuntary commitment. In many jurisdictions, chronic substance use ("chronic inebriates") and dementing illnesses are not so included. You must be aware of local laws and common practices. He is at high risk for alcohol-related neurocognitive disorder, Korsakoff syndrome, and major neurocognitive disorder due to vascular disease. As such, "dementia/delirium" laboratory studies (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, urinalysis/toxicology) and neuroimaging should be done (or recent ascertainments of these at least reviewed).

B. What Do You Focus on in Your Examination?

In addition to routine interview items, formal cognitive assessment (MoCA test or equivalent) is needed, as an assessment of his substance abuse. Since he is rejecting placement, not a medical procedure, this is not an example of decisional capacity for informed consent but, rather, to self-manage on his own or "dispositional capacity" [17]. Therefore, the usual decisional capacity criteria of understanding, appreciation, rationality, and communication of choice do not apply as they would regarding informed consent for a single discrete procedure.

Case continued: You go to see him. He is marginally cooperative but is able to emphatically deny suicidal or homicidal intent, and he has no psychotic symptoms. He is a bit circumstantial but without loose associations or disorganization. His affect is irritable and labile. He cooperates marginally with the MoCA testing and scores a 21/30, with mild deficits in recall and concentration ("because I only completed 6th grade, I hate school and reading and all of that"). He is superficially able to tell you how he would manage to live in a rented room and "beg for food or go to soup kitchen" to survive on a modest welfare check. He denies any family connections and is not particularly connected to social service agencies. CT of the head shows global atrophy and microvascular disease but no acute infarct. Laboratory studies are nonspecific. He acknowledges abuse of alcohol "when I can get it" and is disinterested in a recovery program.

C. What Do You Do Now?

In most jurisdictions, he would not qualify for a psychiatric commitment order. On interview, he shows enough cognitive capacity to probably be able to self-manage. Since this is a dispositional capacity question, it would be advisable to obtain an occupational therapy assessment of life skills (e.g., Kohlman Evaluation of Living Skills (KELS)) to better ascertain his performance of actual activities of daily living

(ADL) and social work assessment for social resources. Take their input into account in your final disposition. If he is very impaired on the KELS assessment, he may need a conservatorship procedure depending on local laws and practices and if so would need to be declared to have "impaired decisional capacity" to be kept in hospital pending these arrangements.

D. What Do You Tell Your Internal Medicine Colleague?

The patient will not qualify for a psychiatric commitment order. He has mild cognitive impairment on exam. Have internal medicine order the occupational therapy and social work assessments, the results of which may guide placement. However, mild cognitive impairment (e.g., MoCA score of 21) is unlikely to be associated with gross impairment on the KELS, so he is probably able to leave on his own. Full documentation of this encounter is needed; should he return repeatedly for failed placements (especially if his cognitive impairment progresses to moderate-to-severe impairment), he may need formal legal proceedings to appoint a conservator (or other local legal team) at that time. If, on a subsequent admission, he is suicidal, homicidal, or disorganized/psychotic per se, a psychiatric commitment order could be considered at that time.

Question 4.18

The patient is a 68-year-old white male who was admitted for unstable angina. A cardiac catheterization reveals critical stenosis of two coronary arteries, and he is scheduled for coronary artery bypass graft (CABG). His psychiatric history is notable for recurrent depressive disorder, first episode in his early 50s in the context of vascular disease. He was treated at that time with a course of sertraline 100 mg per day for 6 months, during which time he recovered.

He subsequently did well until 8 years ago, when, due to increasing functional limitations from both cardiac and peripheral vascular disease, he was obliged to retire. He disliked the forced inactivity ("I feel useless like this") and experienced a second episode of depressive disorder. He again was treated with sertraline 100 mg per day. He again responded, though more slowly this time, and this time was maintained on medication for 2 years.

Approximately 2 years ago, he started experiencing poor short-term recall memory and word-finding difficulties. His Patient Health Questionnaire (PHQ)-9 score accomplished by his primary care physician at the time was 7 (suggestive of minimal depressive symptoms), so treatment was not initiated. In the last few months, he thinks his memory problems are getting worse, to where he is forgetting the names of familiar people and is fearful of driving other than familiar routes. He has gotten lost while driving and had to urgently appeal to his GPS device to find the route home; after this incident, he became increasingly fearful of driving, especially

alone. Once, while walking near his home, he made a wrong turn and was only able to find his way home by a circuitous path.

After this incident, he told his wife that "I really am losing it, I was scared that I was not going to get home." He has also had some occasions of unsafe behavior at home, leaving a burner on the gas stove and failing to safely extinguish a fire in the fireplace.

You are on the consult service at the medical center where he is admitted. You get a call from cardiothoracic (CT) surgery: "This man has unstable angina and needs a CABG. However he has a 'psych history' so we think he is not consentable (sic) due to his depression. Please evaluate and treat him and tell us if he is competent to consent to surgery. If he is not consentable (sic), he must need a psychiatric commitment order."

A. What Considerations Come to Mind Based on the Referral Question?

There are several concerns to sort out in your management of this consult. The fact that the patient has a "psych history" is nonspecific to the issues at hand. Depressive disorders very infrequently result in impaired decisional capacity unless the depressive episode results in cognitive impairment and/or psychotic symptoms. Even then, mild cognitive impairment in most cases of depressive disorder does not impact decisional capacity, and the majority of patients with psychotic symptoms retain decisional capacity, unless their psychotic illness includes delusional beliefs or denial about the illness itself.

There is a legitimate reason to be concerned about his decisional capacity, which may be affected by a previously underappreciated major neurocognitive disorder due to vascular disease; this will need full evaluation. He shows several unsafe "dysexecutive" behaviors consistent with major neurocognitive disorder. Also, any acutely ill medical patient must be assessed for delirium, which, if moderate-to-severe intensity, can impact decisional capacity.

B. How Will You Approach the Interview?

Given that the most common cause of impaired decisional capacity is neurocognitive disorders [17], remember the adage that "every decisional capacity consult is a surreptitious cognitive disorder evaluation." To "only answer the decisional capacity question" is an incomplete evaluation, the same as "only assessing suicidal risk" and not the background psychiatric illness driving suicide risk would be. You should therefore supplement the usual interview with formal cognitive testing and assessment of the four elements of decisional capacity pertinent to the proposed surgery (understanding, appreciation, rationality, and communication of choice) [15].

C. Is There Some Data You Will Request Before Seeing Him?

You should minimally obtain the "delirium screening and dementia assessment" laboratory studies, e.g., metabolic panel, liver-associated enzymes, TSH, B_{12}, and urinalysis/toxicology. Due to the high likelihood of CNS vascular disease, neuroimaging (magnetic resonance imaging (MRI) is preferred, but computerized tomography (CT) scan is acceptable alternatively) is indicated.

Case continued: You go to see him. He is fully alert and not agitated, with RASS 0. There are no reports of sleep-wake disturbance. He says clearly that he is "not depressed" though situationally anxious about the surgery and recovery period. You go over his recent memory complaints which he acknowledges are a recent problem; he does admit to the unsafe behaviors noted previously but blames them on "the stress."

On exam, he is anxious, non-tearful, and mildly perseverative, without suicidal ideation or psychosis. He does struggle with some word finding and is quite superficial about recent historical illness events. MoCA score is 15/30, with deficits in recall memory, executive functions, visuospatial, and concentration. Hamilton Depression Rating Scale (Ham-D) score is 10 (suggestive of mild depression) (owing to sleep and energy problems).

D. How Do You Interpret These Exam Findings?

His Ham-D is well subsyndromal for a depressive episode, so his mood state does not explain the abnormal MoCA score. Moderate cognitive impairment without clear evidence of delirium is consistent with major neurocognitive disorder due to vascular disease.

E. What About His Decisional Capacity?

Moderate cognitive impairment due to major neurocognitive disorder is typically associated with impaired decisional capacity, but decisional capacity needs to be separately ascertained [17]. You would assess his understanding of relevant information about his heart disease and proposed surgery, appreciation of the implications of the illness and surgery for his personal situation (including his appreciation of both risks/benefits/side effects of surgery versus medical management), rationality (the ability to compare the "intervention" to "nonintervention" and its meaning to his personal values and preferences) and to communicate a consistent choice regarding intervention versus nonintervention. If he accomplished these four elements in a manner of a "typically informed patient," then he has intact decisional capacity for the surgery.

Case continued: You discuss the CABG operation with him. He seems to understand the relevant anatomy and physiology and can discuss some of the steps of the surgical procedure ("they open my chest and put new vessels in my heart").

He understands that he "might die" intraoperatively but cannot describe the common and usually well-understood complications of graft failure, infection, bleeding, and anesthetic risk. He says, "I trust my surgeon, she won't let anything bad happen." He says, "I would rather go for it than live so sick," as he sees self as an active person, and he unequivocally wants to pursue surgery "because I have no choice really" (he cannot describe medical management of angina other than "just take pills").

Because of his cognitive impairment and his responses to the decisional capacity discussion, you ask him to identify a surrogate for decision making in case of incapacity. He is able to understand that a surrogate would speak for him if he was clinically incapacitated, that the surrogate is charged with acting as he would have wanted, and that the surrogate (despite this charge) might not actually act as he would. He names his wife as surrogate.

F. What Do You Tell Your Surgical Colleague?

The patient has major neurocognitive disorder due to vascular disease, and he has impaired decisional capacity for the CABG consent. He is, however, able to name his wife as surrogate. You remind the surgeon that the naming of a surrogate is a "lower-capacity" exercise than exercising surgical consent per se. He is highly delirium-prone (as are all CABG patients) and so needs standard delirium precautions (i.e., avoidance of opioids, anticholinergics, benzodiazepines), and you will help with delirium surveillance. There is no role for antidepressants; his mood state is subsyndromal for a depressive episode, and serotonergic antidepressants are not started preoperatively as they may increase bleeding risk.

Question 4.19

The patient is a 75-year-old male with validated Alzheimer disease, moderate severity. He was diagnosed with this neurocognitive disorder "about 5 years ago" and initially was tried on donepezil, but he could not tolerate this due to symptomatic bradycardia, so he was thereafter managed on memantine alone. He no longer drives, and lives with his family, which an arrangement that has been working well until 2 months ago.

Over the last 2 months, he has been increasingly suspicious and frankly paranoid. He is accusing his son (in whose home he lives) of "stealing my stuff, that is why he made me move in with him." He is especially concerned that his son has "taken my car keys, probably wants to sell my car" and has taken his weapons away.

Tonight, apparently suddenly, he ran into the kitchen and grabbed a cleaver and went around the house looking for the son, only to be subdued by several family members. They called the police, who brought him to the ED. You are on duty covering the ED. The ED physician calls you that "some guy is here, all paranoid" and that he "is medically cleared to go to psych right away."

A. What Workup Do You Want to Direct the ED Physician to Do Before You See the Patient?

Delirium must always be considered in an ED presentation of any geriatric patient. Metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, calcium, urinalysis and toxicology, and blood alcohol level should be obtained. CT of the head is needed to rule out chronic subdural bleed, atrophy, and/or vascular disease. MRI is not needed, other than if called for by radiology following interpretation of the CT scan. EEG is not needed unless there is a witnessed seizure.

B. What Accounts for New Onset Psychosis in This Patient?

The two likely causes of acute-onset psychotic disorder in late life are major neurocognitive disorder and delirium. Psychosis is unusual at onset presentation of major neurocognitive disorder, except in Lewy body disease. In typical neurocognitive disorder due to Alzheimer disease, psychosis can occur throughout its clinical course, but it tends to be *less common* in the *early* stages and may become *more common* at *moderate* stages of illness.

C. What Is the Most Common Psychotic Symptom in Alzheimer Disease?

Delusions, usually of a nonbizarre, paranoid nature, often about people in the person's life, are common psychotic symptoms in Alzheimer disease.

Case continued: You see him in the ED. He is alert, restless but not agitated, and preoccupied with wanting to "kill"' his son for "stealing my things," though he cannot say exactly how he would do this. He is not suicidal. He denies hallucinations, saying "I am not crazy or anything." His MoCA score is 12 with deficits in multiple domains. His laboratory studies are unremarkable. His CT scan shows advanced atrophy of the cortex, without bleed or vascular lesion.

D. What Do You Do Now?

He is actively paranoid and continues to threaten his son. His risk of violence is thus high as his impulsivity from major neurocognitive disorder makes him more likely to act on homicidal thoughts.

E. Does the Case Meet the "Duty to Warn" Criteria?

In jurisdictions with this statute and expectation, the usual test for duty to warn or protect is a product of "credible threat and identifiable victim." The intended victim

is clear in this case, and given that he has been assaultive suggests that he continues to be at risk. The fact that his diagnosis is major neurocognitive disorder does not change the duty to warn or protect [26].

F. How Would You Manage Him?

He needs an antipsychotic to calm him and perhaps decrease the paranoia. He needs to be committed to an inpatient service (geriatric psychiatry units will be better able to manage him) with medication trials of optimized memantine. Consider another trial of a cholinesterase inhibitor if he is cardiovascularly stable, along with cautious dosing of an antipsychotic.

He cannot be discharged until he is no longer threatening; this will likely require full treatment of his paranoia. Serial MoCA scores are needed to ascertain if his paranoia was impacting his initial performance and to see if the new medication regimen may improve his cognitive status. He needs to have no access to weapons and cannot drive; his family needs to take steps to be sure he does not have access to weapons (including knives) or vehicles. If he continues to be paranoid about his son, he needs alternative placement.

Question 4.20

The patient is a 70-year-old white male, divorced, unemployed, with a history of alcohol abuse, having returned to drinking despite several completed stays at rehabilitation facilities. Due to his alcohol abuse, he is estranged from his family members, who will have nothing to do with him while he continues drinking. He currently lives in a dilapidated single-room occupancy hotel in the inner city. He is unemployed, with minimal savings, and has pension income both from social security and a veteran's pension. He is brought to the emergency department by the police on a psychiatric commitment order. He was overheard by neighbors on his cell phone, threatening to kill himself if his family did not return to his life.

You are on the consultation liaison service at the hospital where he is brought. The ED physician calls you to see this patient and says "he's done this a million times before. He says he is suicidal every time his family distances from him. He drinks constantly."

A. Based Solely on the Narrative Above, How Would You Estimate His Suicide Risk?

He is among the highest-risk patients for suicide. Specific validated risk factors include:

- White race
- Older age

- Male sex
- Solitary status
- Unemployment
- Active substance abuse
- History of (apparent) suicidal ideation in similar presentations
- Continued alcohol abuse despite opportunities to rehabilitate

B. Before You Go to the ED, What Laboratory and Other Workup Do You Require? What Additional Workup Items Are Worthy of Consideration?

Delirium must always be considered in an ED presentation of any geriatric patient. Metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, calcium, urinalysis and toxicology, and blood alcohol level should be obtained. Given his alcohol use disorder, an international normalized ratio (INR) to check for hepatic enzymatic functions is appropriate. CT scan of the head is not urgent unless there is evidence of head trauma or lateralizing neurologic signs but is needed to rule out chronic subdural bleed, atrophy, and/or vascular disease. MRI is not needed, other than if called for by radiology following interpretation of the CT scan. EEG is not needed unless there is a witnessed seizure.

Case continued: You go to the ED to see him. He is unkempt, poorly groomed, sloppily dressed, dysarthric, and mildly somnolent and smells like alcohol. When spoken to, he opens his eyes for up to 30 s and makes fleeting eye contact (RASS -2). He endorses being "really depressed, hopeless" and that "I just can't stop drinking, nothing helps." He endorses suicidal ideation by "drinking myself to death, or may jump in front of a truck or bus, or something." He denies homicidal ideation or psychotic symptoms. MoCA score is 13/30; he closes his eyes during several of the items and has to be spoken to rearouse to finish the exam.

C. What Is Your Differential Diagnosis at This Moment?

The differential diagnosis includes alcohol use disorder, or alcohol intoxication, with the caveat to rule out depressive disorder due to alcohol use, major depressive disorder, major neurocognitive disorder (due to alcohol use disorder/other factors), and delirium.

Case continued: His metabolic profile is normal; he has mildly elevated liver-associated enzymes, INR, and mean corpuscular volume (MCV). He is mildly anemic and mildly thrombocytopenic. TSH is normal; serum B_{12} level is 200 pg/mL which the ED physician says "is OK, that is normal range"; blood alcohol level is 225 mg/dL or 49 mmol/L; INR is 1.3; vitals are normal; and urinalysis and urine toxicology are negative. CT of the head reveals no subdural hemorrhage, but there is global atrophy (more in cerebellar than cortical regions), with evidence of mild white matter disease.

D. How Do You Interpret the Laboratory Results?

Elevated liver enzymes are likely due to mild alcoholic hepatitis, whereas MCV is consistent with alcohol abuse. Elevated INR suggests liver disease due to alcohol use disorder. "Low normal" range B_{12} is not an acceptable level in a patient with cognitive deficit and needs further supplementation.

E. How Would You Manage Him?

At such a high risk of suicide (given multiple risk factors), you should not assume "he won't be suicidal when he sobers up"; thus he needs to stay on a psychiatric commitment order. He needs B_{12} supplementation and IV thiamine for several days. Consider ultrasound of the liver to rule out cirrhosis. He needs surveillance for alcohol withdrawal risk and Clinical Institute Withdrawal Assessment (CIWA) monitoring.

F. What About Antidepressants in This Patient?

He needs serial assessment of mood. If he remains with depressed affect and suicidality after detoxification, he may meet diagnostic criteria for alcohol-associated depressive disorder, which could justify a trial of antidepressant. Due to low platelet count, SSRI and serotonin-norepinephrine reuptake inhibitor (SNRI) should be avoided due to a bleeding risk. An alternative is mirtazapine.

G. How Would You Decide That He Is No Longer a Suicide Risk?

This is a false hope. Due to the various risk factors, he will always have a higher than population base rate suicide risk. Factors to consider to mitigate risk would be improved cognitive status (serial MoCA scores are needed), improved mood state, denial of current suicidal ideation, acceptance of the need for another attempt at recovery (residential programming is recommended), and any evidence of improved social support/less loneliness.

H. What Are the Ethical Aspects of This Case?

Cases such as this create an ethical tension between patient autonomy, or the patient's ability to make reasoned informed choices, and beneficence, which is the moral obligation to act for the benefit of the individual. In this case, the physician will need to take on a paternalistic stance to ensure the "best interests" of the patient at this time. Currently, it is presumably in the patient's best interests to ensure that

he doesn't impulsively act on his suicidal thoughts by "drinking (himself) to death" or "jump(ing) in front of a truck or bus."

This tension requires serial formal assessment of decisional capacity, which is often temporarily impaired due to intoxication, delirium, or other transient clinical states. It is necessary to explicitly comment on the clinical findings of "impaired decisional capacity" to fully ethically justify limiting a patient's autonomy for self-determination on valid clinical grounds.

When he is not intoxicated or delirious, the patient's mood may still be depressed, but he will probably be less likely to impulsively make a decision to end his life. This patient has survived for many years in this self-destructive pattern of alcohol intake, so it is likely that once sober, he may well also no longer have thoughts of suicide despite his family's distancing themselves from him.

In a culture that highly values individual autonomy, it may be considered an inappropriately paternalistic application of beneficence to force the patient to remain sober once he has decisional capacity. An exception to this would be if the patient has been convicted of drinking under the influence (DUI), in which case he may have temporarily forfeited his right to drink any alcohol. For example, he may be obligated by law to submit to random drug or alcohol screens to ensure his sobriety and, if found to be intoxicated, would be incarcerated or experience some other consequence.

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Topic 5: Late-Life Depressive Disorders, Bipolar Disorders, and Psychotic Disorders

Question 5.1

Aging is accompanied by many changes, including changes in physical health and life circumstances. It is a common misperception that sadness or unhappiness is an essential part of aging. While it is normal to experience good days and bad days, it is *not* normal to feel that everyday is a bad day, no matter what age you are. According to the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (DSM-5), major depressive disorder is defined as feeling depressed most of the day, nearly every day, or experiencing loss of interest or pleasure, along with four or more other associated symptoms, to the extent where daily functioning is affected [1]. The key symptoms are listed in Table 5.1. (For a full review of the diagnostic criteria for major depressive disorder, the reader is referred to the DSM-5 manual [1].) Late-life depression can refer to aging patients who experienced depression initially as a younger adult and then again as an older adult late life. It can also refer to patients who are presenting with depression for the first time later in life (also referred to as late-onset depression).

Table 5.1 Major depressive disorder: highlights of the DSM-5 diagnostic criteria [1]

Five (or more) of the following symptoms present during the same 2-week period, with one of the symptoms being either (1) or (2)	1. Depressed mood 2. Markedly diminished interest or pleasure 3. Significant weight loss/gain or change in appetite 4. Insomnia or hypersomnia 5. Psychomotor agitation or retardation 6. Fatigue or loss of energy 7. Feelings of worthlessness/excessive or inappropriate guilt 8. Poor concentration 9. Recurrent thoughts of death, suicidal ideation (with or without a plan), or a suicide attempt

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_5

What Is the Prevalence of Late-Life Depression?

The lifetime prevalence of major depressive disorder varies in the general population from 1% in Czech Republic to 16.9% in the USA [2]. In Canada, the lifetime prevalence is 9.9% [3]. Most studies suggest that the prevalence of major depressive disorder is lower in older adults compared to younger adults, but numbers range depending on the study, occurring anywhere from 10 to 38% of older adults [3, 4]. The rate of depression is also noted to be higher in older adults in hospitals and living in long-term care settings compared to those living in the community [5].

Question 5.2

How Is Late-Onset Depression Different from Depression with an Earlier Onset?

Depression in late life is generally associated with a more "somatic" presentation compared with depression in the younger cohort [6]. Older patients are more likely to present with complaints of body aches and pains, rather than feelings of sadness. This presents a challenge in the assessment of older adults, as they are also more likely to suffer from medical conditions given their age, and their physical complaints may be the result of other illnesses. Evidence suggests a high comorbidity between depression and systemic medical illness, up to 45% [7]. Older adults are also more likely to have symptoms of sleep disturbance (e.g., shorter sleep duration, more sleep fragmentation), fatigue, psychomotor retardation, and feelings of hopelessness [4, 7]. Anxiety is also another common symptom in older patients with major depressive disorder [7]. Older depressed adults also present more with memory and concentration complaints and diminished executive function similar to that seen in a major neurocognitive disorder [4, 8]. This "depressive pseudodementia" tends to resolve as other depressive symptoms improve. Table 5.2 lists some of the key differences seen in earlier-onset vs. late-onset depression [9].

Table 5.2 Comparison of features in early-onset vs. late-onset depressive disorder. ***Source:*** Cheng T: Late-Life Depression. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; 2018. Used with permission from Springer

Early-onset depressive disorder	Late-onset depressive disorder
More family history of depression	More structural brain changes and cardiovascular risk factors
More depressive thoughts (suicidal thoughts, thoughts of worthlessness)	More anhedonia and apathy
Expression of depressive symptoms (feelings of sadness)	Less expressed depressed mood, more somatic complaints
Moderate to high risk for suicide	High risk for suicide
Mild cognitive changes	More cognitive deficits
Substance misuse is common comorbidity	High systemic medical comorbidity

Question 5.3

You are reviewing a case with a junior psychiatry resident who just started working with you in your outpatient clinic today. Earlier this morning, the resident had assessed a new patient who was referred for assessment for diagnostic clarification. The resident tells you that this patient endorsed feeling depressed and anxious over the past year, with his depression being the predominant issue. The patient also complained of some memory impairment for the past 6 months; he seems to be forgetful of conversations and has a hard time keeping track of all of his medical appointments. The resident feels that the patient not only meets diagnostic criteria for a major depressive disorder but also generalized anxiety disorder and possibly a mild neurocognitive disorder.

The Resident Wants to Know if It Is Possible for the Patient to Have All Three Diagnoses or if All the Symptoms Were Part of the Depression. What Are Some Common Comorbid Psychiatric Disorders?

As noted in Question 5.2, anxiety is a common symptom endorsed by older adults with depression. Anxiety disorders are also common comorbid disorders in older patients with major depressive disorders, with 38–58% of patients with late-life depression also meeting DSM criteria for an anxiety disorder [7]. Major neurocognitive disorders are also often linked to major depression. Studies suggest that depression itself not only increases the risk of major neurocognitive disorders by twofold, with some suggesting that depressive symptoms are an early sign of neurocognitive pathology, but that patients with major neurocognitive disorder also are at risk of developing depression; thus this relationship is reciprocal [10, 11]. It has been reported that about 11–24% of patients with Alzheimer-related major neurocognitive disorder also meet diagnostic criteria for major depressive disorder [12]. Substance-related disorders, anorexia nervosa, bulimia nervosa, and borderline personality disorder are also common comorbidities with depressive disorders [1], though these comorbid diagnoses are more common in younger adults compared to older adults.

Depending on the timeline of the appearance of the various psychiatric symptoms, and whether the patient described in the case scenario met full criteria for major depressive disorder, generalized anxiety disorder, and/or major or mild neurocognitive disorder, the patient could potentially have all three diagnoses. If all of the symptoms occur around the same time (or after the onset of the depressive symptoms), it is likely that the patient's primary diagnosis is major depressive disorder, with anxious distress. The cognitive changes reported would be considered as secondary to the depressive symptoms, given that they started about 6 months after the onset of initial depressive symptoms. This scenario is a common diagnostic dilemma, trying to differentiate whether a patient has a stand-alone major depression diagnosis, with other accompanying psychiatric features, or if the patient truly has multiple "independent" psychiatric diagnoses. In some cases, the management plan would be to treat the depressive disorder first and then reassess for the other

symptoms to see if they improve with resolution of the depressive symptoms. In this patient's case, if the cognitive impairment persists after the depressive and anxiety symptoms resolve, then the diagnosis of an underlying mild neurocognitive disorder would be appropriate.

Question 5.4

Mrs. N, a 69-year-old married female, presents to your office with worsening of her "bad nerves." She tells you that in the past 2 years, ever since she retired from her job as a high school teacher, she has been feeling increasingly "shaky." She is not sure why she feels this way but often wakes up in the morning with this shakiness, where she actually starts to feel discomfort in her stomach. This tends to improve somewhat as the day goes on but never completely goes away. She denies excessive worrying. She does feel "panicky" quite often but denies a full-blown panic attack. Screening for obsessions and compulsions was negative.

Mrs. N admits that she also does not seem to enjoy things as much as she once had. She denies feeling sad, but reports that she has a hard time feeling excited about anything. She really has to "push herself" to get things done around the house. When her husband asks her to do something with him, she would usually decline as she would rather just stay at home. The only thing she really looks forward to is visiting with her grandchildren. This is not really like her as she used to be a very social person and was always active. She has been going to sleep much earlier as she feels that sleep is her only escape. She tells you she has lost about 20 lb in the past 6 months—she has not been eating very much, as food tends to bother her stomach and makes her feel worse. While Mrs. N denies wanting to die or kill herself, she admits there are days when she would wonder "what is the point?"

Mrs. N has no previous history of depressive symptoms or symptoms of mania or hypomania. There is no evidence of psychosis, and cognition is intact (Montreal Cognitive Assessment score of 28/30).

Medically, Mrs. N is relatively healthy. She has hypertension that is well controlled and does have some chronic pain issues in her right knee related to osteoarthritis. Her only medications are ramipril 5 mg daily and over-the-counter glucosamine.

A. What Investigations Would You Order?

Acute management requires ruling out any systemic medical conditions that may be causing Mrs. N's symptoms, especially in light of her complaints about gastrointestinal discomfort, significant weight loss, and the fact that she has no prior psychiatric history. Baseline laboratory studies should include complete blood count, electrolytes, creatinine, estimated glomerular filtration rate, and tests of renal and thyroid function. As she likely has poor nutritional intake, serum B_{12} level, albumin, calcium, magnesium, and phosphate should also be checked. If there is concern about a possible gastrointestinal bleed (i.e., if she is anemic), fecal occult blood and further investigations may be warranted. If pharmacological intervention is to be

considered, it may be worthwhile to do a baseline electrocardiogram as many psychotropic medications can prolong QT interval.

B. What Is Your Provisional Diagnosis?

Even though Mrs. N presented with complaints of her "bad nerves," her diagnosis is likely that of a major depressive disorder, with anxious distress. Most older adults with depressive disorder present with anxiety or somatic complaints rather than primary complaints of depressed mood and anhedonia per se. And while she does not endorse feeling down or sad, she has significant apathy and many of the other neurovegetative symptoms of depression (i.e., loss of interest and motivation, hypersomnia, weight loss, passive suicidality), supporting a primary diagnosis of major depressive disorder.

Question 5.5

Suicide is most commonly associated with depressive disorders. In the USA, there is an average of 14.9 suicides out of every 100,000 people over age 65 annually [13]. In Canada, at least one senior die by suicide every day [14]. Hanging and firearm use are the most common methods of suicide in older men and self-poisoning and hanging in older women [14]. An assessment of depressive symptoms would not be complete without an evaluation of the person's risk for suicide and the presence of suicidal ideation, intent, or plans.

What Are Some Suicide Risk Factors?

Suicide risk factors can be divided into non-modifiable risk factors and modifiable risk factors. A past history of suicide attempt is the strongest risk factor for a future attempt [15]. In treatment of depressive symptoms, one of the goals should be trying to minimize any modifiable risk factors in order to decrease risk. See Table 5.3 for some of the other suicide risk factors.

Table 5.3 Suicide risk factors during a major depressive episode [15]

Non-modifiable risk factors	Modifiable risk factors
• Age > 65 years • Male sex • Previous suicide attempt of self-harm • Family history of suicide attempt • History of legal problems	• Presence of suicidal or homicidal ideation, intent, or plans • Access to means for suicide (e.g., guns, knives) • Stressful life events (e.g., loss of loved one, loss of independence) • Presence of psychotic symptoms • Presence of alcohol or other substance use • Comorbid personality disorders • Chronic systemic medical illness • Presence of functional decline

Question 5.6

You are seeing a patient for follow-up in your office today with your third-year psychiatry resident. Mr. B is someone diagnosed with a major depressive disorder, recurrent, with somatic complaints when you saw him 1 year ago for consultation. You have previously tried him on escitalopram, sertraline, duloxetine, and mirtazapine, all of which he has not been able to tolerate as he would complain of either nausea or feeling worse. You had started him on venlafaxine XR at the last visit, and his is up to a dose of 112.5 mg daily. He comes back today to tell you that he has noticed a slight improvement in his mood as he is not feeling as low or depressed. However, the burning sensation he has on top of his head seems to be the same (he has discussed this burning sensation at length at the last appointment). He complains that it continues to feel like it is on fire and that the only thing that seems to help is some clonazepam (he has a previous prescription from his primary care physician for 0.5 mg BID PRN). He has been taking clonazepam at least 0.5 mg once a day.

Your Resident Asks You Whether Antipsychotics Are Indicated in Mr. B for the Somatic Complaints

With the concern of polypharmacy in the older population, the goal of treatment is to manage the depressive disorder with a single agent if possible. However, in cases of treatment-resistant or treatment-refractory depressive disorder (a term used to describe cases that have failed two or more trials of antidepressants), adjunctive strategies would be a reasonable treatment consideration. There are some studies to support the use of adjunctive second- and third-generation antipsychotics (such as quetiapine and aripiprazole) in the treatment of major depressive disorder [16]. However, in using antipsychotics, one would need to be cautious because of the side effect profiles of these medications, especially in older adults.

In someone with somatic features in the context of a depressive disorder, antidepressants are still first-line [15]. Somatic symptoms are usually not psychotic features; thus, antipsychotics are not commonly used as initial treatment. However, in Mr. B's case, as he has had a number of failed medication trials, a case could be made for the consideration of adding an antipsychotic medication as adjunctive strategy. In cases where the somatic complaint is pain, there is literature supporting the use of duloxetine and other serotonin noradrenergic reuptake inhibitors [15]. Mr. B has tried duloxetine but was not able to tolerate it; he is currently on venlafaxine, which seems to have helped his mood somewhat. It would be reasonable at this time to continue to optimize his dose of venlafaxine XR (e.g., increase from 112.5 to 150 mg/day) before considering augmentation with an antipsychotic medication.

Psychoeducation should also be provided in terms of Mr. B's reliance on benzodiazepines. He should be made aware that the use of benzodiazepines could increase the risk of falls as well as cognitive impairment. Attempts should be made in the

near future to try and taper him off the clonazepam, especially as his mood and somatic symptoms improve with treatment.

Question 5.7

You are seeing Ms. B, a patient that you have been following for the past 4 months for her persistent depressive disorder. The patient tells you during her appointment that her depressive symptoms have been worsening in the past 3 weeks. She feels so low on some days, that getting out of bed to get dressed for the day is a monumental task. She cannot even watch television anymore as she has trouble following a 1/2-h program as she gets distracted by her own negative thinking quite easily. On her drive to the appointment today, she almost drove her car through the garage door when she was backing out of her driveway as she put her car in forward gear rather than reverse gear.

Under What Circumstance Would You Report Someone with Depressive Disorder to the Local Government Agencies Because of Concerns of Driving Risk?

While there are usually defined reportable conditions for risk to drive in various countries, generally speaking, the rules for reporting psychiatric conditions are usually more subjective. For example, when a patient has a seizure episode, the responsible physician is mandated to report the event to the ministry of transportation, in which case, the patient's driver's license will likely be suspended for a period of time. However, in the case of a major depressive disorder, it is not as clear-cut. In people with major depressive disorder, driving risk may or may not be a concern, depending on the endorsed symptoms. For example, in the Canadian Medical Association Driver's Guide, several circumstances are highlighted as potential concerns for risk to driving in patients with depression, including [17]:

- Patients with cognitive impairment secondary to the depressive disorder (e.g., with short-term memory, concentration, or mental processing speed affected)
- Patients who receive electroconvulsive therapy, as there may be concerns with anesthesia post-procedure and memory impairment
- Patients with psychotic symptoms (which may occur in context of a depressive episode)
- Patients with a suicidal plan involving crashing a vehicle
- Patients with an intent to use a vehicle to harm others
- Patients taking medications that may potentially cause sedation

For Ms. B, not only is her mood worsening, but she is also endorsing issues with her concentration, with a near accident today when she came to her appointment. Ms. B should be advised to not drive until these symptoms improve. If she is not compliant with the medical advice to not drive, this should then be reported to the authorities.

Question 5.8

It is normal to experience "ups and downs" in one's life. However, when the ups and downs are to the extent where emotions are extreme and cause dysfunction, this is no longer part of the "normal" experience. Late-life bipolar disorder generally refers to the onset of disorder in patients aged 60 and over. In bipolar disorder, the patient must meet criteria for either a manic episode or a hypomanic episode, as well as a major depressive episode. The DSM-5 divides bipolar disorder into bipolar I disorder, bipolar II disorder, cyclothymic disorder, substance/medication-induced bipolar and related disorder, bipolar and related disorder due to another medical condition, other specified bipolar and related disorder, and unspecified bipolar and related disorder [1].

How Is Mania Different from Hypomania?

The main difference between mania and hypomania is the duration of episode and the severity of the episode. By definition, a hypomanic episode lasts <7 days; the symptoms experienced are less extreme, not severe enough to cause social or occupational functional impairments. The presence of psychotic symptoms automatically denotes a manic episode. As well, if psychiatric admission is warranted, the diagnosis will change from a hypomanic episode to a manic episode. See Table 5.4 for a summary of the diagnostic criteria for a hypomanic episode and a manic

Table 5.4 Hypomanic episode vs. manic episode: highlights of the DSM-5 diagnostic criteria [1]

Hypomanic episode	Manic episode
• Distinct period of persistently elevated, expansive, or irritable mood lasting at least 4 days • Three or more of the following symptoms (4 if mood is only irritable): • Inflated self-esteem or grandiosity • Decreased need for sleep • Pressured speech or more talkative • Flight of ideas/racing thoughts • Distractible • Increase in goal-directed activity • Lack of regard for consequences	• Distinct period of persistently elevated, expansive, or irritable mood lasting at least 1 week • Three or more of the following symptoms (4 if mood is only irritable): • Inflated self-esteem or grandiosity • Decreased need for sleep • Pressured speech or more talkative • Flight of ideas/racing thoughts • Distractible • Increase in goal-directed activity • Lack of regard for consequences

Table 5.5 Potential causes of secondary mania. ***Source:*** Cheng T, Saperson K: Late-Life Bipolar Disorders. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; 2018. Used with permission from Springer

Category	Examples
Systemic medical conditions	Anemia, hyperthyroidism, vitamin B_{12} deficiency, niacin deficiency
Medications/ substances	Antidepressants, corticosteroids, captopril, stimulants, amphetamines, cocaine, opiates
Infectious diseases	Neurosyphilis, encephalitis, human immunodeficiency virus, or acquired immunodeficiency syndrome
Neurological disorders	Major neurocognitive disorders, multiple sclerosis, epilepsy, Parkinson disease, traumatic brain injury, brain tumors, normal pressure hydrocephalus, Wilson disease

episode. (For a full review of the diagnostic criteria for manic and hypomanic episode, the reader is referred to the DSM-5 [1].)

Question 5.9

What Are Some Causes of Secondary Mania?

Secondary mania is considered as mania that is due to another underlying condition. For example, exposure to certain medications such as corticosteroids and stimulants may induce a manic episode. If a person's manic symptoms stem from an underlying etiology, it would be diagnosed as a substance/medication-induced bipolar and related disorder or a bipolar and related disorder due to another medical condition, depending on the cause. Some possible conditions leading to secondary mania are listed in Table 5.5.

Question 5.10

You are seeing Mr. K in the acute inpatient psychiatric unit. He was admitted to the hospital last night as he was brought to the hospital by his family as he was exhibiting paranoid delusions in the past week. Mr. K was quick to tell you this morning that he did not sleep a wink last night (his family actually tells you that Mr. K has not been sleeping very much at all for the past 2 weeks). He was concerned that his neighbor, who works as volunteer in the hospital, may come and "do things" to him last night. He reported that he has never gotten along well with this neighbor, but this neighbor has started a campaign to get him to move out of the area in the past 2 weeks. Mr. K believes the neighbor has been placing garbage on Mr. K's lawn in the middle of the night. He also accused this

neighbor for paying kids in the neighborhood to come and knock on his door incessantly at nights—when Mr. K goes to the door, there would be no one there. Mr. K has not been able to sleep at night as a result. He has been staying by his window at nights, waiting to confront his neighbor if he sees them putting garbage on his lawn.

How Do You Differentiate Between Psychotic Symptoms in Context of a Manic Episode Vs. a Primary Psychotic Disorder?

The psychotic symptoms themselves are usually specific enough to be used as a distinguishing factor between someone who is psychotic due to a manic episode vs. a primary psychotic disorder. However, in a manic episode, the psychosis tends to be that of grandiose delusions and/or may focus on a religious theme. In a primary psychotic disorder, thought disorder may be more of a prominent symptom. The major difference between the two would be whether there is the presence of mood symptoms. If mood symptoms are present, they are prominent in a manic episode and would predate the psychotic symptoms. However, in some cases, the clinician may not be able to ascertain a history of mood symptoms predating the psychotic symptoms (either due to the patient being a poor historian or the lack of collateral information), and a definite diagnosis may be difficult to make.

In Mr. K's case, if he has other accompanying symptoms suggestive of a manic episode such as increased talkativeness, distractibility, racing thoughts, or grandiosity, his diagnosis would be more consistent with a bipolar I disorder, manic episode with psychotic features. His psychotic symptoms are substantial enough that an antipsychotic medication needs to be used as part of the management plan.

Question 5.11

Bipolar disorder is an episodic chronic illness that has no cure. Treatment of the disorder and symptoms can decrease the associated morbidity and mortality [18]. Interventions aimed at psychoeducation therapy, cognitive behavior therapy, interpersonal therapy, and social rhythm therapy have demonstrated benefits in decreasing relapse rates and increasing functioning, as well as improving medication adherence [19]. There is also evidence supporting the use of electroconvulsive therapy (ECT) in bipolar depression [20]. However, the mainstay of treatment for bipolar disorder is pharmacological interventions. There are no medication treatment guidelines for bipolar disorder that are specifically aimed at older adults; the results of current guidelines for the general population are often extrapolated to apply to the older population.

Table 5.6 Recommendations for pharmacological treatment of acute mania. ***Source:*** Cheng T, Saperson K: Late-Life Bipolar Disorders. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; 2018. Used with permission from Springer

Treatment	CANMAT	APA
First-line options	Lithium, divalproex, olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone, asenapine, paliperidone ER, lithium or divalproex + risperidone, lithium or divalproex + quetiapine, lithium or divalproex + olanzapine, lithium or divalproex + aripiprazole, lithium or divalproex + asenapine	Lithium, divalproex, olanzapine, risperidone, lithium + antipsychotic, divalproex + antipsychotic
Alternative options	Carbamazepine, haloperidol, lithium + divalproex, chlorpromazine, clozapine, oxcarbazepine, tamoxifen, lithium or divalproex + haloperidol, lithium + carbamazepine, adjunctive tamoxifen	Carbamazepine or oxcarbazepine in lieu of lithium or divalproex, ziprasidone or quetiapine in lieu of another antipsychotic, clozapine

APA American Psychiatric Association, *CANMAT* Canadian Network for Mood and Anxiety Treatments, *ER* extended release

What Are the Pharmacological Treatment Recommendations for Acute Mania?

Lithium and divalproex are two medications that have been well established in the treatment of acute manic episodes [18, 19]. The American Psychiatric Association (APA) guidelines suggest monotherapy with lithium, divalproex, olanzapine, or risperidone in a manic patient who is less ill. In a severely ill patient, combination therapy of lithium plus an antipsychotic or divalproex plus an antipsychotic is recommended. The Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines recommend monotherapy with lithium, divalproex, olanzapine, quetiapine, risperidone, aripiprazole, ziprasidone, asenapine, or paliperidone ER. Combination therapy with either lithium or divalproex plus an antipsychotic (quetiapine, risperidone, olanzapine, aripiprazole, or asenapine) is also considered first-line therapy [21]. Table 5.6 shows a summary of the APA and CANMAT recommendations for treatment of acute mania.

Question 5.12

What Is the Evidence of Using Antidepressants in Bipolar Depression?

The role of antidepressants in patients with bipolar disorder is very controversial. However, while monotherapy with antidepressants is not recommended, antidepressants remain as a treatment for bipolar depression in both the Canadian and US guidelines when used in combination with lithium or divalproex [18, 19] (see Table 5.7). If antidepressants are being considered, bupropion or selective serotonin reuptake inhibitors are the preferred options [18].

Table 5.7 Recommendations for pharmacological treatment of acute bipolar I depression. ***Source:*** Cheng T, Saperson K: Late-Life Bipolar Disorders. In: Hategan et al. (eds). Geriatric Psychiatry: A Case-Based Textbook, Springer; 2018. Used with permission from Springer

Treatment	CANMAT	APA
First-line options	Lithium, lamotrigine, quetiapine, lithium or divalproex + SSRI[a], olanzapine + SSRI[a], lithium + divalproex, lithium or divalproex + bupropion	Lithium, lamotrigine, lithium + antidepressant
Alternative options	Divalproex, lurasidone, quetiapine + SSRI[a], adjunctive modafinil, lithium or divalproex + lamotrigine, lithium or divalproex + lurasidone, carbamazepine, olanzapine, lithium + carbamazepine, lithium + pramipexole, lithium or divalproex + venlafaxine, lithium + MAOI, lithium or divalproex or atypical antipsychotic + TCA, lithium or divalproex or carbamazepine + SSRI[a] + lamotrigine, quetiapine + lamotrigine	Adjunctive: Lamotrigine, bupropion, paroxetine, another SSRI, venlafaxine, or monoamine oxidase inhibitor

SSRI selective serotonin reuptake inhibitor, *MAOI* monoamine oxidase inhibitor, *TCA* tricyclic antidepressant
[a]Except paroxetine

In the past, patients who experienced a manic episode where they were treated on antidepressants were thought to have an antidepressant-induced manic episode. In recent years, there is growing evidence to suggest that, in fact, these patients have an underlying bipolar disorder [22].

Question 5.13

Mrs. W, a 67-year-old female, was referred to you for an assessment of her psychotropic medications. Mrs. W was diagnosed with bipolar I disorder since her early 20s. For most of her 20s, she would experience either a depressive episode or a manic episode about two times a year. She has had three previous psychiatric admissions. However, for the past 35 years, her mood has been quite stable on lithium carbonate and olanzapine. Mrs. W was wondering if she can come off her psychiatric medications as she has been well for so long now. In the past year, she tells you that her benign essential tremor in her hands has worsened, and she wonders if the lithium could be making that worse. As well, she has put on over 40 lb since being on olanzapine and was recently told by her primary care physician that she has "borderline diabetes." She had requested the referral herself so she can discuss with a psychiatrist about stopping her psychiatric medications.

In Someone Who Has Not Had a Mood Episode for over 30 Years, What Is the Evidence to Continuing Treatment? What Would You Advise Mrs. W?

Medication adherence remains an issue for many patients, especially when considering the possible side effects of pharmacotherapy, patient attitudes, and the stigma of psychiatric illness. It is often difficult for a patient to remain on medications if

they have not relapsed for some time. It is not unusual for 4 years to elapse between the first and second episodes [18], which lulls patients to think that medications are no longer necessary. Maintenance treatment is strongly recommended to prevent relapse, reduce subthreshold symptoms, and reduce suicide risk [18].

In a patient who is considering discontinuing maintenance treatment, it would be important to have a discussion about the risks. The highest risk for relapse is in the 6 months after an acute episode [18]. The more episodes the patient has, the worse the outcome.

For Mrs. W, she was quite unwell in her 20s from her bipolar illness but has been stable on the lithium and olanzapine combination for many years now. However, she now has significant side effects from both medications—worsening hand tremor, weight gain, and possibly onset of diabetes mellitus. Depending on the dosage of her medications, one possible option instead of discontinuing both her psychotropics would be to consider simply reducing the dosage of the medications. As Mrs. W has aged physically over the years, she may no longer require the same dose of lithium (the target serum lithium levels in older adults are generally lower than that of the general population). Lowering lithium may also be enough to improve her tremor. In considering her olanzapine, a trial of lowering the medication dose would not be unreasonable. The pros and cons of discontinuing her medications should be discussed with Mrs. W.

Question 5.14

What Is the Impact of Chronic Bipolar Disorder on Cognition?

In bipolar disorder, cognitive function can be impaired during a depressive or manic episode, mimicking that of a neurocognitive disorder in an older adult. Memory deficits, along with disorientation and confusion, can be observed. These symptoms, referred to as "pseudodementia" can be thought of as a harbinger of neurocognitive disorders. Chronic initial psychiatric illness such as bipolar disorder also leads to a higher risk of developing major or mild neurocognitive disorders. It has been suggested that residual mood symptoms, structural brain abnormalities, long-term side effects of medications, adverse psychosocial conditions, and comorbid systemic medical conditions may all contribute to the cognitive deficits in older adults with bipolar disorder [23]. There is evidence suggesting that the decline in cognition of older adults with bipolar disorder may be due to long-standing neurodegenerative processes compounded by normal aging rather than accelerated cognitive loss in old age [24]. This implies that older adults with bipolar disorder are at risk of cognitive decline by virtue of having less cognitive reserve. In other words, patients with chronic bipolar disorder are at greater risk of having cognitive decline, whether it is due to less cognitive reserve, structural brain abnormalities, medication side effects, comorbid medical conditions, or the impact of having a chronic recurrent mood episodes.

Question 5.15

Mr. Y is a 73-year-old male who presents to the emergency department with his wife tonight while you are on call. When you see Mr. Y, he is very agitated, pacing around the interview room. He tells you right away that he needs to leave and go home so he can make sure his wife is safe. Mr. Y states that over the past month, his new neighbor, who moved in about 3 months ago, has been using a special machine to shoot laser beams at him. The patient tells you he can hear a humming and clicking sound whenever the machine is turned on, and he will start to feel tingly and warm. He is not sure what the laser beams' effects are, but knows they are likely causing him some type of harm. Mr. Y believes that this neighbor is in love with his wife and wants him "out of the way." He is concerned that if he stayed at the hospital any longer, this neighbor may steal his wife away from him.

Mr. Y denied feeling down or sad lately but admits he is angry with his neighbor. He denies any wish to harm this neighbor, and he just wishes all of this would stop. In fact, he had gone next door earlier tonight to confront this neighbor, who slammed the door on him when Mr. Y started accusing him of shooting the laser beams. He was yelling and screaming in his neighbor's yard when his wife came home from the grocery store and that was when she told him they needed to come to the hospital.

Mr. Y tells you he has never needed to see a psychiatrist before and that he does not need one now as he is not "a nut job." His medical history includes hypertension, hyperlipidemia, Crohn's disease, and a previous appendectomy. He was not able to tell you the names of his medications (and his pharmacy is currently closed) but tells you that his wife is the one who manages all his medications so you should talk to her.

When you speak with Mrs. Y, she tells you that her husband has been getting increasingly suspicious over the past 2–3 months. Initially, he would make comments about their new neighbor, saying how a single man should not be living in a large single family home. Over the past few weeks, Mr. Y has mentioned about this laser beam machine more and more. She also tells you that he gets very suspicious these days whenever she goes out on her own, asking her where she has been and who she was with. When she came home this evening and found him screaming on their neighbor's front lawn, she tried to get him to go back into their home. He then accused her of having an affair with the neighbor and stated that she is "in this with him." This was when she decided that "enough was enough" and brought him to the hospital.

She tells you that other than for this suspiciousness, there have been no changes in his behavior. She has noticed him to be a bit more forgetful in the last month, sometimes confusing dates and appointments. For the most part, she has not noticed any other changes in what he does during the day. He has not been sleeping as well lately, but he had told her it was because of back pain. She was not able to name his medications and did not bring his medication list as they left their home in haste but tells you he is on two blood pressure pills, a cholesterol pill, and something for his Crohn's disease. About a few months ago, Mr. Y had a flare-up of his Crohn's disease, and he was put on a "steroid" pill. He is scheduled to follow up with his gastroenterologist next week to reassess.

What Are Some Common Disorders with Psychosis as a Significant Symptom? What Is Your Differential Diagnosis for Mr. Y?

Psychosis can be a common symptom in older adults with bipolar disorder, occurring in about 65% of patients [25]. Psychosis can also be a presenting feature in many other psychiatric disorders, including major depressive disorder with psychotic features and primary psychotic disorders such as delusional disorder, schizophrenia spectrum disorders, substance/medication-induced psychotic disorders, psychotic disorder due to another medical condition, major/mild neurocognitive disorders, and delirium.

As Mr. Y is presenting with first-onset psychosis, possible underlying systemic medical causes would need to be ruled out. His differential diagnosis should include:

- *Delusional disorder*—Mr. Y's predominant psychosis is based on the delusion that his neighbor is trying to harm him, as the neighbor is in love with the patient's wife. While he does endorse auditory hallucinations, this is not prominent and is related to his delusion. However, other medical conditions and the effect of substances or medications would need to be ruled out before making this diagnosis.
- *Major neurocognitive disorder with psychosis*—While this is part of the differential, it would be lower on the list as the forgetfulness is identified as being recent and may be caused by his psychosis rather than the cause of his psychosis.
- *Late-onset schizophreniform disorder*—Mr. Y's symptoms has been present for the past 2–3 months, thus, not long enough to meet criteria for schizophrenia but is within the time frame for schizophreniform disorder. He also meets criterion A as he has both delusions and auditory hallucinations. However, Mr. Y seems to lack the marked impaired function that one would expect to see (although this is not a criterion for diagnosis).
- *Bipolar disorder*—It is possible that Mr. Y may be in a manic episode (he has been sleeping less); however, there is not sufficient history in regard to impulsivity, elated/expansive mood, or changes in energy level to confirm this as the diagnosis.
- *Medication-induced psychotic disorder*—Mr. Y has been on a "steroid pill" for the past few months, which could potentially be the cause of his psychosis.
- Psychotic disorder due to another medical condition—It is possible that Mr. Y has an underlying medical condition (e.g., brain tumor) that could be leading to his psychosis.
- *Delirium*—It is possible that he may have an underlying urinary tract infection, pain (from his back pain), or hyponatremia (depending on which blood pressure medication he is on, he may be at risk for this). The onset of his psychosis is fairly rapid, but other than the wife noting some "forgetfulness," there is no history suggesting issues with fluctuating attention or awareness of environment.

The first steps in confirming Mr. Y's diagnosis would be to rule out the possibility of another medical condition leading to his symptoms and to ensure he does not have delirium. The "steroid pill" should be discontinued (depending on the dose he is on, a quick taper may be needed). If his psychotic symptoms persist, then delusional disorder is likely the provisional diagnosis.

Question 5.16

Delusional disorder is defined as the presence of at least one delusion for at least 1 month's duration in the DSM-5. The delusion is not accompanied by bizarre behavior or functional impairment.

What Is the Prevalence of Delusional Disorder?

The overall prevalence of delusion disorders is low—lifetime prevalence is estimated as 0.18% [26]. In an older adult presenting with non-bizarre delusions (such as paranoia, somatic delusions, grandiosity), and otherwise intact functioning, the clinician should be suspicious of a delusional disorder. Common themes of delusions include those of persecution and conspiracy. Hallucinations are usually not prominent but can be present if related to the delusional thought content.

Question 5.17

What Are Some Risk Factors for Late-Life Psychosis?

Risk factors for late-life psychosis include [27]:

- Female sex
- Social isolation
- Hearing/visual impairment
- Genetic predisposition
- History of previous psychosis
- Comorbid medical illness/deteriorating physical health
- Medications
- Substance misuse/use disorders
- Life stressors
- Premorbid personality structure

Question 5.18

Mrs. C is an 82-year-old widowed female who lives alone in her apartment. She presents today to the clinic with her nephew for a consultation for her delusional thinking. Mrs. C tells you that she has been quite concerned that her neighbors are drug dealers. She reports that she actually moved 6 months ago to get away from drug users. Mrs. C states that she moved 6 months ago as her neighbor that lived above her used marijuana so heavily that she constantly smelled it in her apartment. She tried getting the superintendent involved but told you that the superintendent did not want to do anything as he himself was a marijuana user. She finally could not stand it and ended up moving to another apartment building. Unfortunately,

shortly after moving to the new building, a couple moved into the unit next door, and they were also heavy marijuana smokers. Mrs. C reports that this past summer has been difficult as she was not able to use her balcony, as the marijuana smell would drift over to her unit. She also tells you that she has been getting frequent headaches as the smell would come through the air vents in her apartment. She believes that this couple is actually selling drugs from their apartment as they often have visitors come to their door at all times during the day. She has been considering contacting the police but is concerned that this couple may retaliate if they found out she was the one who reported them to the authorities.

Mrs. C denied any significant mood or anxiety symptoms. No other psychotic symptoms were elicited. Her medical history is significant for diabetes mellitus and hypertension. She is an ex-smoker and a nondrinker. She has never seen a psychiatrist before and has no psychiatric history.

Her nephew was able to tell you that his aunt started complaining about her neighbors a year ago. She had complained of getting headaches from the smell of the cannabis, and that was the reason she ended up moving away. When he had visited her in the past, he was never able to smell anything, though she would tell him that the neighbors usually smoked late at night. He never thought she might be "crazy" until she started complaining about her new neighbors in the new building too. He tells you that the couple his aunt is talking about is actually quite a nice couple. He actually has asked around the other people on the floor, and no one has noticed any marijuana smells.

The nephew also reports that he has noticed a decline in Mrs. C's memory and function over the past 2–3 years. Initially, he had put these changes to Mrs. C's age. But in the past 1½ year, her short-term memory is extremely impaired. He also noticed that she is no longer as meticulous about her appearance as she used to be and that there are times where he would notice her to wear stained and dirty clothes. He also took over managing her finances about 1 year ago as she was forgetting to pay her bills and kept overdrawing on her checking account.

A. What Is Your Provisional Diagnosis?

From the collateral information, there seems to be a convincing history of cognitive decline over the years that predate the onset of the delusions. As Mrs. C has no appreciable mood symptoms, her most likely diagnosis is major neurocognitive disorder due to Alzheimer disease, with behavioral disturbance.

B. What Would Be Your Pharmacological Treatment?

Once you have ruled out other potential systemic medical conditions or medications/substances as the cause of her presentation, and confirmed your diagnosis of major neurocognitive disorder, you would likely consider starting her on a cholinesterase inhibitor. However, evidence suggests that the effect of cholinesterase inhibitors on behavioral symptoms is modest at best [28, 29]. As Mrs. C is quite distressed

by her delusions, it would be reasonable to trial her on a low-dose antipsychotic medication despite its risks to see if her delusions would resolve. Risperidone, olanzapine, and aripiprazole are all reasonable options.

Question 5.19

In Someone Who Cannot Tolerate Antipsychotics, What Are Other Treatment Options for Schizophrenia?

Non-pharmacologic therapies are often used to reduce symptom burden and to enhance adherence to pharmacological interventions. Cognitive behavioral therapy (CBT), social skills training, family therapy, and cognitive remediation are used as treatment interventions [26, 30]. CBT is the most widely used, with studies supporting its use for the reduction of positive and negative symptoms [26, 31]. Other interventions such as supported employment, healthy lifestyle measures including exercise, illness self-management training, assertive community training, and family psychoeducation may also play a role in treatment plan [32]. However, there is limited data on applying these interventions in the older adult population.

Question 5.20

Mr. J is a 77-year-old widowed male you are following on the inpatient unit. He has a history of late-onset schizophrenia (diagnosed at age 68). Over the past 9 years, he has been admitted to the hospital five times due to his psychotic symptoms and disorganized behavior. He has also failed numerous trials of antipsychotic medications. Mr. J was brought to the hospital by his family because they were concerned that he is decompensating. He has not been eating very much over the past weeks and appeared to be depressed. He stays at home all day and will complain to any family visitors that the army is coming after him as he "knows too much," believing in various conspiracies. His family asks you if "shock therapy" would help Mr. J as antipsychotic medications do not seem to have any effect.

What Is the Evidence for ECT in Schizophrenia?

ECT is generally used in treatment-refractory cases. Benefit is noted in patients with catatonic schizophrenia and schizophrenia with a significant depressive component [26]. However, there are a very limited number of studies specifically with older adults. Again, data from the general adult population has been extrapolated to apply to the older population. Maintenance treatment with ECT and antipsychotic has been shown to be associated with lower rates of relapse [26, 33, 34]. Mr. J may benefit from a trial of ECT given his five failed trials of antipsychotic medications.

He also seems to have significant depressive symptoms. Thus he would be a good candidate for ECT consideration.

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Topic 6: Late-Life Anxiety Disorders, Obsessive-Compulsive and Related Disorders, and Trauma- and Stressor-Related Disorders

Question 6.1

A 76-year-old female, who lives alone in a one-story house, complains to her psychiatrist about sleep difficulties and low energy. Six months ago, she sustained a right hip fracture due to a fall caused by tripping over the sidewalk. She underwent rehabilitation after hip surgery and is now able to walk but has developed multiple fears associated with falling. She is afraid she may lose her balance and fall, and that she may "faint" (although she does not feel dizzy) when alone, and consequently she no longer goes out by herself. She now asks that her children accompany her on the rare occasion when she goes out shopping. She feels easily irritable, tense, and "on edge" when her children and grandchildren come to visit her. She describes herself as always being "a nervous person," which has worsened since the death of her spouse 2 years ago. She does not use illicit substances or alcohol. She takes acetaminophen as needed for pain related to her osteoarthritis but is otherwise healthy. She worries about the future and her health and believes that is related to her difficulty to initiate sleep.

A. Which Anxiety Disorders Are the Most Common in the Old Age?

Several of the DSM-5 anxiety disorders (panic disorder, social phobia, and obsessive-compulsive disorder) are not common in late life and rarely begin in old age. However, generalized anxiety disorder, specific phobias (including fear of falling), and agoraphobia are the most common anxiety disorders in older adults [1].

B. What Is the Diagnosis in This Case Scenario?

According to the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5), Table 6.1 highlights the key elements of the diagnostic criteria for the most common anxiety disorders in older adults [2]. (For a full review of the DSM-5

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_6

Table 6.1 Common anxiety disorders in older adults: highlights of the DSM-5 diagnostic criteria [2]

Generalized anxiety disorder	Excessive worry; and ≥3: (1) restlessness; (2) fatigue; (3) concentration difficulty; (4) irritability; (5) muscle tension; (6) insomnia; distress/impairment in important areas of functioning; duration >6 months
Specific phobia	Marked fear about specific object/situation; phobic object/situation is actively avoided or endured with intense fear which is out of proportion to the actual danger; distress/impairment in important areas of functioning; duration >6 months
Agoraphobia	Marked fear about using/being in ≥2 situations: (1) public transportation; (2) open spaces; (3) enclosed places; (4) in line or in a crowd; (5) outside of home alone; these situations are feared and actively avoided to prevent embarrassing symptoms (e.g., fear of falling, fear of incontinence), require presence of a companion, or are endured with intense fear which is out of proportion to the actual danger; duration >6 months

criteria for anxiety disorders, the reader is referred to the DSM-5 manual [2].) This patient meets the diagnostic criteria for generalized anxiety disorder, specific phobia, and agoraphobia. Generalized anxiety disorder is characterized by 6 months or more of excessive worry about a number of daily life domains (e.g., health, relationships, finances), difficulty in controlling the worry, and associated physical symptoms (i.e., insomnia, muscle tension, restlessness, fatigue) that cause distress and impairment in important areas of functioning [2]. Specific phobia is characterized by persistent irrational fear of an object or situation and the desire to avoid the phobic object or situation [2]. Fear of falling is specific to older adults; it occurs in 60% of those who have previously fallen and is associated with significant distress and functional impairment [3]. As in this case, fear of falling and its impact on the patient's daily function can be similar in presentation to agoraphobia in the more severe clinical manifestation. Agoraphobia can also be a common phobia in old age [4]. Late-life agoraphobia may be precipitated by psychosocial stressors and interferes with quality of life. As in this case, agoraphobia can follow a traumatic event such as a fall. These patients can become housebound and have a poor post-fall rehabilitation [5].

Question 6.2

Anxiety and depressive disorders are among the most common psychiatric disorders, regardless of age. Anxiety disorder is also highly comorbid with other psychiatric disorders, especially depressive disorder, and proper screening for identifying and managing these disorders is necessary.

What Are Some Common Rating Scales for Anxiety Disorder and Its Comorbidity?

Anxiety disorders, along with depressive disorders, are among the most common psychiatric presentations in primary care and clinical specialty populations across the life span [6]. Identifying and managing both disorders are necessary. Scales such as Generalized Anxiety Disorder (GAD)-7 and GAD-2 (the abbreviated 2-item

version) for anxiety are brief validated screening and rating tools, with good sensitivity and specificity in detecting generalized anxiety, panic, and social anxiety disorder [6]. The Patient Health Questionnaire (PHQ)-9 is a brief validated screening tool for depressive disorders. The typical syndromal cutoff score is 10 on the parent scales (GAD-7 and PHQ-9) and 3 on the abbreviated versions (GAD-2 and PHQ-2). The PHQ-9 and its abbreviated 8-item (PHQ-8) and 2-item (PHQ-2) versions have good sensitivity and specificity for detecting depressive disorders [6]. Although posttraumatic stress disorder (PTSD) is no longer formally considered an anxiety disorder, but is classified in the DSM-5 category of trauma- and stressor-related disorders, a few common screening tools for PTSD are the following [7, 8]:

- Short form of the PTSD Checklist-Civilian version: it is a 6-item screen used in primary care settings; it has a cutoff score of 14; those screening positive should be assessed with a structured interview for PTSD.
- Short screening scale for PTSD: it is a 7-item screen that was designed for all trauma survivors; it has a cutoff score of 4; those screening positive should be assessed with a structured interview for PTSD.
- SPAN (i.e., Startle, Physically upset by reminders, Anger, and Numbness): it is a 4-item self-report screen; it has a cutoff score of 5; those screening positive should be assessed with a structured interview for PTSD.
- Short Post-Traumatic Stress Disorder Rating Interview (SPRINT): it has a cutoff score of 14; those screening positive should be assessed with a structured interview for PTSD.
- Trauma Screening Questionnaire (TSQ): it is a 10-item symptom screen for survivors of all types of traumatic stress; it has a cutoff score of 6; those screening positive should be assessed with a structured interview for PTSD.
- Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): it is a short screening tool with a cutoff score of 3 for maximized sensitivity, a score of 4 for maximized efficiency, and a score of 5 for maximized specificity.

Question 6.3

Provide Examples of Maladaptive Avoidance Behaviors in Older Adults

Figure 6.1 provides some common examples of age-specific fears and maladaptive avoidance behaviors in the old age [9, 10].

Question 6.4

What Are the Clinical Manifestations of Fear and Anxiety?

In many animal species, fear has survived as an important evolutionary survival mechanism [11]. In humans, fear and anxiety represent normal responses to a real or perceived danger. Anxiety occurs in *anticipation* of threat, whereas fear occurs as a *direct response*

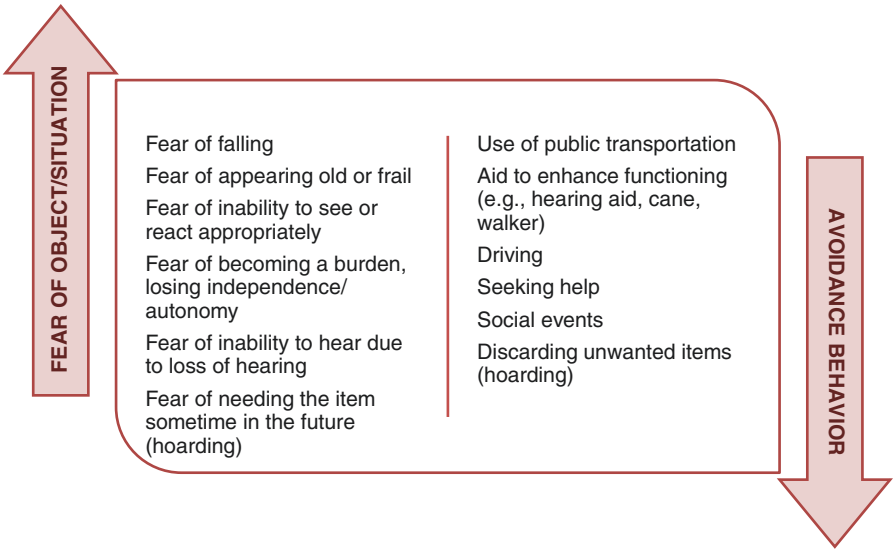


Fig. 6.1 Common age-specific examples of fears and maladaptive avoidance behaviors

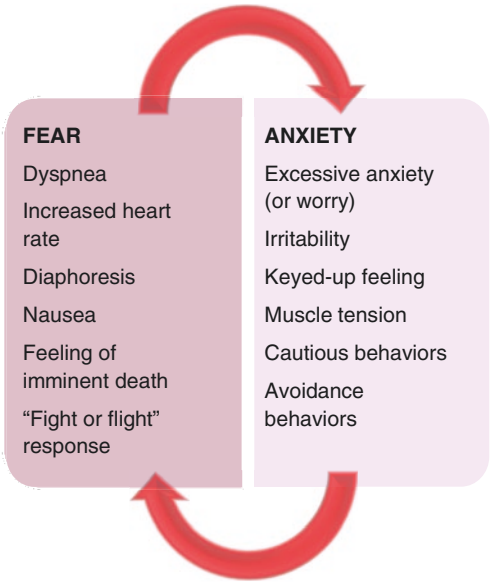


Fig. 6.2 Clinical manifestations of fear and anxiety

to a real or perceived danger. Anxiety is characterized by worry, muscle tension, cautious behaviors or avoidance behaviors, while fear is more related to autonomic responses, including nausea, tachycardia, increased blood pressure, and diaphoresis. A faulty "fight or flight" response is believed to be associated with the predisposition to panic attacks [11]. Avoidance is an important coping mechanism across anxiety disorders. Figure 6.2 lists key clinical manifestations of fear and anxiety.

Question 6.5

What Are the Reasons for Which Anxiety Disorder Is Difficult to Diagnose in Late Life?

Anxiety disorders in late life are difficult to diagnose for a number of reasons, including a difficulty to differentiate adaptive from pathological anxiety in older adults in the context of age-related physiological changes, challenging life circumstances including bereavement and disability, poor quality of life, patient denial or minimization of symptoms, and high prevalence of associated comorbidities, including neurocognitive disorders [12, 13]. The anxiety symptoms in older patients may differ from those in younger patients, which makes recognition rather challenging. For example, older patients may present with more somatic complaints, with anxiety being related to the experience of physical comorbidities [12]. Another reason for this under-recognition is that most anxiety disorders in late life are believed to be chronic and have their onset earlier in life [1]. Unless older adults with anxiety disorders are already engaged in psychiatric care, it is unlikely that these individuals will come to psychiatric attention at such a late stage after the onset of their disorder. For example, agoraphobia in older adults rarely comes to psychiatric attention, and patients themselves often do not consider their fear as excessive or unreasonable. When generalized anxiety disorder has a late onset, it often is associated with a depressive disorder, which can be viewed as the primary problem. As well, patients with phobic disorders in late life may be less likely to come to psychiatric attention than younger adults because it may be easier for them to avoid anxiety-provoking situations because of not having to attend school or work and by having access to home support [1]. Additionally, "ageist" assumptions may also dissuade the recognition of anxiety disorder in late life; e.g., symptoms of agoraphobia occurring after a fall may be minimized or dismissed by the affected individual or family members as an "age-appropriate" adaptation to the fall event [1].

Question 6.6

How Do Anxiety Disorders Present in Late Life?

The DSM-5 does not describe age-specific anxiety disorder phenotypes, despite reports of geriatric-specific anxiety syndromes such as fear of falling [14]. Fear of falling can be viewed as a specific phobia in older adults. Generalized anxiety disorder and specific phobias are among the most commonly occurring anxiety disorders late in life [13]. Almost half the cases of generalized anxiety disorder have a late-life onset, although cases with an early onset tend to have a more severe course characterized by excessive worry and a higher rate of psychiatric comorbidity and psychotropic medication use; physical disability may be a risk factor for late-onset generalized anxiety disorder [15]. Social anxiety disorder typically presents early in life [16]. Older patients with panic disorder, which

involves the fear response, have less distress during panic attacks in relation to body sensations and panic-related cognitive symptoms and emotions than the younger adults [17]. Panic disorder has a lower incidence in older adults than in younger peers [17]. This decrease in incidence may be explained by age-related dampening of physiological autonomic responses [18]. For example, older age is associated with diminished symptomatic and cardiovascular response to the panicogenic agent cholecystokinin tetrapeptide [18]. New onset of panic symptoms in late life should prompt a thorough medical workup to rule out alternative and comorbid conditions particularly systemic medical disorders and medication side effects.

Question 6.7

List the Differentiating Features of Primary Versus Secondary (Caused by Another Condition) Anxiety Syndrome in Older Adults

Differentiating primary from secondary anxiety syndrome is essential for adequate treatment. Table 6.2 shows some key elements to consider in determining whether the clinical presentation is due to a primary anxiety versus secondary anxiety syndrome (caused by another medical disorder and/or medication/substance use) in the context of physical illness [10].

Table 6.2 Differentiating features between primary anxiety versus secondary anxiety syndrome in the context of physical illness [10]

Characteristics	Primary anxiety	Secondary anxiety[a]
Onset of anxiety symptoms	Before onset of physical illness	After onset of physical illness
Presence of symptoms of physical illness known to cause/exacerbate anxiety (e.g., chronic obstructive pulmonary disease, angina, hyperthyroidism)	No	Yes
Comorbidity with depressive disorder	Onset of depression before physical illness	Onset of depression after physical illness
Newly started prescribed/over-the-counter medications or substances (e.g., prescribed and illicit psychostimulants, thyroxine, caffeine)	No	Yes
Polypharmacy	No	Yes
Major life events	Yes	No
Psychiatric history of anxiety disorders	Yes; history of increased anxiety when facing the feared object or situation; history of avoidance behavior	No

[a]Caused by another medical condition, medication, and/or substance use

Question 6.8

A 66-year-old recently retired, single female has recently relocated to another city to be closer to her sister. She has a grade 8 education. She has no past psychiatric history. She is being seen by the consultation-liaison psychiatry team during her admission for a community-acquired pneumonia with *Streptococcus pneumoniae* that has been adequately treated in hospital with an antibiotic and corticosteroid. It appears that during hospitalization, she has continued to manifest unexplained, episodic shortness of breath. Upon psychiatric interviewing, she reports having a poor childhood. She describes herself as a "life-long worrier" but believes that she has always been able to cope with her worry appropriately. Aside from pneumonia, her medical history is significant for chronic obstructive pulmonary disease (COPD), diabetes mellitus, and hypertension. She does not use any substances or over-the-counter medications. Her current medications are albuterol, metformin, glyburide, and ramipril. She is not currently being treated with any psychotropic medications. She described her current health as poor, unable to take care of herself due to physical limitation, and that she does not feel comfortable with discharge to her home until her "shortness of breath is resolved." The psychiatrist is of the opinion that the patient has a late-onset anxiety disorder.

What Are the Risk Factors for Anxiety Identified in This Case?

As in this case, the following risk factors have been found to be associated with increased risk of having an anxiety disorder in late life [19]:

- Female sex
- Single, divorced, or separated (compared to being married)
- Lower education level
- Early childhood adversity
- Stressful life events (e.g., retirement, relocation)
- Personality trait of neuroticism
- Chronic medical conditions
- Physical impairment in daily activities
- Poor subjective health

Question 6.9

What Is the Interplay Between Anxiety and Depressive Disorders in Late Life?

Anxiety disorder is highly comorbid with depressive disorder in the old age [19]. These disorders have significant risk factors and symptom overlap (e.g., impaired sleep, concentration, and energy). Generalized anxiety disorder and

major depressive disorder also have genetic risk factors that significantly overlap. Studies suggest that premorbid genetic factors, accumulating life stressors, and enduring negative affectivity may, solely or in combination, produce patterns of hypo/hyperreactivity [20]. Twin studies suggest that genetic factors relate either to "fear" disorders or to disorders of "anxious misery" (i.e., described as a potential dimension across the anxiety spectrum that may be involved in generalized anxiety disorder, major depressive disorder, and persistent depressive disorder (dysthymia)) [20]. Therefore, in patients with late-life depressive disorder, comorbid anxiety symptoms can be prevalent and contribute to the burden of clinical presentation [21]. Comorbid anxiety disorders are associated with a greater decline in memory and more severe somatic symptoms in late-life depression; anxiety disorders with an onset in later life may be associated with neurocognitive decline [22]. Anxious depression in older adults may represent a relatively treatment-resistant subtype of depression, associated with an increased risk of neurocognitive disorder and, and perhaps most importantly, an increased risk for suicide [22]. Moreover, comorbid symptoms of generalized anxiety disorder in depressed older adults are associated with a more severe presentation of depressive illness [23].

Question 6.10

What Are the Key Elements in Evaluating and Managing Anxiety Disorders in Late Life?

Diagnosing late-life anxiety disorder requires a comprehensive assessment of the patient, including a clinical history, physical examination, and laboratory investigations.

The clinical history should include [12]:

- A review of the onset of anxiety symptoms.
- A review of substance and prescribed/over-the-counter medication use; a careful review of current medications is essential in evaluating anxiety disorders in older adults, especially before prescribing additional medications for treatment.
- Review of previous treatment history and response.
- Collateral information from family members or caregivers to determine the functional impact of symptoms.

Physical examination and laboratory investigations should be targeted based on the clinical presentation and differential diagnosis, including ruling out physical illnesses. As clinically indicated, some suggested laboratory investigations in late-life anxiety disorders include the following [10, 24]:

- Complete blood count
- Extended electrolytes
- Fasting glucose
- Fasting lipid profile

- Thyroid-stimulating hormone
- Liver-associated enzymes
- Toxicology
- Pulse oximetry
- Urinalysis
- Electrocardiogram
- Computed tomography or magnetic resonance imaging of the brain

Table 6.3 lists common factors that can cause or exacerbate anxiety disorders in late life [10]. Figure 6.3 highlights the assessment and also the overall management of anxiety disorders in older adults [10].

Table 6.3 Common factors that can cause or exacerbate anxiety disorders in late life [10]

Category	Examples
Medications/ substances	Prescribed psychostimulants, steroids, alpha- and beta blockers, thyroxine, levodopa, bronchodilators, muscle relaxants, nonsteroidal anti-inflammatory drugs, illicit amphetamines (e.g., crystal meth, cocaine), caffeine, alcohol (withdrawal), benzodiazepine (withdrawal)
Medical conditions	Hyponatremia, hyperkalemia, hypocalcemia, cognitive impairment, Parkinson disease, strategic strokes, seizures, brain tumors, migraine, chronic obstructive pulmonary disease, pulmonary embolism, pneumonia, hypoxemia, dyspnea, sleep apnea, hyperthyroidism, pheochromocytoma, diabetes mellitus, hypoglycemia, constipation, diarrhea, abdominal pain, anemia, angina, mitral valve prolapse, myocardial infarction, congestive heart failure, arrhythmias

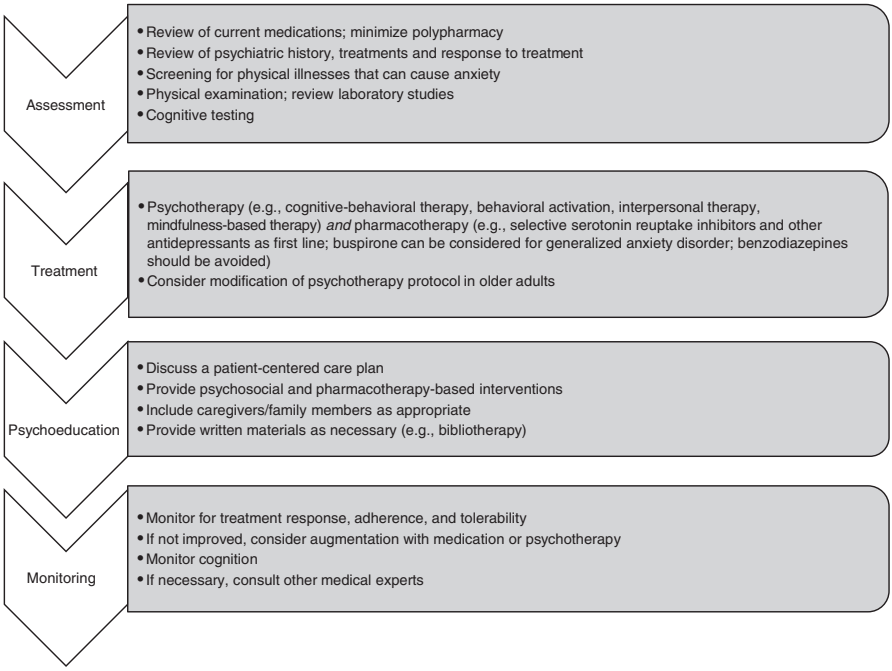


Fig. 6.3 Assessment and management of anxiety disorders in older adults

Question 6.11

What Are the Treatment Recommendations in Older Adults with Anxiety Disorder?

The general principle for prescribing medications for older adults is to start low, go slow, and treat long to remission target. Starting with one-quarter to one-half of the usual starting dose of an antidepressant for anxiety disorder and up-titrating the dose slowly, with regular patient monitoring and reassurance, is often necessary. Antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are recommended but not always tolerated, whereas activating antidepressants (e.g., bupropion) and tricyclic antidepressants (e.g., amitriptyline) are generally avoided in older adults because of side effects and exacerbation of anxiety symptoms. Trazodone can be used for anxiety-related insomnia but can add to the serotonin burden when simultaneously using an SSRI or SNRI. Benzodiazepines and other sedatives (e.g., anticholinergics, antihistaminergics) should be avoided in older adults because of their poor safety profiles including delirium risk [12]. If use is necessary in specific situations, benzodiazepines can provide a rapid anxiolytic effect and are used as a short-term adjunct or on-demand. However, benzodiazepines reinforce a maladaptive behavior that anxiety must be immediately relieved, which represents an avoidance behavior that serves to perpetuate anxiety in the long term [12]. In many cases, monotherapy may not be adequate. Thus, clinicians should consider augmenting with other medications (e.g., gabapentin, pregabalin) or with cognitive behavioral therapy (CBT). To date, there is insufficient evidence to guide augmentation strategies in older adults with anxiety disorders [12]. Improvement in symptoms should be assessed by subjective report from the patient or informant and objectively through standardized questionnaires. An increase in the dose of the antidepressant should be considered at 2 weeks if there has been no subjective or objective improvement and the symptoms remain disabling.

Question 6.12

Late-life anxiety disorders are commonly associated with cognitive impairment.

A. Describe a Proposed Model of How a Biological Stress Response in Late-Life Anxiety Produces Cognitive Impairment

Late-life anxiety disorders are commonly associated with cognitive impairment [13]. Several mechanistic hypotheses have been postulated to explain the cognitive impairment due to persistent stress response seen in anxiety disorders. With aging, there is an altered regulation of the normal physiological response to

chronic stress within the central nervous system, with less ability to downregulate the pituitary adrenocorticotropic hormone (ACTH) receptors and resulting memory and executive dysfunction due to toxic effects of elevated cortisol levels on hippocampus and prefrontal cortex [25] (see Fig. 6.4). Some of these cognitive changes may be reversible, as is the case of hippocampal volume and memory in treated depressive and anxiety disorders. Studies found that cortisol changes during treatment predicted memory improvement [13]. Furthermore, telomere

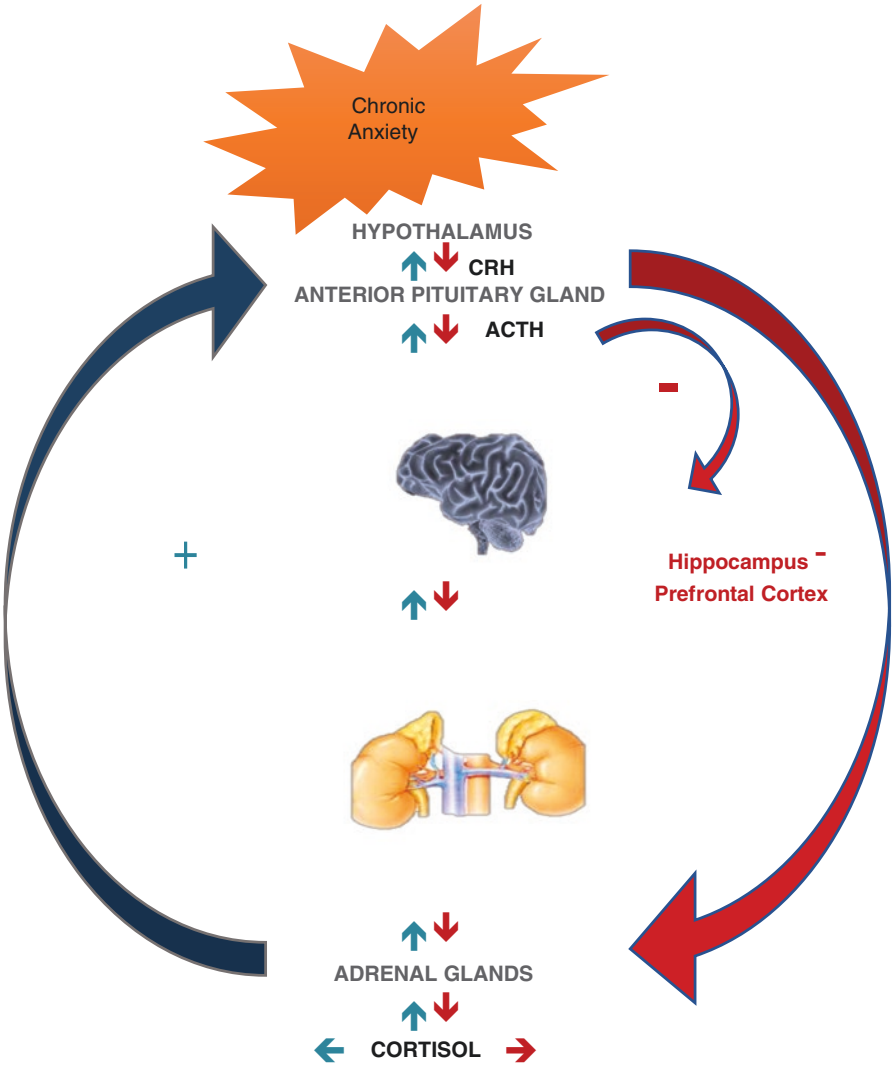


Fig. 6.4 Biological stress response model and cognitive impairment in late-life anxiety. *CRH* corticotropin-releasing hormone, *ACTH* adrenocorticotropin hormone

shortening due to accelerated aging, amyloid plaque accumulation, immune-inflammatory pathways, and oxidative/nitrosative stress have also been associated with late-life anxiety [25]. Although chronic anxiety, stress hyperreactivity, and accelerated aging appear to be convergent concepts, no causality or directionality can yet be drawn [25].

B. How Can Mindfulness-Based Approaches Reverse the Cognitive Impairment in Late-Life Anxiety Disorders?

The aging brain and its lesser ability to downregulate the hypothalamic-pituitary-adrenal (HPA) axis is more vulnerable to physiological insults caused by chronic anxiety and subsequent HPA axis hyperactivity, with deleterious effects on memory and executive function, although some of these changes appear to be reversible with treatment (see Answer A) [13].

There is growing interest in the potential benefits of mindfulness meditation practices for counteracting some of the cognitive deficits associated with aging alone. Pathological worry leads to hyperactive stress response, which may be an ideal target for mindfulness-based treatment. Mindfulness meditation approaches emphasize awareness of present moment experiences as an alternative to dwelling on the past (e.g., rumination) or future (e.g., worry) [26]. One mindfulness-based intervention, called mindfulness-based stress reduction (MBSR), has demonstrated a rumination- and worry-mitigating effect in clinical studies. In studies of MBSR, this therapeutic approach has demonstrated cortisol-lowering effects, suggesting that increasing mindfulness may decrease excessive HPA axis responses including improving memory and executive function [13, 27]. Few studies have directly investigated the effect of mindfulness in geriatric psychiatry, reporting encouraging results in attention, executive functions, and memory, but future studies to overcome methodological limitations are still needed [28]. A randomized controlled study of participants aged 55–75 years has investigated the influence of mindfulness training on executive control and emotion regulation in older adults [29]. These authors concluded that engaging in mindfulness meditation training improves the maintenance of goal-directed visuospatial attention and may be a useful strategy for counteracting cognitive decline associated with aging. Figure 6.5 illustrates a proposed model of how a mindfulness-based treatment for late-life anxiety disorders may reverse this cognitive impairment [13].

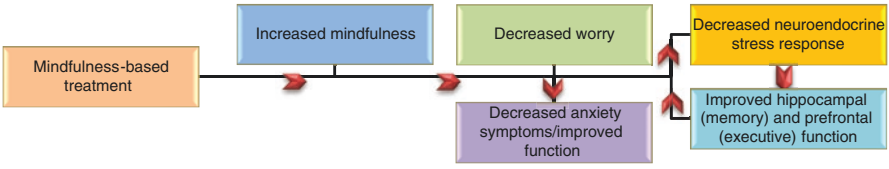


Fig. 6.5 Proposed model of how a mindfulness-based treatment for late-life anxiety disorders may reverse this cognitive impairment

Question 6.13

A 79-year-old man suffered a transient ischemic attack (TIA) a year earlier. A few weeks after his TIA, he developed a phobia of dog feces and recurrent, intrusive thoughts of contamination, compulsions to check the house and visitors' shoes for feces, and compulsions to wash his hands repeatedly. These rituals took 4 h/day to perform. This has affected his mood and he endorsed feeling sad and lacking enjoyment in life. He has anorexia, insomnia, and concentration difficulties. His past psychiatric history indicated that he had a depressive episode at age 29 (following his divorce), which was successfully treated with cognitive behavioral therapy. Upon examination in your psychiatric clinic, he is physically well apart from a mild hand tremor which is worse on the right side. Brain MRI scan shows moderate cortical atrophy and periventricular white matter changes. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score is 29, and the Montgomery-Asberg Depression Rating Scale (MADRS) score is 27.

A. What Is the Diagnosis?

Based on the information obtained, the patient meets the DSM-5 diagnostic criteria of obsessive-compulsive disorder (OCD) (severe intensity) and comorbid major depressive disorder (moderate severity). Table 6.4 lists the highlights of the diagnostic criteria for OCD [2]. For diagnostic criteria for major depressive disorder, please see Topic 5 on depression. For a full DSM-5 review of OCD criteria, the reader is referred to the DSM-5 manual [2].

Case continued: The patient has responded to treatment with citalopram 20 mg daily. His symptoms have resolved over a period of 4 months and he remained well after 12 months. The Y-BOCS score is now 7 (subclinical case), and his MADRS score becomes 4 (normal/symptom absent).

B. Describe the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and How It Is Used in This Case

The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is a 10-item instrument designed to measure the severity and type of symptoms (obsessions and compulsions) in patients with OCD over the previous 7 days [30]. This scale is

Table 6.4 Obsessive-compulsive disorder: highlights of the DSM-5 diagnostic criteria [2]

DSM-5 diagnostic criteria	Diagnostic specifiers
– Presence of obsessions, compulsions, or both – Obsessions/compulsions are time-consuming (>1 h/day) or cause significant distress/impairment – Symptoms are not attributable to or better explained by other psychiatric or medical conditions (e.g., excessive worries as in generalized anxiety disorder, difficulty discarding or parting with possessions as in hoarding disorder, guilty ruminations as in major depressive disorder, delusional preoccupations as in psychotic disorder, cognitive impairment as in neurocognitive disorder)	– With level of insight: good/fair; poor; absent/delusional – If it is tic-related

useful in screening and monitoring OCD symptoms during/after treatment. The severity of this patient's OCD symptomatology has changed with treatment from a score of 29 (severe) to a score of 7 (subclinical symptoms). His depressive symptoms were evaluated using the Montgomery-Asberg Depression Rating Scale (MADRS) [31]. His MADRS score was 27 (moderate severity), with a follow-up score of 4 (normal/symptom absent) after improvement of his symptoms.

Question 6.14

What Are the General Characteristics of Obsessive-Compulsive Disorder (OCD)? How Does It Present in Older Adults?

With the arrival of the DSM-5 in 2013, obsessive-compulsive disorder (OCD), previously considered an anxiety disorder in the preceding DSM classification system, became part of a new category called obsessive-compulsive and related disorders. Hoarding and excoriation disorders are diagnostic entities added to the DSM-5 in this same, new category. In the general population, OCD and hoarding disorder are among the more commonly recognized psychiatric diagnoses. However, OCD has been less studied in older adults. Older adults with OCD are more likely than younger adults to have obsessions of having sinned and compulsions of hand washing [12]. Compared to other late-life anxiety disorders, OCD in later life is more prevalent in men and is associated with greater social impairment [12] (see Table 6.4 for a summary of the DSM-5 diagnostic criteria for OCD).

Question 6.15

A 71-year-old divorced man is referred to a psychiatric clinic for collecting various objects that are deposited in an unorganized manner in the patient's house. The attic, basement, garage, and surroundings of his house are cluttered with these objects. He reported to get anxious when someone else attempted to discard these items despite acknowledging many of these objects have no actual value. The living areas such as bathroom and kitchen were recently uncluttered through an intervention by local authorities while he was admitted to hospital for a fall at home (he slipped on papers which were lying on the floor). However, his living conditions deteriorated rapidly after hospital discharge with relapse of extreme clutter in living areas that compromised their intended use. This behavior to accumulate worthless objects has started 40 years ago and has worsened with time. On mental status examination, the patient is calm and oriented; his speech is organized, logical, and coherent; his affect is euthymic; and there are no psychotic symptoms. He has no known systemic medical conditions.

What Is the Working Diagnosis?

Hoarding disorder is a chronic condition associated with moderate to severe impairment in health and functioning level. Hoarding disorder has been primarily studied in younger adults, and there is limited research on this condition in later life [32]. This patient has a persisting difficulty discarding or parting with objects, regardless of their actual value. There is distress associated with discarding the objects. The difficulty discarding objects results in the accumulation of objects that clutter active living areas and substantially compromises their intended use. This patient's living areas were uncluttered only because of the interventions of third parties (e.g., local services, authorities). The hoarding causes significant distress or impairment in important areas of functioning (including maintaining a safe environment for self and others). His hoarding is not attributable to another medical condition (e.g., brain injury, cerebrovascular disease) or other psychiatric disorders (e.g., cognitive impairment in major neurocognitive disorder, decreased energy in major depressive disorder, obsessions in obsessive-compulsive disorder, delusions in psychotic disorder, restricted range of interests in autism spectrum disorder). Therefore, the patient meets criteria for a diagnosis of hoarding disorder. See Table 6.5 for a summary of the DSM-5 criteria for hoarding disorder [2]. For a full review of the DSM-5 diagnostic criteria, the reader is referred to the DSM-5 manual [2].

Question 6.16

Hoarding disorder must be differentiated from systemic medical and neuropsychiatric disorders.

What Is the Differential Diagnosis of Hoarding Disorder?

Geriatric hoarding disorder is characterized by the presence of severe functional impairment and systemic medical and neuropsychiatric comorbidities, including cognitive dysfunction, which make the differential diagnosis rather difficult [32].

Table 6.5 Hoarding disorder: highlights of the DSM-5 diagnostic criteria [2]

DSM-5 diagnostic criteria	Diagnostic specifiers
– Accumulation of possessions resulting from persistent difficulty discarding clutter in active living areas to the point of congestion and substantial compromise in their intended use – Behaviors cause significant distress or functional impairment – Symptoms are not attributable to or better explained by another psychiatric or medical conditions (e.g., obsessive-compulsive disorder, major depressive disorder, psychotic disorder, neurocognitive disorder, neurodevelopmental disorders, brain injury, cerebrovascular disease, genetic syndromes)	– With level of insight: good/fair; poor; absent/delusional – With excessive acquisition

Table 6.6 Differential diagnosis for hoarding disorder [2, 34]

Diagnosis	Clinical characteristics
Hoarding disorder	Maladaptive beliefs that accumulated objects are necessary; distress is associated with having to discard items, not urged to control thoughts; insight is variable (e.g., from good to absent); symptom onset is in adolescence; impairment typically begins in later adulthood
Neurocognitive disorders	Cognitive inability to properly organize/discard objects; onset is later in life, although hoarding behavior can precede cognitive impairment. Up to a fifth of patients aged ≥65 with hoarding disorder have concurrent major neurocognitive disorder [34]
Depressive disorder	Clutter is the result of lack of interest and low energy to clean and organize rather than a result of difficulty discarding; excessive acquiring is unlikely present
Obsessive-compulsive disorder (OCD)	Hoarding obsessions and compulsions associated with contamination or other OCD fear themes; distress arises from need to perform associated hoarding compulsions or obsessions rather than from difficulty discarding; symptoms are typically egodystonic; insight is typically good; symptom onset and impairment typically coincide
Psychotic disorders (e.g., schizophrenia)	Object accumulation is the result of delusions or negative symptoms; items collected likely serve a specific purpose in delusions; insight typically is poor
Neurodevelopmental disorders (e.g., autism spectrum disorder)	Difficulty discarding is typically due to extreme attachment to specific objects rather than difficulty with discarding
Neurodegenerative diseases (e.g., Parkinson disease)	New-onset hoarding and collecting behaviors are common in patients with underlying neurodegenerative disorders; neurocognitive inability to discard and organize things, without attaching meaning to those objects

Older adults with hoarding disorder have more physical illnesses compared to their nonpsychiatric peers [33]. In a study, hoarding severity significantly predicted the total number of medical conditions [33]. The differential diagnosis for hoarding disorder is presented in Table 6.6 [2, 34].

Question 6.17

What Is the First-Line Treatment for Hoarding Disorder?

Cognitive-behavioral therapy (CBT) is considered the first-line treatment for hoarding behavior and focuses on:

- Active exposure aimed at discarding objects and avoiding acquisition of new items
- Managing emotional distress related to discarding
- Addressing maladaptive belief patterns and behaviors related to hoarding
- Addressing problems related to information processing in some cases

Pharmacotherapy for hoarding disorder has been less well studied than the CBT approach. There has been a dearth of randomized, double-blind, controlled trials to investigate the treatment response of hoarding disorder. However, a meta-analysis of seven studies that investigated pharmacological treatment of hoarding disorder found that over half of treated patients responded to medications [35]. This study suggests that, although sample sizes have been small and methodologies have been limited, SSRIs and SNRIs may be effective in some cases for treating hoarding disorder. Other agents (e.g., antipsychotics, cognitive enhancers, psychostimulants) have insufficient data. In conclusion, first-line treatment for hoarding disorder is CBT, modified for hoarding symptoms, although pharmacotherapy may also have a role, but further studies are needed especially with a focus on the geriatric population.

Question 6.18

What Is the Neurocognitive Profile of Patients with Hoarding Disorder?

Neuropsychological studies of hoarding disorder have suffered from small sample sizes and methodological limitations but generally suggest a pattern of clinically significant cognitive impairment in some visually mediated neurocognitive processes including visual memory, detection, and categorization [36]. However, relative strengths in abstract reasoning in both verbal and visual domains have also been reported [36]. In a controlled study of 26 unmedicated patients with hoarding disorder, there was a tendency to use explicit rather than implicit learning strategies for perceptual categorization; however, they performed as well as the normal controls on many other neurocognitive measures [37].

Question 6.19

An 89-year-old man was admitted to the intensive care unit (ICU) for myocardial infarction. He is now being seen by the consultation-liaison psychiatry team for fluctuating agitation and requests to leave hospital against medical advice. He is frustrated due to his long admission and loss of physical functioning. Because he remained alert and fully oriented at all times, his medical team ruled out delirium. His medical history is notable for constipation and occult blood in stool (for which he refused colonoscopy). He has taken diazepam for many years (prescribed by his primary care physician for “the nerves”). He is guarded, irritable, and reluctant to answer the psychiatrist’s questions, but his son provided collateral information over the phone with the patient’s consent. His supportive wife suddenly died a few months ago from a surgical complication of hip fracture, and he felt guilty because he avoided visiting her at the hospital. The patient was involved in an accident as a child, in which his younger brother died by drowning when they were playing outside their house near a creek. He suffered from guilt and had flashbacks of the tragedy for a long time after that. Although he never talked about his combat experience,

Table 6.7 Posttraumatic stress disorder: the main DSM-5 diagnostic components [2]

DSM-5 diagnostic components	Diagnostic specifiers
Exposure Re-experiencing Avoidance Negative cognitions and mood Arousal Duration >1 month Functional impairment Symptoms are not attributable to substance use (e.g., medication, alcohol) or another medical condition	With dissociative symptoms: depersonalization/derealization With delayed expression

he had been a prisoner of war during World War II. He had started drinking heavily shortly after coming back from the war in order to cope with any reminders of the war. He also used to abuse opioids following receiving prescriptions for his chronic back pain. He never sought formal help, because he believed "you have to pull yourself up by your bootstraps," but he continued to take diazepam from his primary care physician. He was afraid of doctors and avoided hospitals and medical follow-ups until his current admission for myocardial infarction. He is eventually diagnosed with posttraumatic stress disorder (PTSD).

A. What Are the Main DSM-5 Diagnostic Components of PTSD?

The most familiar type of posttraumatic stress disorder (PTSD) occurs in veterans exposed to combat, and it can recur or worsen in the setting of other stressors in late life, including severe medical illness. Although most older adults adapt after catastrophic medical diagnoses and treatments, a significant number may in fact develop posttraumatic stress symptoms or PTSD [38]. Table 6.7 lists the key components of the diagnostic criteria for PTSD [2]. For a full review of the DSM-5 criteria for PTSD, the reader is referred to the DSM-5 manual [2].

B. What Are the Risk Factors for Medically Induced PTSD in This Case? Generally, What Medical Conditions Have Been Associated with PTSD?

Although studies vary as to whether age increases risk for medically induced PTSD, several other factors are consistently associated with an increased risk. As in this case, the literature lists several risk factors for medically induced PTSD, including [38]:

- Past trauma or negative life stressors
- Preexisting psychiatric disorder
- Higher exposure to trauma (e.g., prolonged ICU stay, prolonged cancer treatment)
- Loss of physical functioning due to medical condition
- Pain

Several conditions have been associated with medically induced PTSD, including [38]:

- Myocardial infarction
- Cancer
- Stroke
- Delirium
- Fall
- Cardiac surgery
- Multiple sclerosis

Question 6.20

What Is the Pharmacotherapy for PTSD in Older Adults?

The pharmacologic interventions should target the core symptoms of PTSD with special attention paid to the systemic medical comorbidities and the risks and benefits of medications in older adults. To date, the US Food and Drug Administration (FDA) has approved only the selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine for the treatment of PTSD. Paroxetine may not be the best choice for PTSD symptoms in older adults due to its anticholinergic activity. Comorbid systemic medical illnesses (e.g., renal and kidney disease, cardiac disease, neurocognitive disorders) increase risks for adverse drug effects in the geriatric population. All other agents trialed in the management of PTSD are used off-label. Benzodiazepines pose multiple risks in older adults including dependency, tolerance, delirium, and withdrawal and are best avoided in older adults [38]. Table 6.8 lists some common medications for PTSD prescribed in older adults [38].

Table 6.8 Common medications for PTSD in older adults [38]

Symptom target	Medication (daily dose)	Geriatric considerations
Hyperarousal, nightmares, sleep disturbance, anxiety	Prazosin 1–3 mg qhs Trazodone 12.5–100 mg qhs	Adverse effects: orthostatic hypotension, slow heart rate, dizziness, headaches, priapism Monitor for blood pressure, falls
	Mirtazapine 7.5–30 mg qhs	Adverse effects: orthostatic hypotension, dizziness, weight gain Good choice for cachectic, ill patients
Re-experiencing, depressed mood, avoidance	Sertraline 12.5–100 mg daily Escitalopram 5–10 mg daily	Adverse effects: hyponatremia, risk for QTc prolongation at higher dose If daytime sedation, consider switch to qhs
	Venlafaxine XR 37.5–150 mg daily	Adverse events: increased hyperarousal due to noradrenergic activation, hypertension Monitor for discontinuation syndrome (taper slowly if ineffective)
Fatigue, depressed mood, avoidance	Bupropion XL 150–300 mg daily	Adverse events: insomnia, worsened hyperarousal No sexual side effects

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Topic 7: Substance Use Disorders in Older Adults

Question 7.1

What Is the Definition of a Substance Use Disorder According to the Diagnostic and Statistical Manual, 5th Edition (DSM-5)?

The DSM-5 describes a substance use disorder as a "cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems" [1]. The DSM-5 lists ten classes of substances, including alcohol, caffeine, cannabis, hallucinogens (e.g., phencyclidine or PCP, lysergic acid diethylamide or LSD), inhalants, opioids, sedatives, hypnotics or anxiolytics, stimulants, and tobacco. A diagnosis of substance use disorder applies to all of these classes except caffeine.

Question 7.2

What Major Assumptions Do Many Clinicians Make About the Geriatric Population, Increasing the Chance That Significant Substance Use Disorders Go Unrecognized?

The major assumptions are:

- Older people generally do *not* abuse drugs.
- But *if* they use drugs, they certainly do not use illicit substances.

The prevalence of substance use disorder was previously believed to decrease with aging [2]; however, available literature suggests otherwise [3–5]. In their review of published papers between 1967 and 2011 regarding illicit substance use among older adults, Taylor and Grossberg found that illicit drug use among the geriatric population is increasingly common [5].

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_7

In another study, Chhatre et al. completed an analysis of data of all admissions to publically funded substance abuse treatment programs in the USA between 2000 (n = 60,112) and 2012 (n = 121,015) for those aged 55 years and older at the time of admission. They found that the proportion of older adults admitted to these programs increased from 3.4 to 7.0%. The majority of admissions were for alcohol as the primary substance of abuse, but the proportion of alcohol decreased from 77 to 64%, while the proportion of other substances increased by the following percentages—cocaine/crack (63%), marijuana/hashish (150%), heroin (26%), non-prescription methadone (200%), other opiates/synthetics (221%), and benzodiazepines (67%) [3]. Alcohol was the most common substance of abuse (65%), followed by heroin (15%), cocaine (8%), and opiates (5%) [3].

Using data from three large national data sources, Mattson et al. presented information about substance use in adults aged 65 years and older on a "typical" or "average" day. They estimated that on an average day in the USA, 6,000,000 drink alcohol, 132,000 use marijuana, and 4300 use cocaine [6].

Question 7.3

What Medical and Psychiatric Problems Do Older Individuals with Substance Abuse Problems Have Compared to Their Younger Counterparts?

Older adults are more likely to have comorbid chronic medical problems, polypharmacy, increased risk of suicide, impaired cognitive function and increased vulnerability to psychoactive substances, increased physical disabilities, and overall worse outcomes [7–11].

Question 7.4

What Factors Affect Adherence to Medication Regimens, Contributing to the Development of *Substance Use Disorders* When Not Addressed?

In 2003, the World Health Organization (WHO) proposed that there are five interacting dimensions that affect medication adherence [12]:

- Socioeconomic factors
- Health system/healthcare team factors
- Condition-related factors
- Therapy-related factors
- Patient-related factors

Building on these five dimensions, the American College of Preventive Medicine (ACPM) developed a medication adherence tool for prescribers to improve health outcomes of their patients [13]. According to the ACPM tool, socioeconomic factors include language proficiency, health literacy and/or overall literacy, stability of the living situation, transportation to the pharmacy, medication cost, and cultural beliefs about illness and treatment [13]. The health system/healthcare dimension includes the nature of the patient-prescriber (or "provider") relationship, communication skills of the healthcare team members, and formulary restrictions. Condition-related factors include the complication of treatment regimens (e.g., with meals, prior to meals, timing, frequency); lack of symptoms, which can lead patients to avoid taking their medications; and duration of therapy. Patient-related factors include physical factors such as visual or hearing impairments, cognitive impairment, and impaired mobility or dexterity [14]; and psychological or behavioral barriers include knowledge about the condition/disease, perceived risk/susceptibility to disease, and confidence in ability to follow treatment recommendations. Even mild cognitive decline in healthy older adults significantly impacts the ability to adhere to medication regimens [15].

Older patients take significantly more medications than do younger patients, complicating medication adherence. Although accounting for only 13% of the population, older (age 65 and over) adults account for one-third of all prescriptions in the USA [16].

Question 7.5

Polypharmacy is common in geriatric population.

A. How Does Polypharmacy Intersect with Substance Use in Older Adults?

The definition of polypharmacy varies from discrete numbers set by researchers (≥4–6 medications), to a generalized statement that polypharmacy is the use of "more medications than are medically necessary" [17, 18]. The practice of "deprescribing" has taken hold to combat the problem of polypharmacy [19, 20]. It is defined as the "act of systematically identifying and tapering, reducing or stopping medications that are not indicated… or are causing, or have considerable potential to cause, adverse effects" [21].

Polypharmacy is common in older (age 65 and over) adults, who have multiple underlying systemic medical disorders [22], and is associated with an increased risk of medication misuse and nonadherence [23–26]. Data from the National Ambulatory Medical Care Survey ($n = 97{,}910$) for the years 2004–2013 were reviewed for outpatient visits that included three or more central nervous system (CNS)-active agents

[27]. Gerlach et al. [27] used the Beers criteria of polypharmacy to mean three or more CNS-active medications including antipsychotics, benzodiazepines, non-benzodiazepine benzodiazepine receptor agonist hypnotics, tricyclic antidepressants, selective serotonin reuptake inhibitors, and opioids (see Question 7.9 for a description of the Beers criteria). They found that of CNS polypharmacy visits between 2011 and 2013, 76.2% included an opioid, 61.8% included a benzodiazepine, 66% of the polypharmacy visits with benzodiazepines included opioids, and 53.3% of the polypharmacy visits with opioids included benzodiazepines. Between 2004 and 2013, the proportion of polypharmacy visits with opioids rose from 69.6 to 76.2%.

B. What Are the Clinical Consequences of Polypharmacy?

Polypharmacy is associated with higher healthcare costs [28], increased risk of adverse drug events [29, 30], drug-drug interactions [31], medication nonadherence [32], and reduced functional capacity.

Question 7.6

Prescription drugs can be misused or abused by older adults.

A. What Is the Definition of Prescription Drug Misuse and Abuse?

According to the Substance Abuse and Mental Health Services Administration of the US Department of Health and Human Services, prescription drug misuse and abuse is the "intentional or unintentional use of medication without a prescription, in a way other than prescribed, or for the experience or feeling it causes" [33].

B. What Are the Most Commonly Misused or Abused Drugs by Older Adults?

The most commonly abused or misused drugs by older adults are prescription drugs [34, 35]. Of the nearly 3500 older adults who were screened for alcohol, medication, and illicit substance abuse problems in Florida, Schonfeld et al. [34] found that prescription misuse was the most common substance use problem identified (26.4%), followed by alcohol (9.7%), and various illicit substances (1.14%). The specific medications were not identified in this study, but general category of prescriptions misused were pain medications (29.5%), anxiolytics (22.9%), and sleep aids (21.7%).

Among the geriatric population in the USA, Colliver et al. [35] estimated that the misuse of prescription medications, or nonmedical use of prescription drugs, would double from 1.2% (911,000) in 2001 to 2.4% (2.7 million) in 2020. In 2009, about

half of the 1.2 million emergency department (ED) visits involving the *misuse or abuse* of pharmaceuticals in those aged 21 years and older involved opioid pain relievers; and about a third was due to medications to treat anxiety or insomnia, primarily benzodiazepines [36]. In those over age 21 years old, ED visits involving misuse or abuse was highest for oxycodone products (71.9%), followed by alprazolam (55.7%), hydrocodone products (43.3%), and antidepressants (41.2%) [36].

Question 7.7

To What Extent Is Opioid Use Disorder a Problem in the Geriatric Population?

In the USA, deaths from opioid overdose overall were five times higher in 2016 than in 1999 [37]. The US Centers for Disease Control (CDC) estimated that 40% of opioid deaths in 2017 were attributed to prescription opioids. The most common opioids leading to death are methadone, oxycodone, and hydrocodone [38, 39].

An analysis of the National Center for Health Statistics' multiple-cause-of-death file for 1999 to 2014 indicated that individuals born between 1947 and 1964 and between 1979 and 1992 had an increased risk of death from overdose due to prescription opioids and heroin compared to other age groups [40]. An analysis of Medicare Part D data demonstrated a significant increase in opioid prescriptions in this population between 2007 and 2011. The percent of Part D recipients receiving prescriptions for combined schedule II/III opioid for more than 90 days per year increased from 4.62% in 2007 to 7.35% in 2012 [41].

Question 7.8

What Are the Complications Associated with Opiate Misuse Among the Older Population?

For adults over age 60 years who misuse prescription opioids, rates of serious medical outcomes are more than twice that of their younger counterparts [42], have increased rates of hospital admission [43], and have increased risk of mortality [44].

Larney et al. conducted analyzed mortality data of patients in the Veterans Health Administration with opioid use disorders between 2000 and 2011 [45], comparing older patients (≥50 years, n = 36,608) with opioid use disorder, younger patients (<50 years, n = 23,662) with opioid use disorder, and older adults (≥50 years, n = 36,608) with no opioid use disorder. They found that the cohort with opioid use disorders aged 50 years or older were more likely to die from any cause than younger adults with opioid use disorder.

In contrast to younger people with an opioid use disorder, older people with an opioid use disorder are more likely to die from chronic illness than drug-related causes, which the authors suggest it leads to these older individuals having more

complex health needs than younger adults with opioid use disorder and older adults without an opioid use disorder. Older adults with opioid use disorder have been found to have high rates of psychiatric illness and chronic diseases [46–48].

Question 7.9

There have been concerted efforts to mitigate prescribing potentially inappropriate medications in older patients, including benzodiazepines. Several medication screening tools have been developed in this regard, including the Beers criteria and the STOPP/START criteria.

A. What Is PIP, and How Is It Related to Polypharmacy?

PIP is an acronym used in the medical literature for potentially inappropriate prescribing, which refers to medications that should generally be avoided in geriatric patients and doses and dosing frequencies that should not be exceeded based on up-to-date data regarding health outcomes and safety parameters such as rates of adverse drug reactions [26]. Until relatively recently, studies of PIP were primarily based on US indicators such as the Beers criteria due to the lack of European specific indicators.

However, since about 2010, the literature about PIP has increasingly included data from Europe using indicators such as STOPP/START criteria developed by researchers in Ireland. In a retrospective national population study (n = 338, 801) using the Health Service Executive Primary Care Reimbursement Service (HSE-PCRS) pharmacy claims database, Cahir et al. found a significant association between polypharmacy and the risk of PIP [26]. In this study, polypharmacy was defined as the number of different repeat drug classes (≥3 prescriptions) per claimant. The most common PIP drugs were proton pump inhibitors at maximum therapeutic dosage for >8 weeks (40 mg daily omeprazole, pantoprazole, and esomeprazole, 30 mg daily lansoprazole, and 20 mg daily rabeprazole), nonsteroidal anti-inflammatories for >3 months, long-acting benzodiazepines for >1 month, and drug duplication within the same therapeutic class.

B. What Are the Beers Criteria and STOPP/START Criteria?

The Beers criteria is a list of potentially inappropriate medications for older adults [49]. Developed and published by the American Geriatrics Society (AGS), the Beers criteria was updated in 2015 and is named after the lead author of a paper published in the *Archives of Internal Medicine* in 1991 about the development of criteria for determining inappropriate medication use in nursing homes [50]. The list has since been expanded to be used in inpatient and outpatient settings.

The Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment (STOPP/START) criteria were developed in Europe as an alternative to the Beers criteria and are also guidelines for the appropriateness to use medications in older adults [51]. While acknowledging that the Beers criteria was the first well-organized list of commonly prescribing errors in the geriatric population, developers of STOPP/START sought to correct a number of deficiencies that were unaddressed by the Beers criteria [52]. Unlike the Beers criteria, the STOPP/START criteria medications are associated with adverse drug events and are meant to be applied in an inpatient admission.

Question 7.10

What Are the Major Trends in Benzodiazepine Prescribing for Older Patients?

Benzodiazepine use in the USA is common [53, 54], increases with age [55], and has not changed despite efforts to curb its use among the geriatric population. Olfson et al. reviewed 2008 LifeLink LRx Longitudinal Prescription database (IMS Health Inc) [55]. In their analysis of this database, which includes approximately 60% of all retail pharmacies in the USA, Olfson et al. found that, overall, about 5.2% of US adults (18–80 years) used benzodiazepines. Of this group, the percentage of those who used benzodiazepines increased with age, from 2.6% (18–35 years) to 5.4% (36–50 years) to 7.4% (51–64 years) to 8.7% (65–80 years). More troubling was that the rate of long-term use—which they defined as ≥120 days of medication dispensed during the year—*increased* with age, from 14.7% (18–35 years) to 31.4% (65–80 years), while the proportion that received a benzodiazepine prescription from a psychiatrist decreased with age from 15% (18–35 years) to 5.7% (65–80 years). Benzodiazepine use was nearly twice as prevalent in women as men.

In their analysis of national benzodiazepine prescription data, Maust et al. completed an analysis of national prescription data between 2007 and 2010 and found that few older adult benzodiazepine users received a clinical psychiatric diagnosis, and virtually none were referred for psychotherapy [54].

Despite the presence of sound data indicating that psychotherapy and non-benzodiazepine medications are effective and preferred, benzodiazepines continue to be the most commonly used treatments for anxiety and insomnia [56–58].

Question 7.11

What Problems Are Associated with Benzodiazepine Use in Older Adults?

Use of benzodiazepines in older adults is associated with multiple unfavorable outcomes, including cognitive impairment [59], increased risk of major neurocognitive

disorder [60, 61], falls [62–64], fractures [65], motor vehicle accidents [66], complications and need for revision of total hip replacements [67], and increased risk of pneumonia for patients with Alzheimer disease and chronic kidney disease [68, 69]. As with opioid medications, efforts are underway to "deprescribe" sedative-hypnotic drugs in older adults [70].

Question 7.12

What Are the Major Trends in Alcohol Use Patterns as People Age?

In an analysis of data from the National Health and Retirement Study, Bobo et al. found that overall consumption of alcohol decreased with age, but the consumption of alcohol significantly increased for a minority of this retiree population [71]. Those who increased their intake of alcohol were more likely to be affluent, highly educated, male, Caucasian race, less religious, and unmarried. Interestingly, those who increased their alcohol intake also perceived themselves to be in excellent health [71].

Question 7.13

A. What Are Two Broad Categories of Illicit Substance-Abusing Older Adults?

Older adults appear to have a unique profile compared to that of younger drug users. Roe et al. describe two groups of older illicit drug users: early-onset and late-onset [7]. "Early-onset" users, which represent the more common group, include individuals with a long history of drug abuse that persisted into older age; "late-onset users" developed substance abuse problems later in life. Late-onset use is estimated to account for <10% of substance abuse in older adults [72].

The onset or worsening of systemic medical and psychiatric illnesses (e.g., depressive disorder, major neurocognitive disorder/dementia, and chronic systemic medical problems) and social factors (e.g., social isolation, financial stressors, poor support) are associated with late-onset illicit substance use [5]. The use of illicit substances among older adults appears to be increasing in the USA. Between 2002 and 2009, the use of illicit drugs for adults ages 50–59 nearly doubled from 5.1 to 9.4% [73].

B. What Are Some Common Brief Screening Tools Used for Geriatric Substance Use?

Brief screening tools can assess the level of risk caused by substance use. Some screening instruments for substance use are adaptations of instruments initially

designed for younger adults, whereas others have been particularly created for older adults. Interviewing screening tools, or self-report instruments, are less intrusive to the older adults than blood or urine tests. Additionally, laboratory tests used for screening (e.g., liver function) have limited utility and can be problematic in older adults, because differentiating impaired functions due to alcohol use or other substances versus due to prescribed medications may be difficult. Some of these instruments with applicability to older adults are listed in Table 7.1 [74].

Table 7.1 Select brief screening tools for geriatric substance use [74]

Screening instrument	Description
CAGE and CAGE-Adapted to Include Drugs (CAGE-AID)	A four-item question tool: (1) Have you ever felt you should *c*ut down on your drinking or drug use? (2) Have people *a*nnoyed you by criticizing your drinking or drug use? (3) Have you ever felt bad or *g*uilty about your drinking or drug use? (4) Have you ever had a drink or used drugs first thing in the morning (*e*ye opener) to steady your nerves or get rid of the hangover? Cutoff score: two affirmative answers; some suggest only one affirmative answer when screening the older patients. CAGE and CAGE-AID do not distinguish between current and lifetime substance use
Michigan Alcoholism Screening Test—Geriatric Version (MAST-G)	A 24-item tool that includes age-specific consequences. Cutoff score: five affirmative responses. Its length may hinder routine use even in shortened form (ten questions with cutoff of two positive responses). It is sensitive to capturing alcohol use disorders in older adults but does not distinguish recent from remote drinking behavior
Alcohol Use Disorders Identification Test (AUDIT)	A ten-item tool that focuses on consumption. Cutoff score: eight affirmative responses in the general population (five for older adults). It is less sensitive than the CAGE
Alcohol-Related Problems Survey (ARPS)	An 18-item, self-administered tool developed for use in geriatric patients with medical comorbidity or who used medications that placed them at risk for adverse events. It detects hazardous and harmful drinkers usually not identified by the CAGE-AID, MAST-G, and AUDIT
The Comorbidity-Alcohol Risk Evaluation Tool (CARET)	Its precursor is the Short ARPS. It identifies at-risk or problem alcohol use among older adults with more sensitivity than the AUDIT and the MAST-G
Screener and Opioid Assessment for Patients with Pain (SOAPP)	A brief, self-administered tool used to assess suitability of long-term opioid therapy for chronic pain patients
Current Opioid Misuse Measure (COMM)	A brief, self-report measure of current aberrant drug-related behavior

Adapted from Hategan A, Bourgeois JA, Saperson K, Chiu S. The chief psychiatric complaints. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 101–140; used with permission from Springer

Question 7.14

The patient is a 65-year-old white male with a history of IV heroin abuse, which has been treated in a methadone maintenance program with daily observed administration of methadone, current dose of 75 mg per day. He is admitted to the hospital after a compound fracture of the tibia requiring external fixation. Postoperatively, he required higher than typical doses of morphine for pain relief, despite the orthopedic team continuing his previous dose of methadone. Your consultation team is called to "see him because he is drug seeking, even though we gave him methadone. Make him stop requesting pain meds and transfer him to psychiatry for an evaluation."

A. Given the Above Narrative, What Items Do You Want to Obtain on Chart Review Before Seeing the Patient?

Chart review should include medication administration record for the actual doses received of methadone and any other opioids; in addition, any medications which have the potential for drug-drug interactions with methadone and other opioids need to be searched for. Due to the possibility of methadone affecting the QTc, a 12-lead electrocardiogram (ECG) is needed. In any substance abuser, it is reasonable to obtain a urine toxicology.

Case continue: You go to see him. He is writhing on the bed in obvious distress, with some restlessness verging on mild agitation (Richmond Agitation and Sedation Scale (RASS) +2). He denies any psychiatric illness other than opioid use disorder. He says that his injured extremity "is a 10/10 pain, the only thing that helps is morphine, the methadone is not enough, and only the IV morphine works very much."

B. What Are Some Items You Want to Focus on in Your Formal Interview/Mental Status Testing?

He has a high delirium risk, so assessment of attention and concentration, formal cognitive assessment (e.g., Montreal Cognitive Assessment (MoCA)) and psychotic symptoms only noted since the injury and surgery should be done. He has a high risk of depressive disorder, so assessment of depressive symptoms (ideally with a Hamilton Depression Inventory (Ham-D)) is indicated. Chronic substance users have an increased risk of major neurocognitive disorder, which would render an abnormal MoCA score without other clinical signs of the delirium syndrome. He needs to be screened for suicidal ideation; such could be seen in concert with an elevated Ham-D score attributable to a major depressive episode or, without an elevated Ham-D score, could represent maladaptive coping with the stress of injury, leading to adjustment disorder.

Case continued: His affect is anxiously dysphoric, occasionally tearful, and nonmelancholic. He denies suicidal ideation "right now, but if I don't get my pain meds,

I don't know what will happen." He scores a 22/30 on the MoCA and denies psychotic symptoms. Ham-D is 20 (moderate severity), with notable sleep-related symptoms and physical complaints noted.

C. What Is the Differential Diagnosis at This Point?

The diagnosis is opioid use disorder. There is no evidence of a withdrawal syndrome nor intoxication per se. His Ham-D is supra-threshold for a major depressive episode. He is not psychotic. His cognitive impairment is nonspecific; this score is not unusual in depressive disorder or could represent mild delirium or mild neurocognitive disorder.

D. What Are Some Useful Interventions at This Point?

While he is not delirious (or at least, not clearly delirious at present), he remains delirium-prone, so standard delirium precautions are indicated (e.g., avoidance of anticholinergics and benzodiazepines, minimization of opioids). It is extremely unlikely that he would tolerate a decrease in methadone dose so the habitual 75 mg daily dose should continue; a cautious increase could be considered due to the acute pain. Alternatively, brief use of other opioids (e.g., morphine) to treat the acute orthopedic injury in the short term can be considered. Adjunctive pain treatments (e.g., noradrenergic antidepressants, pregabalin, gabapentin) can be considered so as to minimize the burden of opioids.

E. What About Psychotherapy?

He should participate in a substance abuse group; more acutely, a cognitive behavioral therapy (CBT) approach to pain management is indicated. Techniques such as mindfulness, biofeedback, and relaxation training can help to address some of the pain from the acute trauma in a patient with opioid use disorder.

Question 7.15

The patient was a 65-year-old white male. He had a long history of alcohol use disorder, with typical consumption of a fifth of vodka per day (approximately 750 mL per day). He was unemployed and lived in a single room occupancy hotel in an impoverished part of the city. He was estranged from his family members and had little social support. He frequently presented to the ED in an intoxicated state. Despite repeated attempts at rehabilitation, he continued to use alcohol daily.

He was brought to the ED yet again intoxicated. You are covering the ED for the consultation-liaison service. The ED physician calls you "This guy is here,

drunk again. He is clearly self-destructive, drinking himself to death, like Nicholas Cage's character in *Leaving Las Vegas*. He must be suicidal, so place him on a psychiatric hold for 'danger to self'."

A. What Initial Evaluation Is Needed in the ED?

Delirium must always be considered in any ED presentation, especially in a geriatric patient. Despite the clear history of alcohol use disorder in this case, delirium (possibly attributable to other illness(es)) must be ruled out. As such, a metabolic panel, liver-associated enzymes, complete blood count (CBC), thyroid-stimulating hormone (TSH), B_{12}, urinalysis and toxicology, and blood alcohol level should be ordered. CT scan is not routinely indicated, unless there is evidence of a traumatic brain injury (TBI) or lateralizing neurological signs. Electroencephalogram (EEG) test is not indicated.

B. What About the ED Physician's Request for a Psychiatric Commitment Order Based on Self-Destructive Drinking?

The usual context of psychiatric commitment orders on the basis of "danger to self" is usually interpreted as acute suicidal ideation with *imminent* intent of self-destruction. In most jurisdictions, and by usual practices, *chronically* self-destructive behavior by substance use is not considered to meet the "imminent" standard. Some jurisdictions may allow for involuntary commitment of "chronic inebriation," but the specifics of these laws may not allow for acute commitment in this context. In the case where a patient is acutely suicidal in the context of substance abuse, a psychiatric commitment may be appropriate.

Case continued: You examine him. He is disheveled, somnolent, and poorly groomed and makes scant eye contact, and his affect is blunted. He is oriented to person, place, and time and denies acute suicidal ideation or psychotic symptoms. He admits to daily alcohol use. He says he is "depressed because I can't manage to stop drinking." He struggles to score an 18/30 on the MoCA. His laboratory studies include a blood alcohol level of 200 mg/dL (43.4 mmol/L). Of note, over 80 mg/dL (>17.4 mmol/L) is considered positive for driving under the influence (DUI) in most countries. Other laboratory studies are unremarkable.

C. What Should You Do Acutely to Manage Him?

He is at high risk for Wernicke-Korsakoff syndrome so he should receive IV thiamine 500 mg TID. He needs to be monitored for alcohol withdrawal.

D. What About His Mood State?

His mood may be dysphoric due to the acute effects of alcohol. As he detoxifies, his mood state may improve as the alcohol level decreases. A depressive episode that persists well after detoxification may be diagnosed as alcohol-associated depressive episode. Some patients may be acutely suicidal while intoxicated; with detoxification, suicidal ideation may abate.

E. What Else Would You Do to Manage Him?

He needs to be monitored for alcohol withdrawal with a Clinical Institute Withdrawal Assessment for Alcohol (CIWA) or CIWA-Ar (revised version) protocol at least until he is no longer intoxicated and no longer at risk for withdrawal. Physical examination is necessary to screen for the stigmata of alcohol use disorder (e.g., liver disease, telangiectasia).

F. What About His Psychiatric Management?

He needs continuing monitoring of his mood state. He needs motivational interviewing to ascertain his interest in rehabilitation. Due to his inability to persistently stop drinking with prior attempts at rehabilitation, he may well be a candidate for inpatient or residential alcohol rehabilitation. During his time in rehabilitation, social services will need to arrange for appropriate aftercare to include outpatient substance use services.

Question 7.16

The patient was a 65-year-old white male, well known to the local ED for his prodigious alcohol binges "atop" his daily use of alcohol. At his peak of alcohol consumption, he would drink 2 gallons of whiskey a day. His wife, not wanting him to drive while impaired (he had had many DUIs, a license suspension, and incarceration for impaired driving) would purchase gallons of whiskey "by the case" and keep a steady supply at home "that way, at least I know he isn't driving impaired. I know he won't stop drinking, it's hopeless, so at least he isn't hurting anyone."

He was brought to the ED by his wife in a state of agitated confusion. When you speak to her, she reports "he can only (sic) drink a gallon of whiskey a day for the last week; he says his alcoholic gastritis and pancreatitis are worse, that makes him nauseated." She denies that he has been using any other drugs ("He is just an alcoholic, not an addict or anything") and he has not been taking any new medications.

A. How Much Is It Safe to Drink in Older Age?

Some of the characteristics of substance use among older adults are presented in Table 7.2 [75]. According to The National Institute on Alcohol Abuse and Alcoholism, the low-risk drinking limit, or the recommended consumption of alcohol, in those aged 65 years or older is lower than for younger adults [75]. The low-risk drinking guidelines for older adults who are healthy and do not take medications should not have more than:

- Seven standard drinks in a week

The guidelines for "a standard drink" are shown in Fig. 7.1. Drinking more than these amounts puts people at risk of serious alcohol problems. However, women

Table 7.2 Characteristics of substance use among older adults [75]

Abstinence	Low-risk use	At-risk (hazardous) use	Problem use
No substance use	Drinking within recommended guidelines (≤7 standard drinks per week; ≤2 drinks on any one occasion) Use of only appropriate/ prescribed or over-the-counter medications No guidelines for low-risk illicit substance use	Drinking beyond recommended guidelines Drinking while taking medications Taking medication that is not prescribed directly for that patient Any use of illicit substances	Substance use that results in social, psychological, or medical consequences, regardless of quantity or frequency of substance use Problematic substance user may or may not meet criteria for substance use disorder

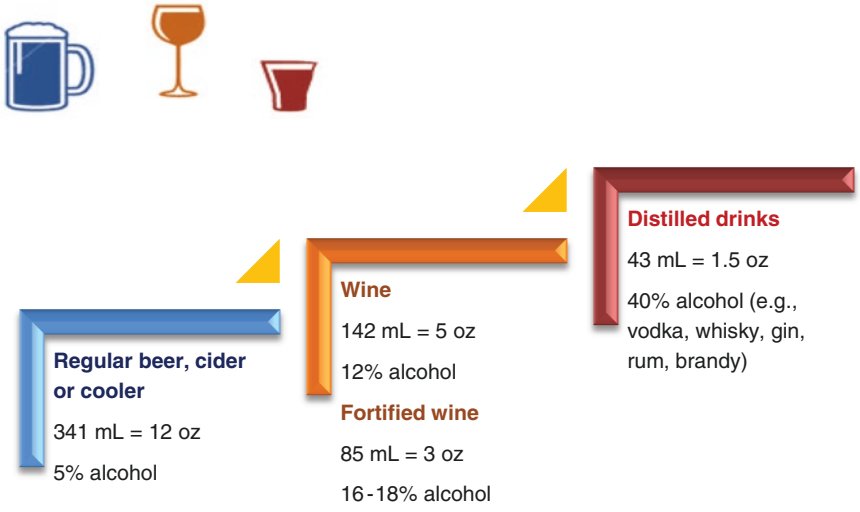


Fig. 7.1 Guidelines for one standard drink

should drink less than men. This is because women, on average, have less water in their bodies than men. Because alcohol disperses in body water, blood alcohol concentration in women tends to be higher than in men.

B. What Are the Diagnostic Possibilities to Consider in This Case Scenario?

He may be intoxicated despite the relatively "lower" levels of alcohol consumption (compared to his baseline), particularly if he is experiencing liver failure rendering him unable to metabolize his usual doses of alcohol. He may be in withdrawal (despite 1 gallon of whiskey/day) if this represents a *decrease in his habitual dose*. He may have taken other drugs that his wife is unaware of, or she may not be disclosing other substance use. He is highly delirium prone, so a delirium workup is needed.

Case continued: The ED physician calls you. "He's here again. When is he going to knock it off? Please evaluate him."

C. What Studies Do You Want the ED Physician to Order Before You See Him?

A minimum laboratory panel would be blood alcohol, urinalysis and toxicology, metabolic panel, liver-associated enzymes, CBC, amylase/lipase, TSH, and B_{12}. Neuroimaging can be considered; it should be done urgently for any history of TBI or lateralizing neurological signs. EEG is not indicated unless seizure activity is noted.

Case continued: You go to the ED. He is hypertensive, febrile, and tachycardiac, with a coarse tremor and diaphoresis. He is hyperalert, restless, and mildly agitated, consistent with a RASS of +2. He denies suicidality but complains of "seeing bugs all over the place, right over there (he gestures toward the corner of the room)" and also says "how did all those guinea pigs get in here? There must be a dozen of them, running around!" His affect is anxiously perplexed, he is perseverative, and he scores only 12/30 on the MoCA.

D. What Is the Likely Cause of His Symptoms?

The hyperadrenergic vital signs, restless agitation, and visual hallucinations are classic for alcohol withdrawal delirium (see Table 7.3 for common benzodiazepine withdrawal symptoms) [76]. Other causes of delirium need to be ruled out as well.

E. How Can He Have Alcohol Withdrawal Delirium with 1 Gallon of Whiskey per Day?

While admittedly a bit paradoxical and counterintuitive, the mechanism of alcohol withdrawal delirium fits this case. His habitual dose of alcohol of 2 gallons of

Table 7.3 Symptoms suggestive of benzodiazepine withdrawal [76]

Benzodiazepine withdrawal symptoms	Perceptual distortions (e.g., false sense of movement, distortions of body image)
	Depersonalization
	Derealization
	Paresthesias (e.g., numbness, tingling)
	Formication (i.e., crawling sensation on the skin, as from ants)
	Sensory hypersensitivity (e.g., to light, sound, taste, smell)
	Abnormal motor activity (e.g., myoclonic jerks, twitches, fasciculations)
	Tinnitus
	Psychotic symptoms (e.g., visual and/or auditory hallucinations)[a]
	Delirium[a]
	Withdrawal seizures[a]

From: DeVido J, Hirsch CH, Sanger N, Rosie T, Samaan Z, Bourgeois JA. Substance Use Disorders in Late Life. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018; used with permission from Springer

[a]Usually limited to rapid or abrupt withdrawal from a high dose of benzodiazepine

whiskey a day establishes a "set point" of GABA agonism that becomes the "new normal" over time. When the habitual dose of alcohol in an alcohol-dependent patient is abruptly decreased, the relative GABA agonism is decreased, triggering a hyperadrenergic response that is clinically manifesting as alcohol withdrawal delirium.

Case continued: His laboratory studies are back. He is mildly anemic and has elevated liver-associated enzymes and increased INR, amylase, and lipase. Blood alcohol level is 234 mg/dL (50.8 mmol/L), and toxicology, TSH, and B_{12} are all negative.

F. How Can He Be in Withdrawal with a Blood Alcohol of 234 mg/dL (50.8 mmol/L), Which Is Three Times the Legal Limit for Driving a Motor Vehicle?

Despite the paradox, it is likely that his "usual" blood alcohol level is well above the current level, triggering a hyperadrenergic alcohol withdrawal delirium. This illustrates that the manifest blood alcohol level in the usual "intoxicated" range is not necessarily reflected in the patient manifesting alcohol intoxication syndromally; in fact, he is in *withdrawal*.

G. How Would You Manage Him?

Other causes for delirium need to be considered and standard delirium precautions are needed. He is at profoundly high risk for alcohol withdrawal seizures

and aspiration so needs to be admitted to ICU for CIWA-Ar protocol and management with IV benzodiazepines. Due to the profound alcohol dependence, extremely high doses of benzodiazepines may well be required; benzodiazepine dosing is primarily driven by the degree of vital sign elevation and delirium symptoms. He needs IV thiamine 500 mg TID for 3 days and then oral thiamine thereafter.

H. What About the Bugs and Guinea Pigs? Does He Need an Antipsychotic?

If he only is psychotic in the context of the hyperadrenergic state of alcohol withdrawal, the primary treatment (even for the psychosis) is benzodiazepines. Should psychosis persist after the vital signs renormalize, one can consider cautious dosing of an antipsychotic considering the probability of impaired hepatic clearance, but recall that antipsychotics can lower the seizure threshold, so caution is advised.

Question 7.17

The patient was a 68-year-old white male. He had a long history of polysubstance abuse since his early 20s. In the past years, he was a heavy user of alcohol and heroin and contracted hepatitis C virus (HCV) from the use of IV heroin. Later in life, he switched to primary abuse of methamphetamine, which he would take orally or IV with a binge/crash pattern.

During a several day binge, he would become psychotic (with delusions of grandiosity, hyperkinetic states, and little need for sleep) which naïve clinicians interpreted as "bipolar disorder" though he never had sustained mood episodes in the absence of stimulant abuse. To finance his habit, he became a methamphetamine producer and dealer. Unfortunately, while intoxicated and preparing methamphetamine with an open flame, he caused an explosion that left him with facial and truncal burns and led to his home burning down. Due to his intoxication and facial swelling which impaired his vision, he was barely able to cooperate with the first response crew from the fire department and briefly became belligerent when told that he needed to be hospitalized.

He was initially brought to a community hospital ED near his home in a remote area of the state. They provided initial care and stabilization but quickly ascertained that his burn injury would require transfer to a burn unit. He was urgently sent by medical helicopter to an academic medical center burn unit several hundred miles away.

You are on call for the consultation-liaison service at the academic medical center. The trauma surgery fellow managing the patient calls in a consult and speaks to you: "You need to see him right away. He blew himself up. This must be a suicide attempt. Once he is cleared he will need a transfer to inpatient psychiatry."

A. Based on This Narrative Alone, What Psychiatric Differential Diagnoses Are to Be Considered?

Any acutely seriously ill and/or injured patient needs to first be evaluated for delirium. Delirium is especially common in acute burn injury patients, due to various factors including risk of infection, use of often prodigious doses of opioids, fluid and acid-base disorders, and other injuries. In his case, chronic use of methamphetamine puts him at risk for major neurocognitive disorder due to vascular disease. The narrative is clear for psychostimulant use disorder; at present you need to ascertain if he is acutely intoxicated or in active withdrawal.

With more subtlety, as this does not require acute management, recall that adult residual attention deficit hyperactivity disorder (ADHD) often leads to patients self-medicating with psychostimulants. Lastly, due to his other (perhaps mostly past) abuse of substances, he needs assessment for other substance use disorders.

B. Based on the Referral Narrative, How Would You Approach the Laboratory Workup?

Delirium rule out is the primary need. Therefore, standard delirium surveillance laboratory studies are ordered; metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, calcium, urinalysis and toxicology, and blood alcohol level are needed. Based on his history of HCV, a hepatitis panel and ammonia are reasonable. While it would not change the acute management, neuroimaging to look for cortical atrophy and/or vascular disease is indicated. There is no role for EEG at this time.

Case continued: You go to the burn ICU to examine him. Vitals are normal. He exhibits psychomotor retardation. His eyes are closed; he arouses only fleetingly to speech and cannot maintain eye contact for more than 20 s. He is dysphoric and tearful but denies suicidal ideation or homicidal ideation. He does endorse paranoid-spectrum fears of "the authorities" who he claims "have it in for me," but he denies hallucinatory phenomena per se. He struggles to score a 14/30 on the MoCA. Laboratory studies reveal methamphetamine on toxicology, mildly elevated white blood cell (WBC) count, and increased aspartate transaminase (AST) to alanine transaminase (ALT) ratio.

C. What Is Your Differential Diagnosis at This Time?

The altered level of consciousness (LOC) and moderately impaired MoCA are consistent with delirium. Major neurocognitive disorder cannot be accurately diagnosed while a patient is delirious. Methamphetamine intoxication in isolation would produce hypertension, tachycardia, and psychomotor restlessness/agitation. It is not possible at present to completely separate psychostimulant withdrawal from delirium (a urine toxicology for methamphetamine is positive for several days after last administration so a withdrawal state must be diagnosed clinically).

He is at risk for depressive disorder associated with stimulant use. He is at risk of adult residual ADHD. A depressive episode is possible, even probable, but cannot be diagnosed at present. From the trauma of the explosion and injury, he is at risk for acute stress disorder/posttraumatic stress disorder.

D. How Will You Manage Him Presently?

Management of burn patients, who have a high risk for delirium categorically, is challenging. Routine burn unit procedures (e.g., debridement, dressing changes) require premedication with opioids and benzodiazepines, which increases delirium risk. Often, dressing changes are done every few hours, which can interrupt needed sleep, further potentiating the delirium risk. With that in mind, a minor modification of standard delirium precautions is needed. An antipsychotic administered on demand (PRN) for agitation (which makes burn injury management much more challenging) is needed. Serial reassessment and monitoring of MoCA scores for checking cognitive status is needed.

Case continued: You effectuate the above plan. When you see him the next day, he is still somnolent with psychomotor retardation. He still struggles to open his eyes to participate in the interview. His MoCA score is 16/30, and he denies suicidal ideation and delusions today. You talk to the general surgery resident. His burn injuries will not require surgery but he will need frequent dressing changes for at least 2–3 weeks.

Over the next several days, his LOC gradually improves to where he is spontaneously awake when you see him. His is distressed over his circumstances but not suicidal nor psychotic. With occasional PRNs of quetiapine, he is generally sleeping well, other than when his dressings are changed. On subsequent examinations, his MoCA score improves to 22/30 and plateaus at that score.

E. What Is the Diagnosis at Present?

He is likely no longer delirious, or at least it is much improved. His MoCA score of 22 is not consistent with a major neurocognitive disorder. His gradual improvement in mood and affect and improved LOC/psychomotor state are consistent with resolving stimulant withdrawal, although he remains delirium-prone.

F. What Are the Intervention Imperatives Now?

Continued delirium precautions and use of PRNs for control of agitation are necessary. Continue to monitor his mood and cognitive state and be vigilant for onset of acute stress disorder. In this circumstance, the traumatic experience leading to acute stress disorder could be the explosion and fire or "iatrogenic" acute stress disorder induced by painfully traumatic medical/surgical procedures.

You need to engage him on the topic of substance abuse rehabilitation to see where he stands on stages of change model. This may be a fortuitous time to consider inpatient or residential substance use treatment given the seriousness of his

injuries experienced during a period of uncontrolled substance use. Continued vigilance for acute stress disorder and depressive disorder with a low threshold to offer psychopharmacologic and other psychiatric interventions is necessary if he rules in for depressive disorder in the context of substance abuse. Regarding ADHD, if he rules in for this, you could offer him a psychopharmacologic intervention that does not include psychostimulants due to the risk of misuse of prescribed medications.

Other medications are also available to assist patients like this one in maintaining their sobriety (see Table 7.4 for a list of maintenance medications for substance use disorders approved by the US Food and Drug Administration and Health Canada [76]).

Table 7.4 Maintenance medications for substance use disorders approved by the US FDA and Health Canada [76]

Maintenance medication	Indicated substance use disorder	Proposed mechanism of action
Naltrexone (oral and available in long-acting injectable (Vivitrol®) formulation[a])	Opioid use disorder Alcohol use disorder	Competitively antagonizes mu-opioid receptors, decreasing reinforcement from endogenous opioids (alcohol) and blocking binding of exogenous opioids (e.g., heroin)
Disulfiram[b]	Alcohol use disorder	Irreversible inhibition of aldehyde dehydrogenase, resulting in toxic accumulation of acetaldehyde when alcohol is consumed
Acamprosate	Alcohol use disorder	Central glutamate and GABA modulation
Bupropion	Tobacco use disorder (smoking cessation)	Weak reuptake inhibition of norepinephrine and dopamine, but the mechanism of action relating to smoking cessation is unknown
Nicotine (available in transdermal, sublingual/transbuccal, intranasal, inhaled formulations)	Tobacco use disorder (smoking cessation)	Nicotinic cholinergic receptor agonist replacement
Varenicline	Tobacco use disorder (smoking cessation)	High affinity nicotinic acetylcholine receptor binding, producing agonist effects
Methadone	Opioid use disorder	Mu-opioid receptor full agonist replacement
Buprenorphine (available in diversion-deterrent formulation in combination with naloxone)	Opioid use disorder	Sublingually available, mu-opioid receptor partial agonist replacement

From: DeVido J, Hirsch CH, Sanger N, Rosie T, Samaan Z, Bourgeois JA. Substance Use Disorders in Late Life. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018; used with permission from Springer

[a]Approved for use in the USA

[b]No longer approved for use in Canada

Question 7.18

The patient was a 65-year-old white female with a long history of "terrible anxiety." She experienced onset of illness in her 20s, in the context of establishing her family and career. Resisting pursuing psychotherapy at the time, she was treated by her primary care physician with diazepam, initial dose 5 mg "two or three times a day" with improvement in symptoms and better social function. She was advised not to co-administer alcohol with diazepam, and other than "social drinking, a glass or two of wine now and then," she largely complied. She continued her use of diazepam for 40 years, with gradual dose escalation to 10 mg three times a day. Admonished by her primary care physician to get the dose under control, she occasionally attempted to decrease her dose, only to experience "return of the terrible anxiety, I would just go to pieces and tremble" when lower doses were tried.

Her primary care physician is unwilling to continue the current dose of diazepam. Resisting this intervention, she refused to see the primary care physician again. While seeking a new, perhaps more compliant, primary care physician, she ran out of her diazepam. She presented to the ED complaining of "terrible anxiety, like I want to jump out of my skin, tremors, I can't cope with this, I need my diazepam."

Your consultation-liaison team is covering the ED. The ED physician calls you "This patient is new to us. She is drug seeking and has been using diazepam forever. She must have a psych disorder. She needs to be admitted to psychiatry to get her under control."

A. What Initial Laboratory Data Do You Want the ED Physician to Order Before You See Her?

With any acute change in mental status, delirium is the first consideration. She may well have acquired cognitive impairment from her chronic use of benzodiazepines which would predispose her to delirium. A screening physical examination and screening laboratory assessments are indicated. Metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis and toxicology, and blood alcohol level would be a minimal delirium screening workup.

B. What Are the Diagnostic Considerations Based on the Case Narrative So Far?

Benzodiazepine use disorder, benzodiazepine withdrawal, alcohol use disorder, major neurocognitive disorder, delirium, generalized anxiety disorder, and panic disorder all must be ruled out. Depressive disorder can have a substantially anxious presentation.

Case continued: You go to the ED to see her. Vital signs include mild tachycardia and systolic hypertension and fine tremor in the distal upper extremities and voice. RASS is +1. Her affect is anxious, non-tearful, and non-melancholic; there are no suicidal or homicidal ideations and no evidence of psychosis. MoCA is 21/30 with 0/5 on delayed recall and 0/3 on concentration. Laboratory studies reveal benzodiazepines on urine toxicology; other laboratory findings are negative or nonspecific.

C. How Do You Interpret the Mildly Decreased MoCA Score?

This score is consistent with mild cognitive impairment, which could represent mild neurocognitive disorder due to chronic benzodiazepine use (which could be reversible with benzodiazepine discontinuation), mild neurocognitive disorder due to other mechanism (e.g., early Alzheimer disease), and/or mild delirium in the context of benzodiazepine withdrawal.

D. How Do You Manage Her at This Point?

If she does not have a history of medically complicated benzodiazepine withdrawal (e.g., withdrawal seizures) or other acute systemic illness substantiating an admission, she could be managed as an outpatient. Assuming she is safe for outpatient management, there are two imperatives: (1) managing the benzodiazepine withdrawal state and (2) developing a different plan for chronic anxiety management.

Acute withdrawal is best managed with cautious dose of benzodiazepines under a taper. An initial daily dose approximating her last daily dose of diazepam is reasonable, with close clinical follow-up with the expectation of a weekly (or even slower) taper until the benzodiazepine can be stopped completely. She needs to be confronted that her cognitive status is mildly impaired, and the use of benzodiazepines are likely culpable, and that continued use of benzodiazepines are associated with major neurocognitive disorder, falls, hip fracture, and increased mortality. Concurrently with the benzodiazepine taper, alternative chronic psychopharmacologic treatment for anxiety disorder is indicated.

E. What Are the Pragmatic Options for Chronic Antianxiety Treatment?

Two approaches, which can be combined, include an antidepressant and buspirone. Due to their other side effects, tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) are not indicated. Assuming that she does not have a risk for acute bleeding or syndrome of inappropriate antidiuretic hormone secretion (SIADH), a trial of a selective serotonin reuptake inhibitor (SSRI) antidepressant is indicated. This should be dosed the same as it would be for a depressive disorder

case. Buspirone can be initiated at 5 mg TID and titrated as needed to an upper limit of 20 mg TID.

F. What if She "Needs" a PRN for Anxiety?

For unequivocal panic disorder (which this narrative does not support), cautious dosing of a short-acting benzodiazepine for PRN use only can be cautiously considered. Non-benzodiazepine alternatives include hydroxyzine, trazodone, and quetiapine.

G. What About Her Abnormal MoCA Score?

To ascertain whether the MoCA score is due to the chronic use of benzodiazepine, reassessment of MoCA in 1–2 months after the last daily dose of benzodiazepine is indicated. Improvement in MoCA score at that point is indirect, but persuasive, evidence of reversible cognitive impairment due to benzodiazepines. If she fails to improve her MoCA score, a full workup for major neurocognitive disorder (to include neuroimaging) is then indicated, as would be consideration of a trial of "cognitive enhancer".

Question 7.19

The patient is a 65-year-old male with a long history of methamphetamine abuse, with both a daily and binge pattern. He is also involved in manufacture and distribution of methamphetamine, for which he has served time in prison. Despite the forced abstinence during prison, he promptly returned to methamphetamine abuse upon release and continues in this pattern of use.

He has a history of highly probable but never treated ADHD with childhood onset poor attention, poor task completion, impulsivity, and irritability. As a result, he repeatedly failed to meet educational milestones and had an irregular career progression, with many job changes, and impulsive relocations for unclear reasons. Interpersonally, he has had four marriages, each of which ended in divorce due to his substance abuse and other impulsive behaviors. He has had episodes (heretofore not treated) of apparent depressive disorder, in the context of ongoing substance abuse and social chaos. He has never been treated with psychotropic medications and has never been hospitalized.

He presents to the ED after yet another binge on methamphetamine. He was using methamphetamine essentially around the clock for 4 days, with no sleep, irritable grandiosity, visual hallucinations, and motoric hyperactivity. He was disruptive in his neighborhood, yelling and causing a disturbance, which led neighbor to call the police. Upon apprehension by the police, he was irritable and marginally cooperative.

The police, aware of his substance abuse history from multiple prior similar encounters, placed a psychiatric commitment order rather than arresting him and brought him to the emergency room. The ED physician calls you "This meth guy is here again, he is acting out, really psychotic this time. The police put him on a psych hold. He is medically cleared; get him out of the ED and onto psych right away. He is bothering all the patients with real illnesses."

A. What Are the Diagnostic Possibilities to Explain This Presentation?

Acute change in mental status especially in an older patient can always represent delirium, which is the most important psychiatric illness to consider in ED presentations. A manic episode is possible but new onset bipolar disorder is extremely rare in an older patient. Intoxication with many types of abusable substances (e.g., alcohol, psychostimulants, opioids) can explain this. Acute stroke can cause disinhibited behavior, as can the effects of medications (e.g., corticosteroids, immunosuppressants).

B. What Medical Evaluations and Laboratory Studies Are Needed?

Standard delirium screening laboratory studies (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis and toxicology, and blood alcohol levels) are needed. Brain CT scan is not acutely indicated unless there are lateralizing neurologic signs or history of head trauma. EEG is not indicated. Vital signs and a screening physical exam are needed.

Case continued: You go to the ED. The nurse tells you that once he got to the ED, despite the agitated behavior he has exhibited, "he has been sleeping mostly, ever since he got here. We thought he might get all agitated so we had a lorazepam PRN written, but he hasn't needed it." Per chart review, his pulse and blood pressure have been normal and he is afebrile.

You go to the room to interview him. His is asleep and only awakens with repeated calls of his name. He struggles to maintain eye contact, frequently falling back asleep, and you need to keep waking him up, consistent with a RASS of −2. He can orient to place and partially to time (he cannot tell the exact date but month/year are accurate). He denies suicidality or psychosis. He does admit to daily methamphetamine use with the recent binge but does not recall the events of the last 24 h very well other than the police bringing him to the ED. He struggles with the MoCA, only scoring a 14/30.

C. How Do You Interpret the Current Exam Findings?

Altered level of consciousness makes either intoxication with a sedative or withdrawal from a psychostimulant more probable, as a manic episode will produce a

persistently hyperaroused state. Delirium, which classically features fluctuations in level of arousal, still must be ruled out.

Case continued: You review the laboratory results. His toxicology is positive for methamphetamine but not for other substances of abuse. All other laboratory studies ordered are normal or nonspecific.

D. What Is the Likely Diagnosis at This Point?

The vital signs and normal screening laboratory studies make delirium less likely but vigilance for delirium needs to continue. Given the level of arousal plus positive toxicology, this is likely psychostimulant withdrawal.

E. How Do You Manage Him in the ED?

He does not need scheduled psychotropic medications at this point. You would tell the ED physician that he needs continued observation and conservative management until his level of arousal improves. You would write a PRN antipsychotic (rather than a benzodiazepine) for breakthrough agitation or psychosis.

Case continued: The ED physician tells you, "see, I told you he is a meth abuser. He needs to go to psych and get out of the ED."

F. How Do You Respond?

Depending on the capabilities and practices of the local inpatient psychiatry unit, an admission to monitor mental status is reasonable. Psychostimulant withdrawal is generally benign (unlike sedative withdrawal), with monitoring of oral intake of fluids and electrolyte status and mental status as the primary clinical needs. Depressed mood and neurovegetative signs simulating a major depressive episode are likely; if a major depressive episode persists well past the few days typical of a withdrawal state, a trial of antidepressant is indicated.

Case continued: While not pleased that the patient needs further monitoring in the ED, the ED physician agrees to keep him under observation. You provide observation instructions to the nurses and continue the psychiatric commitment order and tell the ED physician you will see him in several hours.

You return to see him that evening. At this point, he is more alert and now fully oriented, but he is emotionally much worse. He tearfully admits that "this meth thing is like totally out of control. I just can't stop; I feel depressed so much of the time, only meth helps me feel better but only for a while, then around it goes again." He endorses that "sometimes I wish I would die and be done with it."

G. What Do You Do Now?

This new history suggests commingled depressive and substance use disorder. He is unlikely to respond to a treatment solely focused on abstinence only. You would consider the current acute presentation as an opportunity for comprehensive intervention. The best management would be a brief psychiatric admission to begin a course of an antidepressant combined with a recovery focus. Once his mood state is improved, he could be segued to a substance abuse unit (he likely needs inpatient and/or residential care) while continuing the antidepressant indefinitely.

H. What Antidepressant Would You Choose?

Due to his age and delirium risk, you would avoid tricyclic antidepressants (TCAs) and MAOIs. If safe otherwise, a trial of bupropion could be additionally helpful for his chronic ADHD symptoms.

Question 7.20

The patient is a 66-year-old white male with a history of alcoholism and low social function. He has been brought to the ED by the police for public intoxication and agitation. Your team is on call to the ED and receives a call from ED physician: "This guy is a frequent flyer here, big time alcoholic, drinks a gallon of vodka a day, a real mess if you ask me. Please evaluate him and get him to psych. He is medically cleared."

A. What Initial Considerations Come to Mind as You Take This Call?

While there is no reason not to believe the (somewhat superficial to be sure) history from the ED physician, there could be many other reasons for this presentation (none are mutually or collectively exclusive): other substance intoxication/withdrawal, TBI, cerebrovascular event, major neurocognitive disorder, and delirium.

B. What Initial Studies Do You Stipulate Before Going to See the Patient?

A CT scan of the head, blood alcohol level, urine toxicology, metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, calcium, and ECG are minimally needed. An MRI of the head is not necessary but can be considered. There is no role for EEG acutely.

Case continued: You go to the ED. He is grossly disheveled, is somnolent, and makes little eye contact, his speech is dysarthric, and he repeatedly requests "to

leave this hotel, this is not my hotel." He does not directly answer queries about suicidal ideation, appears to be picking at the bedsheets as if removing insects, occasionally turns his head and speaks as to an unseen other, orients only to city, is many years inaccurate on the date, and cannot complete a MoCA test. You try to stand him up and he cannot maintain vertical posture. You note that he has erratic pursuit eye movements. Vital signs include pulse 120 beats/min and blood pressure 160/100 mmHg.

C. The ED Physician Says, "See, I Told You, He Is a Wreck. Well, Get Him to Psych. He Doesn't Need to Be Here." What Do You Do Now?

He is *not* "medically cleared" and needs to stay in ED until this is accomplished and he is safe to disposition.

Case continued: Some of his laboratory studies are back. His CT scan shows severe global cortical atrophy as well as much cerebellar atrophy (vermis more than the lobes), metabolic panel shows mild dehydration, his liver-associated enzymes are elevated to three times the normal, and he is anemic, but TSH and B_{12} are normal. The blood alcohol level is negative, and the urine toxicology is not back yet.

D. How Do You Interpret the Clinical Exam Findings and Physical Exam Findings?

With a negative blood alcohol level, he is by definition not intoxicated on alcohol per se. He is likely in alcohol withdrawal, given his vital signs and altered mental status. His altered mental status and abnormal eye movements are consistent with Wernicke encephalopathy [77, 78]. Wernicke encephalopathy is common in chronic severe alcoholism but is also seen in other nutritional deficiency states. In alcoholic patients, Wernicke encephalopathy can be seen concurrently with alcohol withdrawal or other complications of alcoholism.

E. What Do You Do Next?

While the rest of your workup proceeds, he needs thiamine urgently to prevent him from transitioning to Korsakoff syndrome. He should get thiamine 500 mg IV TID for 3 days then be transitioned to lower doses for maintenance. He needs to receive thiamine before any IV glucose.

F. Then What Do You Do?

Once thiamine is delivered and future doses scheduled, monitor his mental status and physical exam for improvement in altered mental status and eye movement

abnormalities. Continue to assess him for autonomic signs of alcohol withdrawal with a CIWA-Ar protocol and PRN use of benzodiazepines. Of note, the CIWA-Ar symptom checklist contains features common to delirium related to other medical conditions, and therefore these symptoms may be solely attributed to alcohol withdrawal, potentially resulting in excessive use of benzodiazepines.

G. What About Your ED Colleague's Insistence That He Be Transferred to Psychiatry Ward?

This will depend on local resources. As long as he needs IV thiamine and IV benzodiazepines to manage Wernicke encephalopathy and alcohol withdrawal acutely, he needs to be on a unit that is competent to manage IVs. Some inpatient psychiatry units (particularly geriatric psychiatric units and medical/psychiatric units) are capable of this level of medical management. Otherwise, he needs to be admitted to internal medicine and co-managed by internal medicine and consultation-liaison psychiatry.

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Topic 8: Comorbid Systemic Medical and Psychiatric Illness in Older Adults

Question 8.1

Serotonin syndrome. The patient is a 67-year-old white male. He has a long history of anxious depressive disorder, for which his primary care physician initiated fluoxetine 20 mg per day 10 years ago. He initially did well for several years, but with major psychosocial stressors (retirement and illness in his wife), his depressive disorder worsened. In response, his primary care physician then increased the fluoxetine to 40 mg per day. He initially responded well to the dose increase, with less depressed mood and distress, but 6 months later, he experienced breakthrough anxiety. His primary care physician recommended a psychiatry consult, but the patient refused. Seeking to relieve the newly worsened anxiety, the primary care physician then added buspirone 5 mg TID, titrated to 10 mg TID. On this regimen, he was improved for several months.

Unfortunately, his wife then developed a terminal illness and died 6 months later, with the patient caring for her at home during her terminal phase. In the context of bereavement, he was now unable to sleep, ruminating about his loss. His primary care physician again recommended a psychiatric consultation, which he still refused, stating "It's not anxiety or depression, it's the sleep. I will be OK if I can just sleep. Can I have zolpidem?" The primary care physician, wary of using zolpidem in older patients, instead added trazodone, 50–150 mg at bedtime for sleep.

A. What Are Some Strategies for Managing Sleep in This Patient?

The preferred intervention would be cognitive behavioral therapy (CBT) for chronic insomnia [1]. Alternative therapy models include CBT for depression/anxiety, supportive psychotherapy, or grief counseling. Medication approaches are plentiful, but all have their own risks. Benzodiazepines, zolpidem, and similar GABA-active agents have dependence potential and the risk of precipitating delirium, in addition to falls and somnambulism. Sedating antipsychotics have variable risk of QTc

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_8

prolongation, metabolic syndrome, and nonspecific mortality risk (the latter is only clear when used in major neurocognitive disorder). Sedating antidepressants (trazodone, mirtazapine) can be tried, as can melatonin.

Case continued: He initially experienced improved sleep and stabilization of function and reported that he was doing a bit better in managing his grief. Suddenly, he developed agitated confusion and called 911, fearful that he was having a "heart attack." When the medical team arrived, he was speaking largely nonsensically and was anxiously agitated. He was brought to the emergency department (ED). You are on call for the ED and the ED physician calls you: "This man's depression and anxiety are severe. He cannot think straight and he is very restless and confused. He needs to be admitted to psychiatry for ECT as his psychiatric medications are obviously not working." You ask for a review of his medications, which the ED physician tells you over the phone.

B. What Are the Diagnostic Probabilities?

Acute change in mental status always leads to a rule out of delirium, though you do not know if he has had prior episodes of delirium and there is no evidence of a diagnosis of major neurocognitive disorder (formerly dementia). Substance intoxication needs a rule out. Depressive disorder with psychotic features is unlikely to develop in the context of his robust antidepressant and antianxiety treatment. Bipolar disorder would not typically have an onset at this age. Panic disorder can cause an acute presentation of agitation, but a panic attack would last less than 1 h.

C. What Laboratory Studies Do You Ask the ED Physician to Order?

Standard "delirium assessment laboratory studies" include renal panel, liver-associated enzymes, complete blood count (CBC), thyroid-stimulating hormone (TSH), calcium, vitamin B_{12}, electrocardiogram (ECG), blood alcohol, urinalysis, and urine toxicology. A brain computed tomography (CT) scan, although reasonable, is not necessarily indicated in all routine delirium management, nor is an electroencephalogram (EEG) test.

Case continued: You see him in the ED. He is hyperalert, flushed, tremulous, and restless with RASS of +1. He is able to orient to place/time but on formal cognitive testing only scores 15/30 on the MoCA, with deficits in multiple domains. His affect is anxiously perplexed and occasionally tearful. His thought process is perseverative but not grossly disorganized. He is able to tell you that he has taken his medications as directed "but I feel really sick now." On the ED physician's exam, bilateral ankle clonus of unclear significance was found. The laboratory studies are normal except for tachycardia on the ECG.

D. What Is the Diagnosis?

Given the physical and mental status findings, plus negative urine toxicology, the diagnosis is delirium. The context of presentation with the use of multiple seroto-

nergic medications and delirium with ankle clonus is classic for serotonin syndrome [2]. Figure 8.1 shows the spectrum of signs and symptoms in serotonin syndrome [3].

E. How Would You Manage Him?

He needs admission to the hospital for close monitoring, serial exams, and fluid management. All serotonergic medications need to be stopped immediately; reversing the serotonin syndrome is more critical to manage than concern about withdrawal from serotonergic medications. Due to their somewhat similar appearances, neuroleptic malignant syndrome (NMS) is a rule out in serotonin syndrome cases [4]; serial creatine phosphokinase can be followed (see Table 8.1 for main similarities and differences between the serotonin syndrome and neuroleptic malignant syndrome [5]). Lorazepam on-demand (PRN) for agitation can be given, with atypical antipsychotics as an alternative (once NMS is clearly ruled

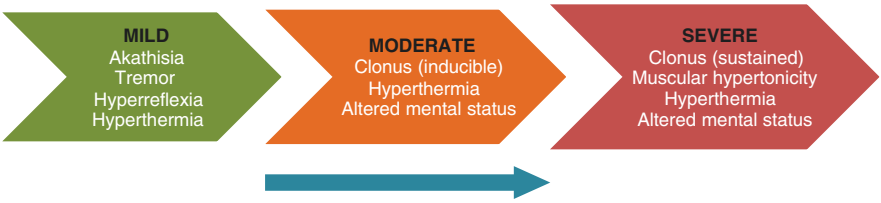


Fig. 8.1 The spectrum of signs and symptoms in serotonin syndrome. Adapted from Hirsch CH, Maharaj S, Bourgeois JA. Pharmacotherapy: safe prescribing and adverse drug events. In: Hategan A et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook. Springer; 2018; Used with permission from Springer

Table 8.1 Similarities and differences between the neuroleptic malignant and serotonin syndromes

Clinical findings	Serotonin syndrome	Neuroleptic malignant syndrome
Vital signs	Hypertension, tachycardia, tachypnea Hyperthermia (T° > 40°C/104°F)	
Skin	Diaphoresis	
Pupils	Normal or mydriasis	
Mucosa	Sialorrhea	
Muscle tone	Increased, primarily in lower extremities	Marked rigidity in all muscle groups
Bowel sounds	Hyperactive	Normal or decreased
Reflexes	Hyperreflexia Clonus	Bradyreflexia
Mental status	Alert to stupor and coma Delirium	

The shaded rows predictably differentiate the two [5]

out). Upon recovery, he needs to not be on this particular combination of serotonergic medications again; though with recovery, cautious restart of one serotonergic medication could be considered, with continuous vigilance for recurrence of serotonin syndrome.

Question 8.2

Neuroleptic malignant syndrome. The patient was a 70-year-old white male with a 45-year history of schizophrenia. He had the onset of psychiatric illness in his 20s, with florid hallucinations and delusions and thought disorganization. He was initially managed with chlorpromazine, then with haloperidol. He had several decompensations over the years, often following minimally disruptive social events. He was never able to manage to maintain employment and was hospitalized in both acute care and chronic care psychiatric facilities. His symptoms never completely resolved. When clozapine became available in the USA in 1990, his psychiatrist recommended a trial, but the patient was unwilling to tolerate the needed blood draws, so it was never started. Some years later, when risperidone became available, he was transitioned to risperidone 2 mg at bedtime. On this regimen, he did relatively well for 10 years or more and was during this time able to avoid rehospitalization. He lived with supportive family members, who sheltered him from social stress and were able to tolerate his paranoid ideation and odd interpersonal style.

A. What Routine Monitoring Should Be Done with Chronic Use of Atypical Antipsychotics?

Irrespective of specific illness indication, ECG (for prolonged QTc), metabolic panel, lipid panel, CBC, and weight assessments should be obtained. With risperidone, it is reasonable to monitor prolactin level, which can be elevated [6].

Case continued: Years later, his psychotic symptoms increased, with more problematic paranoia. To manage these symptoms, his risperidone was increased to 2 mg twice a day. Two weeks later, he is brought to the ED with altered mental status. The ED physician calls you: "This schizophrenic patient is getting psychotic again. He needs to be admitted to psychiatry immediately for a medication adjustment. Please see him right away."

B. What Studies Do You Want to Have Ordered Before You See Him? What Are the Diagnostic Considerations?

Despite his clear history of psychotic illness, *acute* change in mental status needs to be evaluated for delirium. Delirium-associated laboratory studies minimally include renal panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, blood alcohol, urinalysis, and urine toxicology.

C. In Addition to Standard Delirium Laboratory Studies, Does His Illness and Medication History Require Additional Emergent Laboratories?

Delirium in any patient on antipsychotics needs to first be ruled out for neuroleptic malignant syndrome (NMS) with a creatine phosphokinase (CPK); due to his being on risperidone, an ECG to rule out QTc prolongation is also needed. You can consider a prolactin level, but this is not routinely done. EEG would not be needed, but a CT scan would be reasonable.

Case continued: You see him in the ED. He is somnolent, with only fleeting eye contact, RASS −2. His tone is increased with significant, but not "lead pipe" rigidity. His temperature is 102 °F (38.8 °C), and he is tachycardic and hypertensive. Reflexes are decreased. He is oriented to person only. He speaks in nonsensical phrases. Suicidal ideation and psychosis cannot be ascertained. MoCA is 2/30, as he can only identify two animals.

D. What Is the Diagnosis?

The following diagnoses are entertained: neuroleptic malignant syndrome, delirium, and chronic schizophrenia.

Case continued: His laboratory studies reveal pre-renal azotemia, mild anemia, CPK of 2145 IU/L, with negative urine toxicology. All other laboratories are negative or nonspecific.

E. How Do You Manage Him?

Not all elevated CPK cases are NMS [7]. Moreover, there is no agreed-upon clear cutoff point for an elevated CPK level in NMS; however, some use a cutoff point of 1000 IU/L [7]. Due to the dangerousness of NMS in this case, he needs to be admitted to ICU for close monitoring and fluid management. All antipsychotics are held. He needs serial CPKs to monitor clearance of CPK and repeated physical exams for improvement in rigidity. He needs monitoring of renal function due to the risk of rhabdomyolysis. He needs serial psychiatric assessment to monitor progress of delirium. He also needs standard delirium precautions.

F. What About His Antipsychotic Treatment? Won't He Get Extremely Psychotic Without Medication?

He may be well, though his mental status is acutely more affected by delirium than the underlying psychotic illness. For acute agitation, he needs lorazepam PRNs with monitoring for possible worsening of delirium. For prolonged and/or extreme rigidity, dantrolene or bromocriptine can be given.

G. Once He Is No Longer Delirious and His NMS Is Cleared, How Would You Manage Him?

Typical management of post-NMS patients includes several elements. He needs to be admitted to psychiatry unit once he is medically recovered from the delirium, as alternative antipsychotics need to be considered. A common practice is to monitor CPK daily until it is in the normal reference range. Two weeks after that, another antipsychotic medication can be tried.

H. How Do You Decide on an Antipsychotic Post-NMS?

He should not receive the specific NMS-provoking antipsychotic again (in his case, risperidone), which should he labeled as an "allergy" in the electronic medical records (EMRs). The next antipsychotic should be one with a lower propensity to block D_2 receptors, as NMS risk is proportional to D_2 blockade. You can consult standard psychopharmacology texts for complete advice (especially for newly available agents), but a typical medication option in this case would be quetiapine. Even so, vigilance for recurrence of NMS is needed, as there are reported cases of recurrent NMS even with relatively low D_2-blocking agents [8].

Question 8.3

Catatonia. The patient is a 65-year-old white male with a long history of major depressive disorder. He had his first episode in his 30s following social stressors. He was initially treated with nortriptyline 100 mg at bedtime with an eventual good response. He was then maintained on medication for 2 years and then tapered off while clinically stable. His first recurrence was 6 years later, at which time he was restarted on nortriptyline 100 mg at bedtime. This episode proved more resistant to treatment and only responded once lithium 900 mg daily was added. His third episode was in his mid-50s. This episode included melancholic and psychotic features and was ultimately managed with nortriptyline 100 mg at bedtime, mirtazapine 15 mg at bedtime, and aripiprazole 15 mg in the morning. After recovery, his psychiatrist maintained him on all three medications indefinitely.

The patient had been doing relatively well until a month ago, and his family assures you that he has been compliant with medications. Fairly rapidly, however, he has been doing "much worse than ever." He is not sleeping and eating very much, and during the day, "he just sits and stares off, doesn't talk at all unless you talk right to him, even then he doesn't say much." His family continues to struggle to get him to function even at a minimal level. Suddenly, he "just shut down, won't talk, won't even look at us, he is like a zombie." Given that they could no longer manage him, they called the police to bring him to the ED "because he won't even cooperate with his own family. What is going on with him?"

Your team is covering the ED and you get a call from the ED physician: "This depressed patient is doing terribly. He won't even talk, just stares off. He is medically clear and needs psychiatric admission right away."

A. What Are Your Diagnostic Considerations Given the Previous Narrative?

Given the history, recurrent major depressive disorder with melancholic and catatonic features is very likely. Indeed, the association between severe depressive disorder and catatonia is classic. However, catatonia is a "protean" syndrome that can be the "final common pathway" for many psychiatric illnesses (including delirium) and neurologic illnesses [9, 10]. Therefore, even after the syndrome of catatonia has been diagnosed, the *antecedent* illnesses need to be elaborated. Secondarily, catatonia patients are, by definition, at high risk of systemic medical complications due to poor self-care, which themselves need management. In other words, catatonia could be both a "cause" and "effect" of delirium, for instance.

B. What Workup Do You Want the ED Physician to Obtain Before You See the Patient?

Despite the ominous recurrent depressive disorder history, this has to be initially approached as a "delirium rule out" case. As such, standard delirium assessment laboratory studies would include at a minimum a metabolic panel, liver-associated enzymes, CBC, TSH, calcium, urinalysis, and urine toxicology. A CT of the head is indicated. Since you need to consider antipsychotics, an ECG for a QTc baseline is needed. There is no need for an EEG in initial workup.

C. What Examination Modifications Should You Use in Your Session with This Patient?

You should use your standard interview, being mindful that such a regressed patient will not fully engage with all routine examination elements. Since major neurocognitive disorder can also occur in a patient with recurrent severe depressive disorder, plus knowing that delirium can present as catatonia, a MoCA or other standardized cognitive assessment is indicated. More specifically, when there is any concern for catatonia, the Bush-Francis Catatonia Rating Scale needs to be done.

Case continued: You see him in the ED. He is extremely regressed. He sits motionless in the chair, fully alert with a blank, perplexed, and vacuous appearance. He does not make eye contact. He has no spontaneous speech, he perseveratively repeats your words back to you, cannot complete any MoCA items, and has increased tone in his upper extremities with nonsensical movements of the hands. On the Bush-Francis Catatonia Rating Scale, he is positive on six items.

D. What Is the Diagnosis?

The diagnosis is catatonia, with rule out delirium, and rule out recurrent major depressive disorder with psychotic and melancholic features.

E. How Do You Manage His Workup?

Many things need to be done simultaneously. You need to obtain and interpret the delirium laboratory panel and neuroimaging. If there are notable positives on laboratory or other assessments consistent with a systemic illness that may be a cause for delirium, he needs admission to internal medicine for further assessment and management. He is grossly decisionally impaired, so he needs a surrogate for decision making. He cannot leave against medical advice, and (depending on local laws and medical/judicial practices) he may need a psychiatric commitment order.

F. How Do You Intervene?

For the manifest catatonia, irrespective of the causal psychiatric and/or neurologic illness (even if due to delirium), the initial intervention is IV benzodiazepines. This is counter to the usual advice of avoidance of benzodiazepines in delirium (the one other exception is delirium due to sedative/alcohol withdrawal). The usual regimen is initiated with lorazepam 1 mg IV q6h, with doses increased daily to a usual maximum recommended dose to 8 mg IV q6h (though such a high dose in a geriatric patient requires close monitoring), and with serial Bush-Francis Catatonia Rating Scale assessments to monitor catatonic symptoms.

G. How Do You Monitor Response?

Regular (at least daily) repeat vital signs and Bush-Francis Catatonia Rating Scale are required. Once the patient no longer is positive for catatonia on the Bush-Francis Catatonia Rating Scale (i.e., less than 2 of the first 14 items positive [11]), then reassessment with treatment of the likely manifest antecedent psychiatric illness is needed.

Case continued: His workup is otherwise negative or nonspecific. He is started on lorazepam 1 mg IV q6h. One day later he is no better so the dose is increased to 2 mg IV q6h. On the third day, with a dose of 3 mg IV q6h, he improves, begins to speak, orients to person/place/time, has normal muscle tone in the upper extremities, and no longer shows staring, stereotypies, or posturing behaviors. His affect is now dysphoric and blunted, non-tearful. His Bush-Francis Catatonia Rating Scale is now negative. His MoCA score is 15/30.

H. What Do You Do Now?

Assuming he is otherwise medically stable, this would be a good time to restart his antidepressant medications and transfer him to psychiatry unit. With the formulation of major depressive disorder with melancholic and catatonic features, he may need a course of ECT. The lorazepam can be continued briefly until he is fully established on an antidepressant regimen and/or evaluated for ECT [12]. Recall that catatonic patients need deep venous thrombosis prophylaxis and are at significant risk of deconditioning, so may need physiotherapy and occupational therapy evaluation as part of their care plan.

Question 8.4

Depressive disorder versus major neurocognitive disorder. The patient is a 65-year-old white male with a heretofore negative psychiatric history. He presents to your clinic with a complaint of "losing my memory. I think I am getting Alzheimer's like my father did. I feel hopeless because I cannot remember things. I just can't function anymore." He has never had memory impairment before, and until 6 months ago, he was functioning well, planning for retirement from his business career. He did have some ambivalence regarding retirement, as he enjoyed his work, but he was "beginning to show may age, I didn't have my usual energy somehow" so he felt it best to retire. As a retiree he struggles to find meaningful activity, spending time with family and friends, but missing his daily routine. He began to have some struggles with sleep (a new problem for him). He denied any substance use. Later, he noted that his interest in activities and appetite were not as robust, "but I needed to slow down and lose some weight anyway." Increasingly, his major concern is memory and concentration difficulties. He has difficulty sustaining attention in conversation and forgets things he has just learned, and it takes much longer for him to recall names of people, names of places he has been, and news items. He denies unsafe behavior, problems with driving, and wandering.

His medical history is notable for chronic hypertension and mild hyperlipidemia, both of which are treated with medications. He has no history of strokes, cardiac events, or diabetes mellitus. He has no psychiatric history. His family psychiatric history is positive for vascular neurocognitive disorder in his late father. His social environment is stable; he and his wife own their home and his two adult children live in the area. He has no financial problems and is well insured.

On exam, he is mildly anxiously dysphoric, non-tearful, non-labile, and non-melancholic. He denies suicidal ideation or psychotic symptoms. He has clear psychomotor retardation without a movement disorder. He is organized and mildly perseverative and tends to repeat himself. On formal cognitive testing with the MoCA, he scores 21/30, with 0/5 recall memory, 1/3 concentration, 0/1 attention, and 0/1 word generation. Notably, he quickly gives up if he struggles with an individual item and reacts with a catastrophic statement; e.g., "see, I told you I am just

unable to function, I am losing it." Hamilton Depression Rating Scale (Ham-D) is 24 (moderate/severe depressive disorder).

A. What Are the Main Diagnostic Probabilities at This Time?

The main diagnostic probabilities in this case are major neurocognitive disorder, due to Alzheimer disease, vascular disease, or mixed mechanism; major depressive disorder; and depressive disorder due to thyroid and/or vascular disease.

B. What Workup Would You Propose at This Time?

Due to the first lifetime episode of mood symptoms with cognitive impairment on formal testing, he needs neuroimaging to rule out surreptitious vascular disease and/or Alzheimer disease. He also needs TSH; other screening laboratory studies include renal panel, liver-associated enzymes, CBC, B_{12}, urinalysis, and toxicology. His alcohol use is not helping, but there is not persuasive evidence of alcohol use disorder per se.

Case continued: He initially balks at the recommendation for neuroimaging, but then says "it will prove that I have Alzheimer so we had better do it." The brain magnetic resonance neuroimaging (MRI) shows diffuse white matter disease, no focal areas of atrophy, but questionably slight diffuse cortical atrophy. Other laboratory studies are normal.

C. How Does the Results of Neuroimaging Refine Your Diagnosis?

The positive neuroimaging, vascular disease risk factors, and cognitive impairment mean that this is not "typical" major depression. Alzheimer disease may have more notable atrophy than vascular findings, but is possible. Normal range for TSH value rules out hypothyroidism that could have affected his mood and cognition.

D. What Would Be Your Clinical Approach Now?

With this constellation of findings, empirical treatment of his depressive disorder is imperative. Venlafaxine should be avoided in hypertension. A selective serotonin reuptake inhibitor (SSRI) or the serotonin and norepinephrine reuptake inhibitor (SNRI) duloxetine can be considered. Given the significant insomnia and appetite loss, the first approach should be mirtazapine, which will address these neurovegetative signs promptly. At follow-up, reassessment of cognitive status is needed.

Case continued: He reluctantly accepts that depression is present and hopes "that you are right about this, otherwise I have Alzheimer and it's hopeless." You prescribe mirtazapine 15 mg at bedtime, with indication to increase to 30 mg in

2 weeks' time. He returns in 4 weeks, stating that his sleep and appetite seem better, and though he is not sure if his memory is much better, he says "at least it isn't worse, and maybe the sleep is helping me to think better and be less stressed." On exam he is a bit brighter, scores a 24/30 on the MoCA, and his Ham-D has improved to 14 (mild to moderate symptoms), mostly due to less sleep and appetite symptoms.

E. Now What Do You Do?

He should be maintained on mirtazapine indefinitely with serial MoCA and Ham-D to screen for emergence of a major neurocognitive disorder and recurrence of depression. You should communicate with his internist and suggest maximally aggressive control of his vascular risk factors (e.g., blood pressure, lipid status).

Question 8.5

Renal failure. The patient is a 66-year-old female with a history of type 2 diabetes mellitus with nephropathy. She has been managed with diuretics and antihypertensives, but has continued to deteriorate functionally. She was advised to accept hemodialysis, but refused, citing fear of "being dependent on some machine." She has also experienced depressive disorder (treated with citalopram 20 mg daily) and mild memory impairment, which have affected her compliance with her medication regimen. She has continued to experience deterioration in her renal status and rejects dialysis, despite her physicians' advice and the concerns of her family. Relatively suddenly, she developed somnolence, confusion, and complete inability to care for herself. Her family called 911 and has her brought to the ED. When seen in the ED, she is confused, irritable, and intermittently somnolent. She is unable to account for recent illness events. She is only marginally cooperative with the ED evaluation. The ED physician calls you (you are on call for the consultation service) and tells you: "This noncompliant diabetic patient has a history of depression and noncompliance. She is uncooperative with us in the ED. This is obviously her depression. See her and admit her to psychiatry."

A. What Are the Likely Psychiatric Diagnosis(es) at This Point?

Depression is common in diabetes mellitus and can impact patients' self-care due to amotivation and poor concentration. The increased risks of incident depression and prevalent depression among diabetic patients have been noted in community studies [13]. Maraldi et al. showed that diabetes mellitus has been associated with a 30% increased risk of incident depressed mood (OR 1.31; 95% CI 1.07–1.61), which was decreased after adjustment for diabetes-related comorbidities (OR 1.20; 95% CI 0.97–1.48) [14]. Particularly among patients with poor glycemic control, a stronger

relationship has been observed between diabetes mellitus and recurrent depressed mood (OR 1.91; 95% CI 1.32–2.76) [14]. In the case scenario presented, she has been treated for depressive disorder as well.

Similarly, diabetes mellitus is associated with a high risk of Alzheimer disease and vascular major neurocognitive disorder (formerly dementia) [15, 16]. Diabetes mellitus at baseline doubles the risk for major neurocognitive disorder, both of Alzheimer disease and vascular disease type [15]. However, studies show that diabetic patients, compared with nondiabetic individuals, were less likely to have neurofibrillary tangles and amyloid plaques, but more likely to have cerebral infarcts [15]. In this case, the acute presentation of precipitous decline in her mental status makes delirium the primary consideration. For thoroughness, other causes of acute onset changes in mental status (e.g., substance intoxication or withdrawal) are to be considered, especially if the history supports this.

B. What Evaluation Is Indicated in the ED?

The history clearly suggests uremia leading to acute delirium, but given the general vulnerability of a diabetic patient, a full laboratory assessment for delirium is indicated. At a minimum, renal panel, glucose, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis, and urine drug screen are needed. A review of recent medications with particular attention to benzodiazepines, anticholinergics, and opioids should be done. All of these should be accomplished before you see the patient.

Case continued: You see her in the ED. She is somnolent, only transiently able to make eye contact. She has psychomotor retardation and blunted, non-tearful, dysphoric affect. She, with her brief statements, denies suicidal ideation or psychotic symptoms. She does not understand why she is in the ED. Her Montreal Cognitive Assessment (MoCA) score is severely impaired, at 8/30.

C. What Diagnosis Is Confirmed? What Others Are Likely?

Delirium is the index diagnosis. Delirium in uremia is more commonly hypoactive than hyperactive [17]. Hypoactive delirium patients may manifest dysphoric affect and do thus appear "depressed" to observers. In this case, the patient is at high risk for depressive disorder and has been treated for depressive disorder with antidepressant medication. However, depressive disorder does not explain her diminished level of arousal, nor her severe cognitive impairment. She is at risk for major neurocognitive disorder as well (and may well eventually be so diagnosed; however, the acute presentation of delirium completely explains the cognitive impairment). Since she is on a selective serotonin reuptake inhibitor (SSRI), she is at risk for syndrome of inappropriate antidiuretic hormone secretion (SIADH). The best practice would be to manage delirium until the patient is improved and stable, with full assessment for comorbid major neurocognitive disorder at that time. Figure 8.2 illustrates the

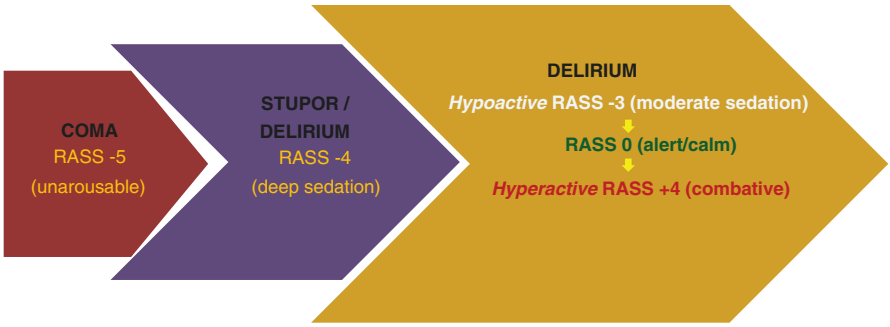


Fig. 8.2 The spectrum of acute cognitive dysfunction based on the Richmond Agitation and Sedation Scale (RASS) [18]

spectrum of acute cognitive dysfunction based on the Richmond Agitation and Sedation Scale (RASS), from hypoactive (RASS < 0) to hyperactive (RASS > 0) delirium [18].

Case continued: Her laboratory studies show renal failure, mildly increased glucose, and anemia. The other laboratory studies are unremarkable or nonspecific. Due to her acute decompensation, she needs urgent dialysis. The nephrologist calls you: "She has been refusing dialysis and you said she is delirious now. What if she gets agitated while being dialyzed? We can't have her acting out in the dialysis suite. Can we treat her before dialysis with something? What about 2 mg of lorazepam?"

D. What Do You Tell the Nephrologist?

You tell the nephrologist that the patient's current state is delirium. She is acutely unstable and has impaired decisional capacity based on her current clinical exam. Therefore, she is unable to refuse treatment. If dialysis is "emergent," no consent is needed. If it is "urgent," then the nephrologist should seek consent from a surrogate decision maker. The patient is unable to appoint a surrogate due to severe impairment, so the nephrologist should seek the closest person to the patient to serve in this role. If the patient recovers from delirium, she will may well regain decisional capacity.

Regarding medication, premedication before the dialysis session is clearly indicated. Benzodiazepines are likely to exacerbate delirium in this case, so the preferred intervention is antipsychotics. Olanzapine is best avoided in diabetic patients. Alternatives to consider include haloperidol, risperidone, ziprasidone, and quetiapine. The antipsychotic should be given at least 1 h pre-dialysis.

Case continued: She is given 1 mg of haloperidol IV before dialysis. After dialysis, her delirium improves rapidly. You reevaluate her the next day. Her MoCA is now 17/30, with deficits in attention, concentration, and recall. She does not recall the events of the last several days. She denies suicidal ideation or psychosis, though she does endorse being depressed and hopeless, despite treatment.

E. What Would You Do Now?

She remains highly delirium prone, so needs continued delirium precautions. Her cognitive status, though improved, is still mild/moderately cognitively impaired [19]. Regarding her cognitive status, studies have shown that MoCA distributes mild neurocognitive disorder cases across a broader score range with less ceiling effect. Depending on the level of sensitivity desired, a MoCA cutoff score of ≥18 out of 30 points may help to capture early and late mild neurocognitive disorder cases [19]. However, her current cognitive status can be explained by continued depressive disorder and/or vascular neurocognitive disorder, as well as the episode of delirium. It is not possible to differentiate among these conditions at this time. Neuroimaging to ascertain the degree of vascular disease (she almost assuredly has significant cerebrovascular disease [20]) may help to clarify this.

F. The Nephrologist Says She Will Now Need to Be on Dialysis, Despite Her Previous Resistance. He Asks if You Can Prescribe Haloperidol Before Dialysis "For an Indefinite Period." What Do You Do with This Request?

It is important to remind your colleague that the pre-dialysis antipsychotic was justified and necessary due to her delirium, which was present when she was initially dialyzed. Now that her delirium is improved, it is not an urgency/emergency any more. She would need to be separately assessed for decisional capacity to accept/refuse dialysis. A patient who is cognitively intact and who has intact decisional capacity to refuse dialysis, even if such a decision leads to death, is typically allowed to refuse dialysis. A discussion with the patient about this issue and ascertainment of decisional capacity for this intervention are indicated. If she has impaired decisional capacity, then surrogate consent would be needed. If there is concern for agitation during dialysis, pre-dialysis antipsychotic may be indicated, especially if an attempted dialysis session needs to be aborted due to behavioral acting out.

G. Beyond the Clinical Implications of Neurocognitive Disorders, How Do You Manage Depressive Disorder in Renal Failure?

The usual management of depression in renal failure is with SSRIs, though the drug-drug interactions with fluoxetine, fluvoxamine, and paroxetine make citalopram, escitalopram, or sertraline the preferred agents. The SNRI venlafaxine should be avoided in hypertension, whereas duloxetine may need a dose adjustment, or be avoided, in renal failure. Bupropion may be considered in such cases. Mirtazapine, if renally dose adjusted, can be considered. Due to their anticholinergic effects, tricyclic antidepressants are best avoided.

Question 8.6

Hypothyroidism. The patient was a 75-year-old white female, with a history of hyperthyroidism due to Grave's disease, which led to a total thyroidectomy when medical management did not fully suppress the hyperthyroidism. For her subsequent iatrogenic hypothyroidism, she took levothyroxine 125 mcg per day with improvement and stabilization of her thyroid status. She was only variably compliant with medication and needed frequent counseling by her endocrinologist to take medication.

She did relatively well for several years, albeit with the compliance problem as previously described, avoiding hospitalization and functioning adequately at home. Subacutely, she developed confusion and psychosis, becoming convinced that "President A is calling me to The White House" and that "Vice President B is coming to my home. I know him when he was a senator from Nebraska." She became uncooperative with family members and disruptive. The police were called and she was placed on a psychiatric commitment order and brought to the ED. The ED physician calls you and says: "She is acutely psychotic. Since she is old, we scanned her head, but nothing was found. Her vitals, renal panel, and CBC were normal. She is medically cleared for an admission to psychiatry."

A. Based on This Narrative, What Are the Likely Diagnoses to Consider?

Subacute to acute mental status changes always need delirium to be considered. She could have developed major neurocognitive disorder with agitation, not necessarily delirium. Drug or alcohol abuse needs to be considered. Thyroid disease, especially with noncompliance, can lead to psychotic and/or cognitive decompensation.

B. What Assessments Do You Need to Have Done Before You See Her in the ED?

A delirium workup has been started. She also needs liver-associated enzymes, TSH, calcium, B_{12}, urinalysis, urine toxicology, and blood alcohol level at a minimum. An ECG is also necessary.

Case continued: When you get to the ED, her family members pull you aside. "She has never ever been psychotic. Is she getting schizophrenia?"

C. What Do You Tell Her Family?

Schizophrenia with onset over age of 60 is rare [21]. The most likely causes of psychotic presentation in older patients are delirium and major neurocognitive disorder.

Case continued: Her family also says she has stopped taking levothyroxine for 4 months ("We can't get her to cooperate with treatment. I know she is supposed to take it"). On exam, she is anxiously dysphoric, fully alert, but psychotic (repeating her delusions about these political figures, very convinced that she has a relationship with each of them) without hallucinations. She denies suicidal ideation. She is mildly tangential and perseverative. MoCA score is 16/30 with deficits in multiple domains. Additional laboratory studies reveal TSH of 85 mIU/L (elevated), with full thyroid panel pending.

D. What Is the Diagnosis?

The diagnosis is neurocognitive disorder due to hypothyroidism. Whether this is delirium per se or neurocognitive disorder with psychotic features due to hypothyroidism is somewhat of an academic point.

E. Obviously She Needs Thyroid Replacement. How Do You Approach Her Psychiatric Management?

She will be admitted to internal medicine to manage her profound hypothyroidism. While classically associated with melancholic depression, profound hypothyroidism can be associated with a primary psychotic presentation, delirium, or major neurocognitive disorder [22, 23]. She should receive standard delirium precautions. She should be started on an antipsychotic (e.g., risperidone 0.5 mg or 1 mg bid) with close monitoring of her psychiatric status, including serial MoCA, as her psychotic symptoms are likely affecting her MoCA score.

Case continued: She was started on thyroid replacement and risperidone. Within 1 week she is no longer as delusional and her MoCA is 20/30. She still cannot take care of herself safely due to residual symptoms. The internal medicine resident says that her TSH is improving but that she is "medically cleared" now and that she can be treated as an outpatient.

F. What Would You Do Now?

The patient needs to stay on an antipsychotic until her delusional symptoms are in complete remission and her thyroid status has renormalized with treatment. Once she is taking oral thyroid medication, she could be transferred to the psychiatric unit if her residual psychiatric symptoms justify this treatment model.

Question 8.7

Post-stroke delirium and major neurocognitive disorder. The patient is a 67-year-old white female with a history of multiple vascular disease risk factors (hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking). She has a history of

recurrent depressive disorder, initially treated in her 20s, but with no recent treatment. She complains of mild memory impairment for several years, as well as some difficulty with word-finding. She has no wandering, disorientation, or vehicular incidents, though she readily admits that "I only drive short distances, you know, to familiar places" and never drives at night. When seen for a routine clinical examination, she denies symptoms of depression, poor sleep, or poor appetite. Her examination is remarkable only for a MoCA of 22/30, with poor concentration and recall memory. No treatment was given at her last visit, though close monitoring of her cognitive status was planned, and she was advised not to use alcohol and to avoid benzodiazepines and opioids, in the name of cognitive preservation.

Suddenly one day, she developed a unilateral facial droop and dysarthria and fell. A bystander called 911 and she was taken to the ED. A "code stroke" was called and she had urgent neuroimaging and thrombolysis. Neuroimaging revealed an emerging ischemic cerebrovascular accident in the distribution of the left middle cerebral artery. She was admitted to the neurology ICU, with continued motor and speech deficits noted. Later that night, she develops agitation and worsening confusion. You are on call for the ICU service and the neurology resident calls you: "She has had a stroke, validated by neuroimaging. We gave her thrombolysis promptly but she still shows neurological deficits, so we don't know how much better she will do. We learned that she has a history of depression; well, she isn't coping well with the stroke at all. This must be her depression coming back, I know post-stroke depression is pretty common."

A. What Is Your Differential for the Current, Acute Presentation?

Acute mental status changes in a hospitalized patient, especially an older patient, need a full delirium workup. While her chronic illness narrative certainly is consistent with (heretofore mild) vascular neurocognitive disorder, the risk of delirium precipitated by the acute stroke is very high [24–26]. You are mindful of her chronic neurocognitive disorder when you go to see her.

Are There More Studies You Want to Order Before Seeing the Patient?

While acute delirium post-stroke can explain the entire presentation, it is best to take a comprehensive approach to delirium assessment. Be sure that the following laboratory studies are accomplished: metabolic panel, liver-associated enzymes, CBC, urinalysis and urine toxicology, TSH, calcium, and B_{12}. Additional laboratory studies can be considered later as needed. There is no role for EEG in acute delirium, absent a concern for new seizure disorder and/or status epilepticus.

Case continued: You see her in the ICU. She is hyperalert and agitated (RASS +1 to +2), needs redirection not to pull her IV lines and ECG leads, has intense eye contact, and appears fearful of "someone out to get me, maybe the nurses here." She cannot tell you that she has a new stroke and does not appreciate her motor deficits.

She denies suicidal and homicidal ideation (she is perplexed by the questions) and hallucinations. She is mildly perseverative. MoCA is 10/30 with impairments in all tested domains. She does not appreciate that she is in a hospital and tries to leave "to get to my home."

B. What Do You Do at This Point?

She is showing a precipitous decrement in cognitive status, with poor insight into her illness and its implications. Her current MoCA score suggests impaired decisional and dispositional capacity. You would be sure that delirium-provoking medications (e.g., opioids, anticholinergics, benzodiazepines, antihistamines) are avoided.

C. The Neurology Resident Says: "We Want to Do Another Procedure. Can We Consent Her?" How Do You Respond?

Her current level of cognitive function is suggestive of impaired decisional capacity. She cannot consent to nor refuse procedures. She needs a surrogate for other than emergency medical decisions.

D. How Would You Manage Her Delirium?

She presently has hyperactive delirium "atop" a baseline vascular neurocognitive disorder. Any acceleration of the rate of cognitive decline from her baseline major neurocognitive disorder can only be ascertained after the acute delirium episode is managed. Usual delirium management with cautiously dosed antipsychotics with close monitoring of QTc, glucose, sedation, and extrapyramidal syndrome is needed. Post-stroke delirium is typically brief.

Case continued: You start her on risperidone 0.5 mg at bedtime. Four days later, she no longer has sleep-wake disturbances and no agitation. She is also less perplexed and more able to converse and to understand medical advice. On repeat exam, she can participate in the clinical interview somewhat better. Her MoCA has improved to 17/30, she is no longer restless or agitated, and she is more organized in her thought process. She now is able to understand that she had a stroke and is struggling to deal with her remaining motor deficits.

E. What Would You Do Now?

With improvement in the delirium, it is likely that her current cognitive status is stable. A decrement in cognitive function after recovery from a delirium episode is common. Continued monitoring of cognitive status over several months is needed to

ascertain new baseline cognitive status. She needs to continue to avoid all delirium-provoking medications and needs aggressive management of vascular risk factors. Her risk for post-stroke depression is high for 12 months after stroke; any significant mood episode needs to be promptly managed [27].

Question 8.8

Delirium in advanced cancer. The patient is a 75-year-old man with a diagnosis of bronchogenic carcinoma following years of smoking. He had no history of psychiatric illness. He was initially treated with surgery and chemotherapy and initially did well. However, in recent weeks he has been exhibiting weight loss, low energy, and debility. His outpatient physician was concerned and communicated with his oncologist, who initiated a repeated workup. Unfortunately, the workup revealed recurrence of his lung cancer, with brain metastatic disease and systemic hyperparathyroidism and hypercalcemia. The oncologist noted: "He is not as mentally sharp either" and requested a psychiatric consultation while the patient was admitted for the cancer recurrence workup. You are on the consultation-liaison service at the hospital and receive the consult. The oncologist says: "Please see him. He is upset and depressed about the recurrence of cancer, which I can appreciate, but he is more depressed than most patients in this situation. Plus, I don't think he understands everything I am telling him. The depression must be affecting his judgment."

A. What Psychiatric Diagnoses Are to Be Considered When You Learn of This Referral?

While depression is common in cancer patients, especially with a worsening prognosis, depression will not typically dramatically affect cognitive function. More to the point is major neurocognitive disorder (from the destruction of cortical tissue from metastatic disease) or delirium (from the cancer, hypercalcemia, perilesion edema, and perhaps hypoxia from compromised pulmonary status). Clear demarcation of delirium from other neurocognitive disorder resulting from direct central nervous system (CNS) disease burden is not always possible with complete confidence.

Case continued: You see the patient in the hospital ward. He is debilitated, wasted, and somnolent. When you speak to him, he is able to arouse and maintain eye contact (RASS −1). Though easily fatigued, with effort he can complete the interview. His affect is blunted and dysphoric. He denies suicidal ideation. However, he says: "There are guinea pigs all over the place here" (he gestures to the corner of the room). He is somewhat perseverative in this thought process. He is aware that he has cancer ("I have had it for years, it's mostly my fault, all that stupid smoking") but is not able to describe the recent recurrence or the CNS findings. His MoCA is 12/30, with notable deficits in recall, orientation, concentration, and attention.

B. What Is the Diagnosis Based on the Interview?

While he manifests dysphoric affect, his level of consciousness and cognitive status are markedly impaired. A depressive disorder cannot account for all of these findings. While it can be argued that he has depressed mood, it is not persuasive that he has a depressive disorder. Recall that *delirium is a "whole brain" disease, which can be responsible for any psychiatric symptom.*

C. What Workup Would You Accomplish?

The usual delirium laboratory investigations (most of which have probably been done by oncology), including renal panel, liver-associated enzymes, CBC, TSH, calcium, and vitamin B_{12}, should be considered.

D. How Would You Manage Him? What Do You Tell the Oncologist?

This is *not* depressive disorder, as the delirium is the most important psychiatric illness at present. Initiating standard delirium precautions (avoid benzodiazepines, opioids, and anticholinergics) is necessary. Serial cognitive assessments are needed. Low-dose sedating antipsychotic given at bedtime (e.g., olanzapine 2.5 or 5 mg) plus PRNs for breakthrough agitation may be considered. Regarding antidepressants, patients with lung cancer and CNS metastases are at particularly high risk for SIADH, so antidepressants such as SSRIs (selective serotonin reuptake inhibitors), SNRIs (serotonin and norepinephrine reuptake inhibitors), or TCAs (tricyclic antidepressants) should be used prudently. If, after recovery from delirium, there is persuasive evidence for a depressive episode separate from delirium, the antidepressant of choice in solid tumor cancers is mirtazapine.

E. How Long Should You Continue Olanzapine, Assuming a Positive Response to Treatment?

With a stage 4 cancer such as this (especially with paraneoplastic syndromes), the risk of recurrence of delirium is very high [28]. Plus, if his course is particularly poor, he may quickly transition to a palliative/terminal phase of illness. Therefore, it is likely preferred that delirium pharmacology be continued indefinitely with serial cognitive assessments.

Question 8.9

Terminal delirium. The patient is a 66-year-old male with amyotrophic lateral sclerosis (ALS), with a rapidly progressive course with quadriplegia and respiratory failure (requiring mechanical ventilation through a tracheostomy), is unable to

speak, and has increasing problems with memory. While he was functioning better cognitively, he agreed to be in do-not-resuscitate (DNR) status. His family members, aware of his disease state, fully supported this decision. As a contingency, his wife agreed to serve as surrogate decision maker if he were to become incapacitated.

A. What Aspects of This Man's Narrative Make Him Particularly Delirium-Prone?

He has several delirium risk factors of note. He is of older age, he has neurological disease, and he is at risk for hypoxia. He is deconditioned and prone to deep venous thrombosis, pneumonia, and urinary tract infections. Less well recognized, in that ALS is often thought of as a "purely motor" illness, is the associated increased risk of cognitive deficits in patients with ALS [29]. Major neurocognitive disorder from any cause is the most important single risk factor for delirium.

Case continued: Despite his frailty, he is managed at home with in-home caregivers supplementing his family's efforts. However, over a period of 2 weeks, he is noted to be subacutely confused, unable to communicate with his message board and other assistive devices, and has a newly altered sleep-wake cycle. Despite his known DNR status, his family brings him to the ED "because maybe there is something that can be treated. We know he is terminal, but this is a sudden change." You are on call for the ED, and the ED physician calls you: "This man is not coping well; I realize he has ALS, so who wouldn't be depressed. He may need an antidepressant."

B. What Workup Do You Want to Order Before You Get to the ED?

Routine delirium management laboratories, including renal panel, liver-associated enzymes, CBC, urinalysis and drug screen, TSH, calcium, and B_{12}, are necessary to obtain. Given his risk for pneumonia, a chest X-ray is indicated. Despite the increased risk of neurocognitive disorder, a CT scan is not indicated as it would not change management.

Case continued: You see him in the ED. He is somnolent, with fleeting eye contact (RASS −2), and he is unable to communicate with his assistive devices. Due to his quadriplegia, he is not capable of agitation, but his somnolence is consistent with hypoactive delirium.

C. What Is a Reasonable Management Strategy in Light of His Poor Prognosis?

Delirium is common in terminally ill patients [30]. Due to his general debility, it may not be possible to ascertain a clear "delirium source." However, illnesses that are reasonably probable that can be easily identified with noninvasive means (e.g., urinary tract infection, pneumonia, dehydration, rhabdomyolysis, renal insufficiency) should

be sought, and noninvasive treatment should be offered. Standard delirium precautions should be accomplished. Psychotropic interventions (e.g., aripiprazole may be helpful in hypoactive delirium due to its non-sedating effects; mirtazapine may help to regulate the sleep-wake cycle; gentle doses of psychostimulants in the morning may increase arousal and attention) may offer meaningful symptomatic relief.

Case continued: His chest X-ray reveals pneumonia. His surrogate decision maker is supportive of a single trial of IV antibiotics, which is initiated. He is given aripiprazole 5 mg in the morning and mirtazapine 7.5 mg at bedtime. He becomes less confused and perplexed, is more alert, and is able to sleep normally. His family thinks he is "back to where he was two weeks ago."

D. Now That He Is Improved, How Do You Manage Him from Here?

Ordinarily, delirium pharmacotherapy is discontinued within 1–2 weeks after delirium recovery. However, in this patient's case, his risk for delirium recurrence is extremely high and his prognosis is poor. Therefore, it is recommended that the medications aripiprazole and mirtazapine be continued indefinitely for maintenance.

Question 8.10

Vitamin B_{12} deficiency. A 70-year-old Asian female presents with gradual onset of cognitive impairment. Her family denies any history of psychiatric illness, insisting that, "she was pretty sharp until a year ago." According to her attentive family members, she has had gradually deteriorating cognitive and social function over many months. Increasingly, family members have to do more and more to help her. She also seems "depressed, withdrawn," and sometimes "we think she is seeing things" as she reaches out to grasp things that are not there. She is also not walking well, stumbling and needing assistance, and says that "the feeling in my legs isn't right," but the family members are not sure what to make of that "as she always has a lot of physical complaints that the doctor can never find a cause for." She was admitted to the general hospital for "failure to thrive." You are the chief of consultation-liaison psychiatry and the internal medicine resident calls you: "She is obviously depressed and 'not dealing', please see her and treat her depression. My attending wants her transferred to psychiatry. She will be medically cleared soon."

A. What Diagnostic Possibilities Do You Entertain Based on the Narrative?

Certainly an episode of depressive disorder can manifest primarily as cognitive and functional impairment being more dramatic in presentation than tearfulness, hopelessness, and other mood symptoms per se, so this needs evaluation.

However, major neurocognitive disorders present in a much similar way, so rule out of neurocognitive syndromes needs to be done concurrently. She has presented with some psychotic symptoms (apparent visual hallucinations); however, new-onset psychosis in older adults is most commonly associated with neurocognitive disorder, less commonly with depressive disorder, and extremely rarely with a new-onset schizophrenia-spectrum disorder.

B. What Diagnostic Workup Do You Want Ordered Before You See Her?

Tell the internal medicine resident that she needs a CT scan of the head, metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, and calcium ordered, as these are standard laboratory studies for major neurocognitive disorder.

Case continued: You go to see her, before the laboratory results are back. She is alert, with good eye contact, no restlessness (RASS 0). She is ill appearing, cachectic, and disheveled, looks perplexed, speaks in soft tones only, and is non-tearful, and affect is blunted. She cannot tell you much about recent events, only that she is "not feeling well" and reliant on her family for most everything. She says that she "sees butterflies in here" (she reaches out as if to catch one which she then "shows" you, obviously certain that it is "real"). Her thought process is concrete but organized. Ham-D score is 20; MoCA score is 15/30 (performed with an interpreter in her native language).

C. What Are the Diagnostic Possibilities?

You need the laboratory data back to be sure, but she currently looks like a "3 Ds" (delirium, depression, dementia (major neurocognitive disorder)) patient, with likely some symptoms of all three. The acute presentation mandates a full delirium workup; the cognitive impairment also directs a workup for major neurocognitive disorder (to include neuroimaging).

D. How Do You Intervene Now?

It seems prudent to at least offer an antipsychotic on a PRN basis for her hallucinatory symptoms, although you do not observe agitated behavior or obvious distress associated with them. A low dose of an atypical antipsychotic (e.g., risperidone 0.25 mg q6h PRN) would be typical.

Case continued: You check the EMRs. CT reveals cortical atrophy and white matter disease. She has evidence of mild dehydration and anemia. Liver-associated enzymes are normal. TSH is normal range. B_{12} is 190 pg/mL (140 pmol/L); the medicine resident tells you "that's good, that is the normal range."

E. How Do You Interpret These Findings?

The CT findings are more consistent with major neurocognitive disorder than depression, though such findings are often incidental in many patients. The normal range for B_{12} may vary among laboratories. However, the B_{12} level in this case, though within reference range, is not "normal" in a patient with depressive and cognitive symptoms. In patients who are symptomatic, B_{12} supplementation is needed to bring the level to at least 350 pg/mL (>250 pmol/L) and then reassess the patient [33, 34].

F. What Do You Do Now?

Have the internal medicine resident order oral B_{12}; a typical dose is 1000 mcg daily. If oral B_{12} cannot reliably be delivered, IM alternatives can be considered.

G. What About Her Psychiatric Symptoms?

It would be prudent to empirically treat her depressive and psychotic symptoms while monitoring her cognitive symptoms as well. If her clinical presentation is actually due to B_{12} deficiency, she may respond symptomatically to B_{12} supplementation and not necessarily require long-term treatment with an antidepressant or antipsychotic medication. Starting doses of mirtazapine 7.5 mg at bedtime and risperidone 0.5 mg at bedtime could be initiated and titrated as needed to optimize response, along with close clinical monitoring and follow-up.

H. How Would You Monitor Her?

Regular follow-up clinical monitoring with serial Ham-D and MoCA tests, at least, is necessary. Once the Ham-D score is no longer in the depressive disorder range (i.e., score < 16 and 50% improvement from initial), she is no longer psychotic, and her B_{12} is now safely above 350 pg/mL (>250 pmol/L); decide whether continued mirtazapine and risperidone are still indicated.

Question 8.11

Corticosteroid-induced psychosis. The patient is a 70-year-old white male with a negative psychiatric history. He is a retired teacher who was widowed 5 years before. He lives near his two adult children (one son and one daughter) and spends time helping with his grandchildren. He volunteers at local social agencies and

participates in retiree activities at the junior college where he used to teach. His medical history is largely benign; he has no history of neurological or vascular disease and takes no regular medications.

Suddenly, he develops arthralgias, fatigue, and swelling on this side of his head. He takes over-the-counter medications without improvement. A few days later, he notices that his vision is affected on the same side. Concerned, he seeks an appointment with his optometrist who discovers reduced visual acuity and diagnoses ischemic optic neuropathy. He is sent to the ED for prompt evaluation by neuro-ophthalmology, neurology, and internal medicine. Full workup leads to a diagnosis of temporal/giant cell arteritis, and a temporal artery biopsy is obtained and confirmatory. He is urgently admitted to the hospital and started on IV dexamethasone 25 mg per day (the equivalent of prednisone 100 mg per day). One day later, the internal medicine resident calls you: "This patient just became bipolar. He is talking fast, agitated, not sleeping, seeing stuff. He obviously is not coping with his illness, he doesn't acknowledge that there is anything wrong with him. Please evaluate him for transfer to psychiatry right away."

A. What Are the Likely Diagnoses at This Time?

Acute onset mania at age 70 is not a typical bipolar disorder. The first consideration is, of course, delirium, but a manic or psychotic episode from his rheumatologic disease and/or its treatment is equally, if not more, likely. Do not attribute *any* psychiatric symptom to "poor coping" with illness until all the physiological explanations have been fully evaluated and managed.

Case continued: You go to see him. Unlike what you have learned about his prior level of function, he is loud, irritably grandiose, saying he is "going to take this place and make it mine due to what they did to me." He is hyperalert, restlessly pacing the room, and threatens to leave. He will not complete the MoCA "because it is a waste of time for someone like me. I am a retired professor, after all." He refuses to answer routine interview questions. When queried about why he is in hospital, he says "that damned eye doctor sent me to the ED, I don't know why, now I am up here for no good reason." You ask him about the temporal artery biopsy, and he says the dressing on his head is "probably a skin cancer from all of the heat." He cannot tell you any of his medications of why he is taking them.

B. What Is the Likely Explanation?

While rheumatologic illness itself can be associated with comorbid psychiatric illness, the likely, more parsimonious, explanation is psychotic/manic episode due to high-dose corticosteroids [35–37]. Corticosteroids, especially at a daily dose exceeding 40 mg of prednisone or the equivalent (his dexamethasone dose is

equivalent to 100 mg of prednisone/24 h), are at high risk to induce multiple psychiatric symptoms, which may or not be frank delirium per se.

C. What Do You Do Now?

Anterior ischemic optic neuropathy is a vision-threatening emergency. The dexamethasone likely cannot be discontinued until his optic neuropathy and peripheral inflammatory markers improve. A full evaluation for other factors that would increase delirium risk (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, urinalysis) is needed, and delirium-provoking medications (e.g., opioids, benzodiazepines, anticholinergics) are discontinued.

D. What Are Your Medication Options?

Even if he met the criteria for a manic episode, lithium is not indicated. Its own risk for renal insufficiency, hyperparathyroidism, and hypothyroidism (in addition to its own risk for delirium) make it contraindicated in medically unstable patients. Better options include an atypical antipsychotic or anticonvulsant (e.g., IV valproate can be administered in the ICU or ward).

E. How Do You Collaborate with the Other Physicians to Manage Him?

At the moment, he has impaired decisional capacity based on his not understanding nor appreciating his illness, so he can be kept in the hospital against his will. You would want very aggressive medication management of his current episode with daily follow-up and reassessment. If his inflammatory disease quickly improves with the corticosteroids (and other immunomodulators), and the corticosteroid dose can be decreased to a safer level (from the perspective of corticosteroid-induced psychiatric side effects), then he may not need indefinite maintenance psychotropic per se.

F. Assuming a Favorable Recovery, How Would You Then Counsel Him?

He needs to understand the phenomenon of corticosteroid-induced psychiatric illness. Given that temporal/giant cell arteritis can be a recurrent condition, future episodes leading to corticosteroids will need repeated surveillance for a recurrent manic/psychotic episode, which would be managed similarly. For a pattern of recurrent episodes, prophylactic psychotropic medication can be considered along with the initial doses of high-dose corticosteroids.

Question 8.12

Immunosuppressant toxicity. A 65-year-old white male is dialysis dependent due to chronic renal failure. After struggling for 5 years on dialysis, during which time he developed depressive disorder and existential despair, hating the dependency on "that darned machine" and sometimes contemplating discontinuing dialysis "to finally be dead and be done with this; this is no way to live." Fortunately, he was willing to take citalopram 20 mg per day and to participate in group therapy with other dialysis patients ("we either go to dialysis together or come to group together; at least at therapy we aren't getting stuck"); he improved and was finally able to qualify for a kidney transplant.

A. What Is the Impact of His Episode of Depressive Disorder on His Candidacy for a Transplant? Won't the Transplant Service Turn Him Down Due to Depressive Disorder?

While standards change over time, the only psychiatric illnesses at present that are a priori disqualifying for organ transplant are advanced major neurocognitive disorder and ongoing substance abuse. Treatable illnesses such as depressive disorder are not disqualifying, as long as the patient is in treatment and functioning well and has acceptable cognitive status. Patients with recurrent suicide attempts will understandably face greater scrutiny and will have to demonstrate improvement in their psychiatric status and behavioral stability in order to be approved for transplant.

Case continued: He qualified for the transplant; part of this qualification required a supportive family and other social circle, a commitment to being free of drugs, and having a commitment to postop medication compliance ("I will do whatever you want. This is a chance at a new life for me. I won't blow the opportunity, you can be sure"). At his last psychiatric evaluation before transplant, his Ham-D was 10 and his MoCA was 23/30 ("the best I have been thinking for years, thank you, doctor").

B. What About His Decisional Capacity for the Surgery Itself? Is His Cognitive Status Good Enough? Does His Depressive Disorder Impact Decisional Capacity?

The literature suggests that patients with mild cognitive impairment can maintain decisional capacity as long as they can persuasively manage the four usual decisional capacity criteria of understanding, appreciation, rationality, and communication of choice regarding the proposed intervention. If you are called upon to render a decision in this area, you would discuss the procedure, indications, and risks/benefits, have him compare intervention vs. nonintervention, and communicate an unequivocal choice for or against intervention. Depressive disorder typically does not affect decisional capacity; given his current Ham-D score of 10 (usual

syndromal threshold is 16), you can be confident that depressive disorder is not adversely impacting decisional capacity.

Case continued: He has the surgery, with a successful procedure, and no operative complications. Fortunately, the graft is working well and there are no signs of incipient rejection. He is started on tacrolimus as an immunomodulator postoperatively. He does well for 3 days postoperatively. Suddenly, he develops behavior consistent with a manic episode. He is not sleeping, has "high energy" all day, is hyperverbal, and is grandiose ("I am going to organize all the kidney patients in the world with me as exalted leader. We are taking over"). Needless to say, this disrupts the transplant surgery team and you are called in haste: "What is going on with this guy? He used to be depressed. How did he become bipolar?"

You hurry to the ICU to see him. His is in fact manic: energetic, restless and agitated, hyperverbal, grandiose, and delusional about his new found charismatic power and mission to organize the kidney patients, and he refuses the MoCA "because I have no time for this. I am taking over. I don't need your damned test." He then refuses further interview and dismisses you.

C. How Did He Suddenly Develop Bipolar Disorder?

This is *not* a bipolar disorder. He is in the throes of an incipient manic episode (though he has not had the episode of mania for the minimal number of days yet). While delirium can cause "any" psychiatric symptom, far more likely is incipient mania due to the immunomodulator tacrolimus, which was started postoperatively [38, 39].

D. What Would You Do Now?

You would always evaluate for delirium first, with routine assessment of a metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, and urinalysis. Empiric treatment of the manic episode is needed. An acute trial of an atypical antipsychotic or mood-stabilizing anticonvulsant is needed.

E. What About Lithium?

Lithium, a classic treatment for bipolar disorder, is not safe in a patient with only one functioning kidney. Lithium can itself provoke renal failure. It is problematic to expose a lone functioning kidney to a medication well known for its risk of kidney disease.

F. Does He Need to Stop Tacrolimus?

Stopping tacrolimus is not necessarily needed. You would have a discussion with the transplant service about this issue. If, for graft preservation, the best immunomodulator is tacrolimus, then the decision may well be to continue it indefinitely,

even with the provocation of a manic episode. He may need therapy for the manic episode indefinitely once stabilized if this is the decision of the transplant service to continue tacrolimus.

Question 8.13

Somatic delusion. The patient is a 65-year-old white female, living alone in the community, with some variable levels of social support. She is seen in the ED at the request of her primary care physician because of declined ability to care for herself at home. You are the on-call consultation-liaison psychiatrist and asked by the ED physician to see this patient after a systemic illness was ruled out as an explanation of her physical complaints and who thinks her complaints "might be delusional in nature." The ED physician tells you that the patient has been somewhat reluctantly cooperative with the evaluation, thinking both "these doctors don't believe me that I am sick" and "they think it is *all in my head*" but "I know it is *real*."

A. Upon Hearing the Referral Question, What Initial Diagnostic Possibilities Need to Be Considered?

Though much less common than mood or cognitive complaints, psychotic symptoms are reported in clinical practice treating older patients including primary care settings [40]. If these patients are able to function and care for themselves, and are not disruptive to their environment, they may not have come to clinical attention with emergency presentations or hospitalizations. While schizophrenia-spectrum illness is rarely initially seen in late life, patients with schizophrenia established at a younger age may become somatically delusional in late life. Such patients will be more likely to present with "bizarre" somatic delusions (e.g., "stomach turning to stone," "being infested by a colony of live crustaceans") rather than a "nonbizarre" delusion (e.g., delusional conviction of "having HIV disease," "having stomach cancer") despite adequate medical workup to the contrary. Also, it must be mentioned that the most common cause of new psychotic symptoms in late life is major neurocognitive disorder; while these patients most commonly experience delusions in the interpersonal sphere (e.g., someone "stealing from me"), somatic delusions are possible. Lastly, severe depression with melancholia may present with comorbid somatic delusions with a depressive theme aspect (e.g., "my body is wasting away").

Case continued: You evaluate the patient. She denies any psychiatric history, mood symptoms, hallucinations, or suicidal ideation. She is convinced that she has a gastrointestinal cancer, as she is "losing weight and have no appetite," which is "obviously due to a cancer that my doctor hasn't found." She says she has had a CT of the abdomen and upper and lower endoscopy, all of which were negative. She also has poor sleep "because of worrying about this." She denies any problematic use of substances. Her affect is anxiously blunted and non-tearful, and her thought process is mildly perseverative on the gastrointestinal complaints.

B. What Additional Evaluations Do You Want to Accomplish on the Initial Assessment?

She is not complaining of a bizarre somatic delusion and has no history of psychotic-spectrum disorder, so schizophrenia is most unlikely. The somatic symptoms she reports could be consistent with a depressive episode. You are mindful of the association between neurocognitive disorder and new-onset delusions in older adults. So, a Ham-D scale to quantitate depressive symptoms and a MoCA test to screen for cognitive status are needed. A brain CT and other workup laboratory studies for major neurocognitive disorder (e.g., renal panel, liver-associated enzymes, CBC, TSH, B_{12}, calcium, urinalysis, toxicology) are needed.

Case continued: Her Ham-D score is 20, with many points referable to sleep and physical complaints, including appetite symptoms. The MoCA score is 22/30, with difficulties with recall memory and concentration. All laboratory studies are normal or nonspecific.

C. What Would You Like to Do Now?

It would be a good idea to contact her primary care physician for background and to share your findings. She does minimally meet criteria for major depressive disorder and has mildly impaired cognitive function, which could be referable to the depressive disorder or be the mild neurocognitive disorder or a forme fruste of an incipient major neurocognitive disorder. She does not have the delusions of persecution, theft, or betrayal by others, which are more common in moderate major neurocognitive disorder.

You explain your findings to her and that you are concerned about her poor sleep and appetite and that she seems distressed by the unexplained gastrointestinal symptoms. You further discuss her depressive and cognitive symptoms and how they might be related. You tell her that you have ideas about medications but you would prefer to talk to her other physician to coordinate care and that you will see her in a week in the outpatient clinic to take the next steps. You also tell her you will order a CT scan of the head as part of the workup.

Case continued: You call the primary care physician, who says "the patient is obsessed about her gastrointestinal distress and is convinced that it is cancer. Her workup has been normal, but she isn't satisfied with that. We don't think any more workup is needed, she needs you because this is all pretty delusional."

D. What Do You Tell the Primary Care Physician?

You share with the primary care physician that this is not the usual context of presentation for schizophrenia and that depressive disorder, mild or major neurocognitive disorder, and isolated somatic delusion are all possible (or commingled). You support the primary care physician in not pursuing more aggressive, high-risk

workup and say that you want to try a medication trial to see if that is of any help. The primary care physician says, "thanks so much, do whatever you want, I can't help her with this. She needs you."

E. What Would Be Your Next Approach to the Patient?

There are two medication approaches to consider initially. One is to treat with an antidepressant (mirtazapine may be the antidepressant of choice for gastrointestinal symptoms and insomnia) and the other is a low dose of an atypical antipsychotic. The cognitive impairment could respond to one or both of these treatments, and you would want to assess that response before committing the patient to pharmacology for a neurocognitive disorder.

Case continued: You see her in a week. The CT is done and reveals mild cortical atrophy and white matter disease. She is still convinced she has a gastrointestinal illness. You tell her that you are working closely with here primary care physician and she is somewhat mollified. You propose a medication trial to help her with her symptoms and to deal with the distress she obviously is experiencing. You also tell her to follow up with her primary care physician. You initiate mirtazapine 7.5 mg at bedtime and risperidone 0.5 mg twice daily.

F. How Will You Monitor Her Response?

Obtaining serial Ham-D scales to assess response to mirtazapine is necessary; an expected robust response would be 50% reduction in the Ham-D score. Serial MoCA tests looking for improvement in attention and concentration are also essential to obtain. Regarding her delusional symptoms, you would hope for less frequently expressed conviction of the intensity of her concerns, less frequent requests for workups, and an ability to question her conviction of a serious illness by statements such as "perhaps I was somewhat exaggerating things" and an ability to accept and be comfortable with the gastrointestinal workup done so far and no more insistence that "something is being missed." These outcomes may take time. Ongoing coordinated care with the primary care physician is highly advisable.

Question 8.14

Acute stress disorder and posttraumatic stress disorder from delirium. The patient is a 66-year-old male who was the victim of a motor vehicle accident with multiple orthopedic traumata, including fractured extremities, pelvic fracture, and pneumothorax. He required a prolonged trauma resuscitation and then a prolonged ICU stay with multiple invasive procedures. He showed intermittently agitated and combative behavior consistent with delirium, which was managed with combined therapy with IV haloperidol, dexmedetomidine, and propofol. With this aggressive treatment, his

combativeness and agitation was brought under control. After several days of managing him in the ICU, he was improved to where the IV sedatives were discontinued and he was extubated.

You have been seeing him throughout the ICU stay to manage his IV sedatives, but have yet to be able to actually speak to him. You have learned through his family members that he is a retired firefighter, and thus he "has seen a lot of bad things" but was able to cope well and only retired at age 60 when the physical demands of the role became too much for someone his age. He does not use alcohol problematically and is not a drug user. He has never been in psychiatric care and has not been treated with psychiatric medications.

When he comes out of sedation, he beckons you to come and talk with you. While he is a bit dysphonic from the effects of the intubation, he tells you that "since they took those meds off, I have been having terrible dreams. Not just about the wreck, but other stuff. I dream about being in a car getting rammed by a truck, the loud noises, the screaming of everyone who got hurt, the shouts of the rescue crew. It is really hard being 'on this side' of a rescue. I rescued people my whole career, it was tough, especially as a young firefighter when we couldn't save someone. But this, it is so strange to be the one getting help. I should be out there helping others. I never should have retired, this wouldn't have happened if I was still working."

He continues: "I get it about the bad dreams of the accident. I know that is kind of normal. But I am having other dreams too that aren't about the accident. I don't get it. For example, I awoke thinking that someone had kidnapped me, taken me somewhere and was shoving a boa constrictor down my throat. I could feel it going down but was powerless. Then, I dreamed that I was being held to a cross and crucified, you know, like Jesus, with nails going through my wrists to hang me by. I couldn't get away."

A. What Accounts for These Symptoms? Is This Continuing Cognitive Impairment from Delirium?

Certainly cognitive impairment from delirium can persist for several months, and you want to clearly monitor and validate recovery from delirium. He should have continued delirium precautions, which might be somewhat challenging in that he may need opioid pain relief for some time, given the severe orthopedic injuries. However, the specificity of the nightmares and sleep disturbances with excessively detailed factual recall more suggests acute stress disorder (due to the less than 6 months duration [41]).

B. How Would You Interpret His Last Two Mentioned Nightmare Narratives?

Given that his actual injuries were not to his pharynx or distal upper extremities, a likely explanation is that he is somatically recalling intubation (the boa constrictor)

and arterial line placement (crucifixion). As he was probably unconscious when these procedures were done, he will not have an organized and coherent narrative by which to explain them. Indeed, at the time he was weaned off IV sedatives, the intubation and arterial line were discontinued, so he has no full consciousness or contemporary awareness of their placement to serve as a substrate for understanding these.

C. How Would You Approach Interpreting These Dreams So as to Help Him Make Sense of Things?

An explanation of the above connection should be done. Psychoeducation about acute stress disorder and posttraumatic stress disorder in the context of injury and medical/surgical procedures should be offered to help him put this into perspective.

D. What Other Considerations Are There for Managing Him?

First and foremost is continued delirium surveillance and prevention. Any recurrence of cognitive impairment, psychosis, or sleep disturbance should lead to reassessment for delirium. Assuming no recurrence of delirium, a clinical pivot to consider the case as acute stress disorder with risk of consolidation of posttraumatic stress disorder becomes paramount. Sleep management with CBT for insomnia, mirtazapine, or trazodone may be needed. A posttraumatic depressive episode may need treatment with an SSRI. Trauma-focused CBT (with focus both on the car accident and the delirium/ICU medical procedures) should be accomplished, with an understanding that the traumatic memories for the medical procedures may in fact be more problematic to the patient than the initial trauma, especially if the index trauma is not remembered in factual detail.

Question 8.15

Geriatric exacerbation of posttraumatic stress disorder. The patient is a 71-year-old male asking to see a consultant psychiatrist during his hospitalization for a medical procedure. He has a history of typical posttraumatic stress disorder with full spectrum symptoms, dating from his service as a combat medic in the Vietnam War in the late 1960s. While he was never wounded, he came under fire repeatedly during his tour of duty. He had persistent flashbacks, nightmares, social isolation, and hyperarousability with onset during the time he was on duty. He went through a period of alcohol abuse in his late 20s and 30s, "trying to numb my head, otherwise I couldn't sleep." While he struggled with his symptoms for some years and had some relapses with alcohol use, he eventually improved. He was able to ultimately have a successful career in medical supply ("I like being part of the medical system, helping people, like when I was a medic") from which he recently retired.

Shortly after retiring, he finds that his nightmares "are coming back, first time in years," which he finds somewhat associated with "watching more TV about the news, all the terrorism" and notes that his symptoms are worse when he learns of mass casualty events "like that place *Pulse* in Florida" which remind him of his combat experience. He has been avoiding drinking but seeks your help "because I don't want to go there again, that road is a loser."

A. You Are the Consultation-Liaison Psychiatrist. How Do You Approach This Case?

Approximately 10% of veteran patients with posttraumatic stress disorder have been reported to have exacerbation of symptoms several decades after the initial traumatic event [42]. Such "recurrent" or "tardive" posttraumatic stress disorder can be cued by vicarious exposure to new disruptive events, even though the patient is by definition not directly threatened by a traumatic event; in the case of a patient with established posttraumatic stress disorder, the trigger for recurrence need not be a threatening circumstance, just a "symbolic" one. Another factor to consider is retirees no longer have daily routine activities to involve themselves in; excess "free time" combined with distressing exposure to other events may conspire to increase frequency of recurrent posttraumatic stress symptoms. Obviously if the patient experiences an actual, life-threatening contemporary event (e.g., illness, surgery, injury), the risk would be expected to be higher, but detailed studies are lacking.

Case continued: You see him in hospital. He describes poor sleep, nightmares, social avoidance, and hyperarousability. His affect is anxious, non-tearful, and non-melancholic. He has no suicidal ideation or psychosis. His Ham-D score is 16 (many points are referable to sleep disturbances and anxiety). His MoCA score is 26/30.

B. Are There Some Other Workups to Consider?

With any new patient and mood symptoms, checking a TSH and B_{12} is reasonable. If you are concerned about alcohol or other substance use, ordering a blood alcohol level and urine toxicology screen is needed. Neuroimaging, while reasonable in many cases, is not urgent. There is no role for an EEG in this case.

C. How Would You Approach This Case?

The psychotherapy of choice for posttraumatic stress disorder at any stage of illness is trauma-focused CBT. The therapist would work on both dealing with older traumatic experiences and work at managing current triggers. This is best done in a group model on an outpatient basis. Couples therapy is also indicated to the degree that his current symptoms impact his intimate relationship. Even if he is not using

alcohol presently, 12-step groups to help maintain social support for sobriety is highly recommended.

D. What About Psychopharmacology for Recurrent Posttraumatic Stress Disorder?

Recurrent posttraumatic stress disorder needs the same psychopharmacological approach as other cases of posttraumatic stress disorder. The psychopharmacology for posttraumatic stress disorder relies on therapeutic combinations; the only categorical recommendation is not to rely on benzodiazepines. For mood and anxiety symptoms, the usual choice is an antidepressant; for patient with concurrent sleep and appetite disturbances, mirtazapine dosed at bedtime is an attractive choice. If he still experiences nightmares once established on an antidepressant, there should be a low threshold to add prazosin, dosed entirely at bedtime, to target nightmares. For irritability that were to persist after optimized antidepressant and prazosin, a trial of an antiepileptic (e.g., lamotrigine) can be considered.

E. What If He Is Readmitted to the Hospital in the Future? What Is His Posttraumatic Stress Disorder Risk Then?

While this has not been adequately studied in a prospective fashion, it is intuitive that his threshold to develop recurrent symptoms of posttraumatic stress disorder associated with medical or surgical illness and/or invasive procedures would be lower than for a patient without such a history. If he is therefore readmitted to the hospital, his outpatient psychotropic medications should be continued in the hospital and the inpatient psychiatry consult service contacted for ongoing management.

Question 8.16

Supervision of house calls teams. The patient is an 80-year-old frail white female. Due to severe osteoarthritis and general frailty, she is largely unable to leave her home. Fortunately, the local academic medical center has a grant-supported geriatric house calls program. In this program, a roving team of geriatric nurse practitioners manages a caseload of housebound patients. They are supervised by a geriatric psychiatrist, who reviews charts, discusses care plans, and occasionally goes into the community to accompany the nurse practitioners. Sensing the high degree of psychiatric illness in these patients, the medical center has engaged you as an additional consultant. The workflow is that you meet with the nurse practitioners weekly to discuss cases that they have seen and advise them regarding clinical interventions. While you have the opportunity to accompany them on their rounds, you generally do not do so, but advise them

based on your case discussions and treatment planning. You have instructed them to complete a Patient Health Questionnaire-9 (PHQ-9) scale, Generalized Anxiety Disorder 7-item (GAD-7) scale, and Montreal Cognitive Assessment (MoCA) on all patients. The nurse practitioners bring blood draw materials to every home visit, but, due to patient mobility limitations, neuroimaging is rarely used in these cases.

You are told of the patient's story. She is widowed, lives alone, and needs shopping and in-home help, although she is alone much of the time. Most of her close friends have died and she has no adult children. Missing her social connection but unable to get out of her home very much, she has become depressed. The nurse practitioner has seen her and reports to you "she really looks depressed, low energy, not sleeping or eating well, hopeless, though she says she wouldn't kill herself, she doesn't have much reason to live."

A. What Else Would You Want to Know?

More details regarding past history of treating this episode is needed. Her initial PHQ-9 was 18 (major depression, moderately severe) and she was started on citalopram. The nurse practitioner reports that "she took it OK and maybe it helped a bit but her sleep and appetite didn't budge." The PHQ-9 only got to 11 (major depression, mild severity) because of the sleep and appetite problem. Her initial GAD-7 was 5 (mild anxiety) ("she isn't anxious, just depressed") and MoCA was 20/30 initially and did not improve. Her TSH level was normal.

B. How Would You Interpret the Nurse Practitioner's Clinical Findings, PHQ-9, GAD-7, and MoCA Scores?

She appears depressed with melancholic features. Her PHQ-9 initially is in the moderate/severe range and only slightly improved; the usual treatment threshold is 10. The GAD-7 of 5 is not actionable. The MoCA of 20, especially in an older patient, is consistent with incomplete response in a depression case; while a MoCA of 20 could also be mild neurocognitive disorder, you would want to fully treat the depressive episode before attributing the score to a mild neurocognitive disorder.

C. What Would You Advise the Nurse Practitioner to Do?

Given the persistence of depressive symptoms and continued poor function, you want to optimize medication interventions within the house calls care model. You would at this point either switch to mirtazapine 15 mg at bedtime or add mirtazapine 15 mg at bedtime to the citalopram trial, monitor compliance and response, and reassess the PHQ-9 and MoCA periodically.

D. What About Acute Safety Concerns?

The nurse practitioner needs to also monitor for suicidal ideation and psychotic symptoms. For suicidal ideation, there would need to be a low threshold to admit her to geriatric psychiatry for a consideration of ECT. Depending on the local jurisdiction's laws, a psychiatric commitment order would need to be written by the clinician (if they are allowed) or by the police. If she responds well and symptomatically and functionally improves, you and the nurse practitioner would have to decide on a pragmatic aftercare and surveillance plan. With older patients who have recovered from severe major depression, it is usually best to continue medication indefinitely.

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Topic 9: Common Major and Mild Neurocognitive Disorders: Alzheimer Disease, Frontotemporal, Lewy Body, and Vascular Types

Question 9.1

Mild neurocognitive disorder (also known as mild cognitive impairment or MCI) is a construct describing individuals who demonstrate cognitive deficits greater than expected for their age but who function relatively independently.

What Are the Subtypes of Mild Cognitive Impairment (Mild Neurocognitive Disorder)? What Are Their "Presumed Outcomes"?

Based on the data from Roberts et al. [1], Fig. 9.1 shows an algorithm used to classify the subtypes of mild cognitive impairment, with "presumed outcomes" characterized by a combination of the clinical syndromes and suspected etiology. The Mayo Clinic Study of Aging reported a 2:1 ratio of subjects with amnestic to nonamnestic types [1].

Question 9.2

The term "dementia" is subsumed under the entity referred to in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) as *major neurocognitive disorders,* which encompasses a group of acquired disorders. *Mild neurocognitive disorder* is a DSM-5-recognized term for the less severe level of cognitive impairment (also referred to as mild cognitive impairment). Patients with mild or major neurocognitive disorders can present with prominent and disabling behavioral disturbances, termed *neuropsychiatric symptoms.* (See Topic 11 for further discussion on neuropsychiatric symptoms due to neurocognitive disorders.) However, neuropsychiatric symptoms can represent early manifestations of emergent mild neurocognitive disorder. Mild cognitive impairment (MCI) can be a

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_9

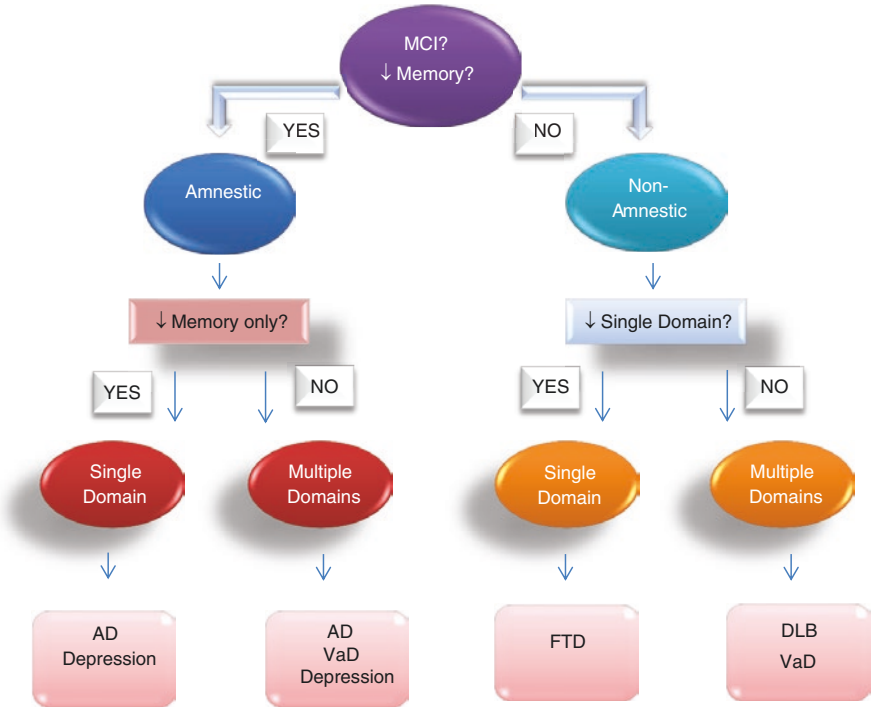


Fig. 9.1 Classification of the subtypes of mild cognitive impairment and presumed outcomes *Abbreviations*: *AD* Alzheimer disease, *DLB* dementia with Lewy bodies, *FTD* frontotemporal dementia, *MCI* mild cognitive impairment, *VaD* vascular dementia

prodrome of major neurocognitive disorder. As with MCI, mild behavioral impairment (MBI) can also be considered a prodromal phase of a major neurocognitive disorder.

A. What Is Mild Behavioral Impairment (MBI) and Its Significance?

Mild behavioral impairment (MBI) is a proposed diagnostic construct aimed to identify patients with or without cognitive symptoms who are at an increased risk of developing a major neurocognitive disorder [2]. More specifically, MBI is a concept to describe late-life onset of neuropsychiatric symptoms that are not better accounted for by other illnesses in the conventional psychiatric nosology and in which other psychiatric symptoms may antedate the cognitive changes.

Neuropsychiatric symptoms are common in major neurocognitive disorder, as well as in prodromal syndromes, such as mild neurocognitive disorder (the terms mild neurocognitive disorder and mild cognitive impairment are used interchangeably in this section). The literature suggests that neuropsychiatric symptoms in MCI confer a greater risk for conversion to major neurocognitive disorder in comparison to MCI patients without neuropsychiatric symptoms. Neuropsychiatric symptoms

Table 9.1 Mild behavioral impairment: highlights of the ISTAART research diagnostic criteria [3]

Criteria		Affected areas
1.	Changes in behavior or personality starting later in life (≥50 years), persisting for ≥6 months, and representing a clear change in at least one of the areas (see right column) Functional changes (not to IADLs) that are attributed to a change in personality/behavior but not to cognitive decline	Motivation/apathy Affective dysregulation Impulse control Social inappropriateness Abnormal perception/thought content
2.	Behavior is of sufficient severity to produce at least minimal impairment in one of the areas (see right column)	Interpersonal relationships Other aspects of social functioning Ability to perform in the workplace The patient should be independent in IADLs
3.	Not attributable to another psychiatric, medical, or substance/medication effect	
4.	No dementia (major neurocognitive disorder); mild cognitive impairment may be present	

Abbreviation: *IADLs* instrumental activities of daily living

in older adults with normal cognition also confer a greater risk of cognitive decline in comparison to older adults without neuropsychiatric symptoms. Although MBI and MCI can co-occur, these constructs are different, and they both can herald a higher risk of progression to major neurocognitive disorder. As with MCI, MBI can be a prodrome to major neurocognitive disorder. However, neuropsychiatric symptoms after the onset of major neurocognitive disorder (discussed elsewhere in this volume) are not considered to be MBI.

B. List the ISTAART Research Diagnostic Criteria for Mild Behavioral Impairment (MBI)

According to the International Society to Advance Alzheimer's Research and Treatment (ISTAART), the highlights for the proposed diagnostic criteria for mild behavioral impairment (MBI) are listed in Table 9.1 [3].

C. Mild Behavioral Impairment Checklist (MBI-C) Has Been Developed to Quantify the Severity of Behavioral Symptoms in Multiple Cognitive Domains. Briefly Describe This Instrument

The mild behavioral impairment checklist (MBI-C) has been developed by Ismail et al. [3] to address the following facts:

- Rating tools used in major neurocognitive disorder did not often differentiate new from chronic neuropsychiatric disorder.

Table 9.2 Highlights of the MBI-C instrument

Items reflected in five MBI domains		Rate
1.	Motivation	Symptom present or absent in the last 6 months
2.	Affect regulation	Is it a change?
3.	Impulse control	If present, note the severity of symptom
4.	Social cognition	Total score + domain scores
5.	Perception/thought content	

Motivation and impulse control are most common
Abbreviation: *MBI-C* mild behavioral impairment checklist

- Rating tools used in major neurocognitive disorder had short reference timelines that might not allow time to rule out reactive states.
- In contrasts with the Neuropsychiatric Inventory (NPI) that initially was developed in context of major neurocognitive disorder, in which the time frame was brief (i.e., 1 month), the MBI-C focuses on a longer time frame (i.e., ≥6 months) (See Table 9.2).

The MBI-C is a 34-item instrument, which can easily be completed by patient, close informant, or clinician. This checklist is designed to quantify the severity of behavioral symptoms in multiple domains. Notably, global and domain-specific scores and thresholds have not yet been developed and validated for clinical diagnosis and assessment. Ongoing validation work will identify scores and thresholds that predict an increased risk of transition to major neurocognitive disorder. To date, this rating scale can be downloaded for no charge and is available in multiple languages (www.MBItest.org).

Question 9.3

Mild cognitive impairment (MCI) may progress to major neurocognitive disorder (also known as dementia) and, therefore, it may be a prodrome of major neurocognitive disorder. However, other neuropsychiatric symptoms may also form part of the prodromal syndrome to major neurocognitive disorder. Therefore, it is essential to recognize these neuropsychiatric symptoms because many patients who eventually go on to develop major neurocognitive disorder were first diagnosed with another psychiatric disorder.

A. What Is the Association Between Late-Life Neuropsychiatric Symptoms and Neurocognitive Disorders?

Woolley et al. [4] found that 28% of their study sample had received a psychiatric diagnosis first, most commonly major depressive disorder, before they went on to develop major neurocognitive disorder (formerly known as dementia).

Neuropsychiatric symptoms in mild neurocognitive disorder (also known as mild cognitive impairment or MCI) increase the risk of conversion to various types of major neurocognitive disorder, in comparison to mild neurocognitive disorder without neuropsychiatric symptoms [2]. Taragano et al. [5] followed older adults with neuropsychiatric symptoms but no cognitive impairment over 3 years and found that 36% developed frontotemporal neurocognitive disorder, 28% developed Alzheimer disease type, 18% developed vascular neurocognitive disorder, and 18% developed another type of major neurocognitive disorder. In a longitudinal study of patients followed annually (median 1.58 years), the estimated conversion rate of MCI with neuropsychiatric symptoms to major neurocognitive disorder is 25% per year, which is higher than the 10–15% conversion rate normally reported for MCI [6]. Other longitudinal studies also have shown that the presence of neuropsychiatric symptoms in patients with MCI increases the risk of converting to major neurocognitive disorder (compared to those with MCI without neuropsychiatric symptoms) [7, 8].

B. What Is the Conversion Rate to Major Neurocognitive Disorder? What Are the Predictors of Progression from Mild to Major Neurocognitive Disorder?

The prevalence of MCI ranges from 15 to 18% in older adults [9]. A significant proportion of individuals later convert to major neurocognitive disorder. The conversion rate is 10–15% per year in clinical studies, but 6–10% in epidemiological studies. Thus, MCI is a risk factor for major neurocognitive disorder/dementia.

The conversion rate is different in clinics versus general population, because in studies using clinics (memory disorder centers), patients seek treatment and thus there is the factor of prior probability of having an underlying disorder; however, in epidemiological (population based) studies, there is more heterogeneity as to the underlying condition. Several factors have shown to predict progression to major neurocognitive disorder/dementia, such as [9]:

- More cognitively impaired states
- Carriers of the e4 allele of the apolipoprotein E (APOE e4)
- Structural changes on MRI including hippocampal and ventricular volume
- PET hypometabolism in temporoparietal regions

Question 9.4

Late-life depressive disorder and major neurocognitive disorder have a complex and often reciprocal relationship—cognitive deficits are common in major depressive disorder, whereas depressive disorders are often seen in the context of mild or major neurocognitive disorders.

A. Is Late-Life Depression a Risk Factor or Prodrome of Major Neurocognitive Disorder?

Both late-life depressive disorder and major neurocognitive disorder present challenges in their clinical assessment where there are mood symptoms, cognitive deficits, and also functional changes present. Common cognitive deficits in late-life depressive disorder include difficulties with processing speed, executive functioning, and memory (encoding/retrieval) (also see Topic 5 on late-life depressive disorders). When late-life depressive disorder usually remits with treatment, cognitive impairments often tend to persist, and most patients meet criteria for mild cognitive impairment [10]. Differences in severity and course between early- and late-onset depressive disorders may suggest different pathogenic processes (see Topic 5 on late-life depression).

In a 28-year follow-up study on trajectories of depressive symptoms before major neurocognitive disorder, the authors found that depressive symptoms later in life were significantly associated with the development of major neurocognitive disorder, while depressive symptoms earlier in life were not [11]. More precisely, those with chronic or recurrent depressive symptoms early in life did not have an increased risk, whereas those with such symptoms later in life did show an increased risk of major neurocognitive disorder. The authors concluded that late-life depressive disorder was either part of the prodrome of major neurocognitive disorder or that the two conditions shared common causes [11]. Therefore, there was no support for the hypothesis that depressive symptoms were a risk factor for major neurocognitive disorder. These findings are consistent with other cohort studies. For example, the 14-year Rotterdam study of 4393 individuals found that risk of major neurocognitive disorder was highest in individuals with depressive symptoms but only at short and intermediate intervals (not beyond 10 years) [12]. In a 14-year longitudinal Australian study of 4922 men, the association between depressive disorder and development of major neurocognitive disorder was only apparent during the initial 5 years of follow-up [13]. Current depressive disorder (with or without past history of depressive disorder) had highest risk of major neurocognitive disorder. Compared with men with no symptoms, the sub-hazard ratios of major neurocognitive disorder were 1.2 (95% CI = 1.0, 1.4), 1.7 (95% CI = 1.4, 2.2), and 2.1 (95% CI = 1.4, 3.2) for participants with questionable, mild-to-moderate, and severe depressive symptoms. Moreover, they found that the use of antidepressants did not modify this risk [13]. For example, the respective adjusted sub-hazard ratio was 1.6 (95% CI = 1.2, 2.1) for men with mild-to-moderate depressive symptoms who were not on antidepressants, 2.5 (95% CI = 1.6, 3.8) for men with mild-to-moderate depressive symptoms on antidepressants, 1.5 (95% CI = 0.9, 2.5) for men with severe depressive symptoms not on antidepressants, and 4.8 (95% CI = 2.3, 9.8) for men with severe depressive symptoms on antidepressants. These authors concluded that depressive disorder is more likely to be a marker of incipient major neurocognitive disorder than a truly modifiable risk factor per se.

Table 9.3 Clinical differences between major depressive disorder and mild/major neurocognitive disorder [14, 15]

Major depressive disorder	Mild/major neurocognitive disorder
Faster/subacute onset	Gradual/insidious onset
No consistent decline over time	Progressive decline over time
Patchy cognitive loss; usually reversible	Progressive cognitive loss; irreversible
Slower rate of forgetting	Faster rate of forgetting
Usually aware of cognitive deficits	May lack insight into cognitive deficits
Patient report > informant report	Informant report > patient report
Oriented to person, time, place	Disoriented, confused
"I don't know, I can't" responses on testing	Guesses and wrong answers on testing
Intact language and motor skills	Aphasia and apraxia
Spared recognition memory ("no" bias—few false-positive errors)	Impaired recognition memory ("yes" bias—many false-positive errors)
Functional impairment—due to insufficient effort	Functional impairment—due to cognitive decline

B. What Are the Differentiating Features Between Major Depressive Disorder and Mild/Major Neurocognitive Disorder?

Table 9.3 presents the clinical characteristics between major depressive disorder and mild or major neurocognitive disorder [14, 15].

Question 9.5

A 77-year-old retired accountant is concerned that his short-term memory has declined over the past year. For example, he returns from the store with the wrong food items, and now he needs to write down a grocery list. Paying the bills and household projects now take him longer to complete, and he feels as if he has lost his confidence in completing these tasks. His father had major neurocognitive disorder due to Alzheimer disease, with onset of symptoms at age 72, in which memory was predominantly affected. The patient had recurrent major depressive disorder 5 years ago and successfully treated with an antidepressant, which was eventually discontinued. He denies any current depressive symptoms. He exercises routinely, never smoked, and rarely drank alcohol. On current examination, the Geriatric Depression Scale 15-item score is 1 (suggestive of no depressive disorder) and the Generalized Anxiety Disorder Scale 7-item score is 6 (suggestive of mild anxiety). On memory testing, he scores below normal when repeating a brief story containing ten details. Laboratory findings are within normal range. Brain MRI shows bilateral temporal (medial, basal, and lateral) and medial parietal lobe atrophy. On genotyping test, he has one apolipoprotein E e4 copy.

A. What Is the Diagnosis?

The patient has subjective and objective cognitive changes and overall preservation of his functional abilities. Therefore, he meets the criteria for mild neurocognitive disorder (see Table 9.4) [14, 16]. Because his family history and cognitive testing are of memory impairment (the typical phenotype of Alzheimer disease) and his topographical biomarker of cortical atrophy is consistent with Alzheimer disease, he meets the criteria for mild neurocognitive disorder due to Alzheimer disease, with an intermediate biomarker probability of Alzheimer disease (see Table 9.5 for biomarkers in Alzheimer disease and Table 9.6 for highlights of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) and National Institute on Aging-Alzheimer's Association (NIA-AA) diagnostic criteria) [14, 16–18]. For a complete review of the DSM-5 diagnostic criteria for major or mild neurocognitive disorder due to Alzheimer disease, the reader is referred to the DSM-5 manual [14].

B. What Should the Physician Advise This Patient Regarding Prevention Strategies and Mitigating Current Risk Factors for Progression to Major Neurocognitive Disorder?

As illustrated in Table 9.7, there are several potentially modifiable and non-modifiable risk factors for Alzheimer disease, specific for each individual [19]. This patient had a first-degree relative with late-onset Alzheimer disease (his father). There was nothing in his family history to indicate an autosomal dominant multigenerational transmission. All this leads to the understanding that he does not require further genetic testing. Apolipoprotein E is a known risk factor for late-onset Alzheimer disease, but data on midlife risk factors that have included apolipoprotein E status have not been found to increase the accuracy of the predictive model

Table 9.4 All-cause major or mild neurocognitive disorder: highlights of the diagnostic criteria according to DSM-5 and NIA-AA classifications [14, 16]

Mild neurocognitive disorder	Major neurocognitive disorder
Modest cognitive impairment in ≥1 cognitive domains	Substantial cognitive impairment in ≥1 cognitive domains
No interference with functional independence (e.g., complex IADLs are preserved, but greater effort and compensatory strategies may be required)	Interference with independence in everyday activities (e.g., requiring assistance with complex IADLs)
Not attributable to delirium or other neuropsychiatric disorders (e.g., major depressive disorder, schizophrenia)	Not attributable to delirium or other neuropsychiatric disorders (e.g., major depressive disorder, schizophrenia)
Specifiers: With or without behavioral disturbance (e.g., psychotic symptoms, mood disturbance, agitation, apathy, other behavioral symptoms)	

Abbreviations: *DSM* Diagnostic and Statistical Manual of Mental Disorders, *IADLs* instrumental activities of daily living, *NIA-AA* National Institute on Aging-Alzheimer's Association

Table 9.5 Biomarkers used to define Alzheimer disease [14, 16–18]

National Institute on Aging-Alzheimer's Association	International Working Group
Amyloid biomarkers CSF: ↓ amyloid beta42 in CSF Amyloid PET: ↑ radiotracer retention	*Pathophysiological biomarkers* CSF: ↓ amyloid beta42 and ↑ t-tau or p-tau Amyloid PET: ↑ radiotracer retention
Injury biomarkers MRI: atrophy in temporal (medial, basal, and lateral) and medial parietal cortex FDG-PET: ↓ metabolism in temporal and parietal cortex CSF: ↑ t-tau or p-tau	*Topographical biomarkers* MRI: atrophy in temporal (medial, basal, and lateral) and medial parietal cortex FDG-PET: ↓ metabolism in temporal and parietal cortex
Biomarker probability of AD etiology: Positive for both biomarker categories: high[a] Positive for 1 biomarker category: intermediate Negative for both biomarker categories: low[b] Unavailable or indeterminate: uninformative[c]	Autosomal dominant mutation biomarkers: APP PSEN1 PSEN2 Apolipoprotein E e4 allele not specific enough to meet criteria

Abbreviations: *AD* Alzheimer disease, *APP* amyloid precursor protein, *CSF* cerebrospinal fluid, *FDG-PET* fluorodeoxyglucose positron emission tomography, *MRI* magnetic resonance imaging, *PSEN* presenilin, *t-tau or p-tau* total tau or phosphorylated tau

[a]Possible major neurocognitive disorder with evidence of AD pathophysiology does not preclude the presence of another pathophysiological process

[b]Unlikely due to AD

[c]Diagnosis is based on clinical criteria

for major neurocognitive disorder, however, more specificity is needed regarding the allele e4 type [20]. A personal history of depressive disorder within the recent past may increase his risk for developing Alzheimer disease later in life. His physician should advise him to control his physical and emotional wellbeing, using evidence-based strategies. However, the patient must be educated that there are no high-quality clinical trials that have evaluated the effectiveness of modifying these risk factors and that there are currently no proven therapies that will fully prevent the development of neurocognitive disorder due to Alzheimer disease. In other words, despite other proven health benefits, he could not be assured that these interventions would eventually decrease his risk of developing Alzheimer disease.

Question 9.6

Based on the National Institute on Aging-Alzheimer's Association Revised Diagnostic Criteria, What Are the Two Categorical Presentations of Alzheimer Disease? Briefly Define These Presentations

According to the National Institute on Aging-Alzheimer's Association revised diagnostic criteria, the two categorical presentations of Alzheimer disease are amnestic and non-amnestic presentations [16].

Table 9.6 Major or mild neurocognitive disorder due to Alzheimer disease: highlights of the diagnostic criteria according to DSM-5 and NIA-AA classifications [14, 16]

Mild neurocognitive disorder due to Alzheimer disease	Major neurocognitive disorder due to Alzheimer disease
Insidious onset, gradual progression; ≥1 cognitive domains	Insidious onset, gradual progression; ≥2 cognitive domains
Probable: Evidence of causative genetic mutation from family history or genetic testing	*Probable*: (1) or (2): 1. Evidence of causative genetic mutation from family history or genetic testing 2. All three are present: (1) decline in memory and learning and >1 other cognitive domain; (2) progressive, gradual cognitive decline; (3) no mixed etiology (e.g., no other neurodegenerative, cerebrovascular, neurological, systemic medical, or psychiatric disorder)
Possible: (1) and (2): 1. No evidence of causative genetic mutation from family history or genetic testing 2. All three are present: (1) clear evidence of decline in memory and learning; (2) progressive, gradual cognitive decline, without extended plateaus; (3) no evidence of mixed etiology (e.g., no other neurodegenerative, cerebrovascular, neurological, systemic medical, or psychiatric disorder)	*Possible:* If above criteria are not met

Abbreviations: *DSM* Diagnostic and Statistical Manual of Mental Disorders, *NIA-AA* National Institute on Aging-Alzheimer's Association

Table 9.7 Non-modifiable and potentially modifiable risk factors for Alzheimer disease [19]

Category	Risk factors	Comments
Non-modifiable risk factors		
Age	Increasing age	Age of early onset vs. late onset in patient and family members
Sex	Females > males	Doubles the risk
Genetic	First-degree relative with AD, Down syndrome Early-onset AD: APP, PSEN1, PSEN2 genes Late-onset AD: APOE4 gene Many other genes of little or unknown significance	Increases four times the risk, trisomy 21 Early age at onset: 30–60 years Gene on chromosome 19: – Three alleles: e2, e3, e4 – Allele e4: – 25% of population – e4/e4: 50% risk in age 60s – e4 heterozygote: 50% risk in age 70s – APOE4 screening not recommended in asymptomatic persons due to low sensitivity/specificity and low positive and negative predictive values

Category	Risk factors	Comments
Mild cognitive impairment	Mostly amnestic forms	80% develop major NCD after 6 years
Modifiable risk factors		
Morbidity factors	Systolic hypertension Serum cholesterol Head injury Depression Diabetes mellitus	At risk: >160 mm/Hg At risk: >6.5 mmol/L (>251 mg/dL) At risk: moderate/severe, with loss of consciousness Independent risk factor: history of late-onset depression Association may be bidirectional
Lifestyle factors	Moderate wine consumption Physical activity Cognitive activity Smoking Diet	Optimal use: 250–500 mL/day At risk: if little/no regular exercise Cognitive training may reduce risk At risk: current use, no conclusive evidence that smoking cessation decreases risk At risk: increased dietary fat intake and reduced omega-3 fatty acids; Mediterranean-style diet associated with better cognitive performance
Sociodemographic factors	Education Occupation	At risk: lower education Inconclusive role; some exposure to environmental toxins (e.g., pesticides, fertilizers, fumigants) increases risk
Statin drugs	Treatment of hyperlipidemia	No evidence of reducing risk of AD; inconclusive results
Other medications and supplements	Nonsteroidal anti-inflammatory drugs, estrogens in women, vitamin B, vitamin C	Studies are inconclusive; no justification for recommending these options; vitamin E dose >400 IU/day had negative cardiovascular effects

Note: *AD* Alzheimer disease, *APOE* apolipoprotein E, *APP* amyloid precursor protein, *NCD* neurocognitive disorder, *PSEN* presenilin
From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

The amnestic presentation involves impairment in *learning and recall* (encoding) of recently learned information.

The non-amnestic presentations can involve deficits in the following cognitive domains:

- *Language*: defined as prominent deficits in word-finding (but deficits in other cognitive domains should be present)
- *Visuospatial*: defined as prominent deficits in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia (but deficits in other cognitive domains should be present)
- *Executive function*: defined as prominent deficits in reasoning, judgment, and problem-solving (but deficits in other cognitive domains should be present)

Question 9.7

A 65-year-old food and wine editor and critic for a major tabloid magazine had a longstanding history of recurrent major depressive disorder managed on maintenance treatment with sertraline 150 mg daily. She reported having difficulties with writing her columns in the past 6 months, attributing this mostly to experiencing progressive dysosmia (loss of sense of smell) and hypogeusia (loss of sense of taste), although the latter has somewhat improved lately. She also believes her concentration and memory have been declining lately in the context of inability to perform her work, along with experiencing depressed mood, anhedonia, and sleep and appetite changes, which she believes could be explained by possible recurrence of depression. Upon history review, 6 months ago, she apparently woke up with the realization that the left side of her face from the forehead to chin was sagging. She could not close her left eye. She believed she had a stroke and called the ambulance immediately. In the emergency department, her neurological examination was normal except for left-sided facial droop (cranial nerve (CN) VII). She could not furrow the left half of her forehead or close her left eye on command. Testing of her olfaction (CN I) was omitted. A CT of her brain was negative for evidence of a stroke but did reveal mild periventricular white matter changes and cortical atrophy considered above average for her age. She was given an aspirin and admitted overnight for observation. By morning, the facial droop had improved considerably, and she was able to close her left eye two-thirds of the way. A diagnosis of Bell's palsy was given. She was discharged home with follow-up with a neurologist. In the following 6 months, her inability to write her column has continued, as did her dysosmia, while her hypogeusia has improved significantly in a few weeks. This patient is eventually referred to a psychiatrist to rule out a depressive episode.

A. What Is the Differential Diagnosis for the Decline of This Patient's Career Following Her Bell's Palsy?

Because CN VII subserves taste on the anterior two-thirds of the tongue, this likely impaired her taste perception for weeks. She met criteria for a major depressive disorder and the loss of taste and smell likely contributed to her stressors leading to the recurrence of depressive disorder. However, after her sense of taste returned, based on objective testing, and loss of sense of smell continued, the quality of her writing continued to be poor. She attributed this to a gradual deterioration in her sense of smell, which is as important as taste for an expert critic of food and wine.

However, another explanation exists in this case. Reduced odor identification (dysosmia) commonly goes unnoticed by patients, whereas physicians often neglect to test olfaction (CN I). This is something a food critic, as in this case, would notice. Odor identification is known to be impaired in both aging and major neurocognitive disorder [21–23]. Diminished odor identification can occur early in the course of major neurocognitive disorder due to Alzheimer disease, with neurofibrillary tangles appearing in the entorhinal cortex, and may be a practical and affordable

biomarker of preclinical Alzheimer disease [24]. An impairment of odor identification can precede the onset of cognitive symptoms and predicts progression from mild to major neurocognitive disorder due to Alzheimer disease [25]. As in this case, neurological examination of older patients presenting with cognitive impairment should include examination of CN I using a substance readily identified by its odor (e.g., fresh, ground coffee). In this case, an alternative diagnostic explanation for the worsening quality of her columns is neurocognitive disorder. The biomarkers on her neuroimaging findings support this diagnosis. Additionally, the mild white matter disease may have made her more vulnerable to concomitant neurocognitive disorder due to Alzheimer disease and vascular disease.

B. Name a Standardized Test of Olfactory Function Used in Clinical Practice

A standardized, simple "scratch-and-sniff" olfactory test is the University of Pennsylvania Smell Identification Test (UPSIT), which is a 40-item self-administered tool, with multiple-choice response forms, which rapidly and accurately assesses general olfactory function [26]. The 40-item UPSIT has been validated in people 5–85 years of age and shows an internal consistency reliability of 0.922; moreover, there are no major sex differences noted [27].

Question 9.8

A 58-year-old female was initially seen by an ophthalmologist for a 2-year history of visual impairment not associated with localized ocular disease. She described difficulties with following the lines of text while reading, double vision, blurred vision, increased sensitivity to bright light and shiny surfaces, problems with depth perception when climbing stairs, and difficulty reaching out to pick up an object. She denied any anxiety or depressive symptoms. Her nonvisual aspects of language were preserved. Three years later, she began to show progressive visuospatial disorientation, affecting her driving ability, and difficulty in using the telephone because she did not see the numbers. She became confused with right and left hands. She had no family history of major neurocognitive disorder. On Montreal Cognitive Assessment (MoCA), she scored 18 out of 30 points. She performed poorly on the Trail Making Test Part B (a test of visual attention and task switching) and Stroop Test (a test of attentional capacity and flexibility, related to the ability to read words more quickly and automatically than naming colors). She had jerky intrusions when attempting to perform smooth pursuit eye movements (ocular apraxia) and had difficulty in performing manual tasks under visual guidance bilaterally (optic ataxia). She did not perceive more than a single object at a time (simultanagnosia) (e.g., she could not see two pens of different colors on the table). She had normal optic fundi. There were no frontal release signs or other neurological signs. Her insight was intact. A neuropsychological evaluation showed visuospatial deficits. Her visual

impairment precluded the evaluation of the other cognitive domains, especially language functions. Laboratory investigations were unremarkable. Brain MRI showed prominent bilateral parieto-occipital atrophy. She was diagnosed with an unspecified major neurocognitive disorder. Three years later, her visual function further deteriorated, and her language functions (reading, writing, naming, and fluency) also deteriorated. She presented bilateral inability to distinguish the fingers on the hand (finger agnosia) and difficulty in performing computations (acalculia). She had difficulty on confrontation field examination, because she often could not see the target (due to simultanagnosia and ocular apraxia). She further deteriorated and presented with worsened basic ADLs. Two years later, unfortunately she died, and at autopsy there was an abnormal accumulation of the proteins amyloid and tau.

A. What Is the Type of Major Neurocognitive Disorder in This Case? Describe this Syndrome

Based on clinical and neuroimaging grounds, a diagnosis of posterior cortical atrophy is made in this case. Posterior cortical atrophy is characterized by progressive impairment of higher (cortical) visual function with neuroimaging evidence of atrophy affecting the occipital, parietal, and posterior temporal lobes bilaterally [28]. In 1988, Benson et al. [29] defined a condition characterized by a progressive visual impairment occurring in the absence of ocular dysfunction. As in this case, these patients may initially see an ophthalmologist, although the visual deficits are due to problems with cortical processing of the information. The visual dysfunction defines this disorder, with classical deficits of the Bálint (i.e., simultanagnosia, optic ataxia, ocular apraxia), and Gerstmann (i.e., agraphia, acalculia, right-left disorientation, finger agnosia) syndromes [28]. Insight is typically preserved until late. With the disease progression, episodic memory, language, and other cognitive functions become impaired, and eventually symptoms of typical neurocognitive disorder due to Alzheimer disease become apparent in the very late stages [30]. Notably, neuropsychiatric manifestations of posterior cortical atrophy can also occur, and include visual hallucinations in about 25% of cases, and seizures in later stages of the disease [30].

B. What Is the Pathological Cause in Posterior Cortical Atrophy?

Most cases prove to have Alzheimer pathology [28]. Therefore, posterior cortical atrophy is typically considered the visual variant of Alzheimer disease and is one of the atypical variants of Alzheimer disease (see Question 9.9). In the case presented, the pathological report showed an abnormal accumulation of amyloid and tau that formed plaques and tangles, as is seen in Alzheimer disease. Although less frequently present, pathological entities such as Lewy body disease, corticobasal degeneration, and prion disease have also been described as underlying causes of posterior cortical atrophy [30].

C. What Is the Epidemiology of Posterior Cortical Atrophy?

Posterior cortical atrophy affects less than 5% of patients with Alzheimer disease, although it tends to be under-recognized [31]. Patients with posterior cortical atrophy have their initial onset of symptoms in their mid-50s or early 60s, but there can be a considerable delay to diagnosis owing to the unusual presenting symptoms and younger age of onset than the typical Alzheimer disease. Life expectancy is approximately similar to patients with typical Alzheimer disease or longer [30].

Question 9.9

Atypical forms of Alzheimer disease rarely present initially with memory impairment, which may not prompt the diagnosis of a major or mild neurocognitive disorder, thus delaying an accurate diagnosis and management.

A. What Are the Atypical Variants of Alzheimer Disease?

Typical Alzheimer disease manifests with progressive impairment in episodic memory and other cognitive domains, but a proportion of patients present with atypical phenotypes. Table 9.8 summarizes the common atypical variants of Alzheimer disease [19, 32, 33].

B. Why Is It Important to Recognize the Atypical Variants of Alzheimer Disease?

Atypical variants of Alzheimer disease are important to recognize for the following considerations:

- It necessitates referral to specialized clinics for a more in-depth evaluation.
- Clinicians may feel less knowledgeable about the disorder's management and require further follow-up with specialized clinics.
- It may require referral for genetic testing (especially the early-onset types) and family counseling, if appropriate.
- It may qualify for a trial of a cognitive enhancer.

Question 9.10

Because Alzheimer disease represents the most common cause of major neurocognitive disorders, it is reasonable to presume that a cognitive impairment actually is caused by Alzheimer disease. However, this is not always the case, and misdiagnosis can impact treatment.

Table 9.8 Atypical variants of Alzheimer disease [19, 32, 33]

Atypical Alzheimer disease	Characteristic features
Posterior cortical atrophy	Deficits in visual processing, praxis, calculation, and spelling, in various combinations; early anxiety; preservation of memory, naming, and executive function Parieto-occipital atrophy with relative sparing of medial temporal lobes Low incidence of family history; present in middle age Pathology: >80% Alzheimer disease; some corticobasal atrophy, Lewy body disease, or prion disease
Frontal Alzheimer disease	Frontal more than posterior deficits: more behavioral changes Frontal, anterior temporal atrophy Onset at younger age
Language-associated Alzheimer disease	Progressive language decline Language-associated syndromes: Alzheimer-associated logopenic aphasia, progressive nonfluent aphasia, or semantic variant Asymmetrical atrophy Biomarkers can confirm Alzheimer pathology
Young-onset Alzheimer disease	<5% of Alzheimer disease cases; includes autosomal dominant Onset age < 65 years More rapid progression usually More non-amnestic phenotype (visuospatial, attention, executive deficits); early prominent myoclonus
Familial Alzheimer disease	<1% of Alzheimer disease cases Early-onset, familial autosomal dominant: APP, PSEN1, PSEN2 genetic mutations Onset at younger age (e.g., fourth decade) Myoclonus, seizures: more common than in sporadic form
Rapidly progressive Alzheimer disease	10% of Alzheimer disease cases Decrease in MMSE: >6 points/year Predictors of rapid decline: low education, younger age, male, severe cognitive impairment at onset, focal signs, seizures, psychotic symptoms (e.g., delusions, primarily visual hallucinations), cortical signs (e.g., apraxia), subcortical signs (e.g., apathy, executive dysfunction), behavioral changes (e.g., aggression, agitation, wandering), biomarkers (e.g., positive PSEN1 and other genes, high CSF tau)
Corticobasal syndrome due to Alzheimer disease	20% of cases have Alzheimer pathology Medial perirolandic dysfunction: asymmetric, akinetic-rigid, levodopa-resistant syndrome Atrophy extends into temporoparietal cortex and precuneus

From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission from Springer

What Is the Differential Diagnosis of Major or Mild Neurocognitive Disorder Due to Alzheimer Disease?

Alzheimer disease is the most common cause of major neurocognitive disorder [34]. However, several other medical conditions can seemingly resemble neurocognitive disorder due to Alzheimer disease, and the differential diagnosis of these clinical presentations is summarized in Table 9.9 [33, 35].

Table 9.9 Differential diagnosis of neurocognitive disorder due to Alzheimer disease [33, 35]

Disorder	Clinical characteristics
Neurocognitive disorder due to Alzheimer disease	Clinical evidence of progressive cognitive and functional decline, with early loss of insight; amnestic and non-amnestic phenotypes; atrophy pattern on MRI: temporal (medial, basal, and lateral) and medial parietal cortex; hypometabolism on functional neuroimaging (temporal and parietal cortex)
Other neurocognitive disorders (e.g., frontotemporal neurocognitive disorder, Lewy body disease, Parkinson disease, progressive supranuclear palsy, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, cerebrovascular disease, cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL))	Non-Alzheimer-like atrophy pattern on MRI, non-Alzheimer-like hypometabolism on functional neuroimaging; abnormal dopamine transporter scan; significant vascular burden or strategic infarcts on MRI; typical presentation in Creutzfeldt-Jakob disease (myoclonus, typical EEG pattern, and CSF 14–3-3 protein); NOTCH3 gene on chromosome 19 in CADASIL
Delirium	Clinical evidence of rapid onset; fluctuating mental status; changes in level of arousal, cognition (i.e., orientation, attention, memory), psychomotor activity, and perceptual abilities; a change from baseline is often key to diagnosis of delirium in those with preexisting neurocognitive disorder
Anxiety disorder	Clinical evidence of anxiety; typical neuropsychological profile; normal MRI
Depressive disorder	Clinical evidence of depression; personal and family history of depression; life stressors; typical neuropsychological profile; normal MRI
Endocrine, metabolic, nutritional disorders (e.g., thyroid disease, diabetes mellitus, B_{12} and thiamine deficiencies)	Typical blood screen pattern
Korsakoff syndrome	History of alcohol misuse; history of Wernicke encephalopathy
Central nervous system infections (e.g., herpes simplex, HIV, syphilis)	Typical serology pattern

(continued)

Table 9.9 (continued)

Disorder	Clinical characteristics
Autoimmune encephalopathies (e.g., voltage-gated potassium channel complex receptor antibodies, *N*-methyl-D-aspartate (NMDA) receptor antibodies)	Identifiable antibodies; abnormal MRI; typical neuropsychological profile
Sleep apnea	History of snoring; abnormal sleep study
Epilepsy	Clinical evidence for seizures; transient amnesia; epileptiform changes on EEG
Brain lesions	Focal neurological deficits; neuroimaging findings
Neurodevelopmental disorders	Onset in developmental age

Question 9.11

A primary care physician referred to you an 82-year-old man with a mild stage of major neurocognitive disorder due to Alzheimer disease for an opinion regarding fitness to drive. He came accompanied by his daughter and son-in-law who lived with the patient since he became a widower 3 years previously. You learned from the referral note and collateral informant that his family members noticed a progressive decline in his memory and functioning over the previous year and that, more recently, he had difficulties with changing lanes safely. An on-road test was already scheduled by his primary care physician and is yet to be completed. Recently, on Montreal Cognitive Assessment, he scored 18 out of 30 points. Now, his family members are wondering whether he was even fit to attempt to take the driving test due to this low cognitive score.

A. What Do You Tell the Family and the Patient Regarding Fitness to Drive in This Case?

You inform them that there is no cognitive test which has sufficient sensitivity or specificity to be used as a single determinant of driving ability. However, abnormalities on the Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), clock-drawing test, and Trail Making Test should trigger further in-depth testing of driving ability. MoCA scores are translatable to the MMSE to facilitate comparison. MoCA distributes mild neurocognitive disorder cases across a broader score range with less ceiling effect. A MoCA cutoff of $\geq$17 may help capture early and late mild neurocognitive cases; however, a cutoff of $\geq$18 could be used depending on the level of sensitivity desired [36]. A functional assessment can help exclude cases of major neurocognitive disorder. A recent study demonstrated that in cognitively impaired older adults, a MoCA score of $\leq$18 in cognitively impaired individuals was associated with greater likelihood of failing an on-road driving assessment, although its predictive ability was not strong enough to recommend its use as the sole instrument for identifying unfit drivers [37].

In summary, the clinician needs to convey the following to the concerned family members and the patient:

- There is no single office-based test that can reliably be used alone to determine whether it is safe for a patient with cognitive impairment to drive; a multifaceted approach helps to ensure that these cognitive test findings are interpreted in a clinical context.
- On-road testing may be advisable, and it remains the most accurate way of determining fitness to drive, although such testing can be expensive, and it is not available in all areas; however, the clinician needs to emphasize that, if the patient is deemed fit to continue driving, these findings could be considered time limited, and thus, the driving evaluations may be repeated at 6-month intervals or more frequently if a noticeable decline is observed.
- The clinician also needs to comply with the disclosure laws to local motor vehicle departments regarding notification of patients with impaired driving due to a major neurocognitive disorder [38].

B. The Trail Making Test (Part A and Part B) Is a Cognitive Screen for Problems That May Indicate Impaired Fitness to Drive in Patients with Mild Neurocognitive Disorder or Early Major Neurocognitive Disorder and May Be Suggestive of the Need for Further Testing (e.g., Performance-Based Road Testing). Briefly Describe the Tool, and Outline the Evidence for Its Use for This Purpose

Driving fitness assessment in older adults requires functional evaluation of cognitive, motor, perceptual, and psychiatric domains. It represents a particular challenge among older adults with progressive neurocognitive disorders, a group at increased crash risk. Notably, there has been no single test shown to be sufficiently robust as a predictor of driving performance that it could be used as a sole screening measure to determine fitness to drive in cognitively impaired individuals.

The Trail Making Test (TMT) is a cognitive test of visual attention and task switching. The TMT is a two-part pencil-and-paper test (Part A and B) commonly used in driving research studies due to its brevity, ease of administration, low cost, and availability in the public domain. Part A (TMT-A) is a visual, attention, and motor-speed task that involves connecting a series of randomly distributed circles containing numbers in numeric order. Part B (TMT-B) additionally requires switching attention sets by connecting a series of randomly distributed circles containing numbers or letters in alternating order. Many international guidelines have recommended use of the TMT-B to assess driving safety [39]. A systematic review concluded that there is support for using TMT-B cutoffs of 3 minutes for completion or three or more errors: the "3 or 3 rule" [40]. The TMT-A may also be helpful in discriminating between safe and potentially unsafe cognitively impaired older drivers, but more precise screening

measures need to be analyzed critically. A study demonstrated that inability to complete the test within a reasonable time frame (e.g., TMT-A > 48 s, TMT-B > 108 s) may suggest the need for further screening or on-road testing [41].

Question 9.12

List the Instrumental Activities of Daily Living (IADLs) and Basic Activities of Daily Living (ADLs)

Instrumental activities of daily living (IADLs) typically begin to decline at the stage of mild neurocognitive disorder and include shopping, management of finances, household chores performance, meal preparation, driving, and using public transportation [42]. Basic activities of daily living (ADLs) are impaired in the moderate-to-severe stages of major neurocognitive disorder and include eating, dressing, grooming, bathing, toileting, and ambulating [42]. The IADLs and basic ADLs are listed in Fig. 9.2 [19].

Question 9.13

Mrs. A, a 64-year-old teacher, has been seen by you in the outpatient psychiatric clinic for a depressive disorder occurring in the context of caregiver burnout. Mrs. A had been the primary caregiver for her mother suffering from major neurocognitive disorder due to Alzheimer disease until 4 weeks ago, when Mrs. A had to move her mother to a skilled nursing facility. At today psychiatric follow-up visit, she reports to you: "I am worried about getting Alzheimer disease, just like my mother. It is really taking a toll on me. I have been caring for her at home while she slowly deteriorated. So, I often wonder what the risk of developing this serious disease is for me. I really want to do everything I can to avoid my mother's misfortune." Mrs. A then goes on to report that her mother (now 86 years old) had her first cognitive symptoms 8 years previously. To her knowledge, no other biological family

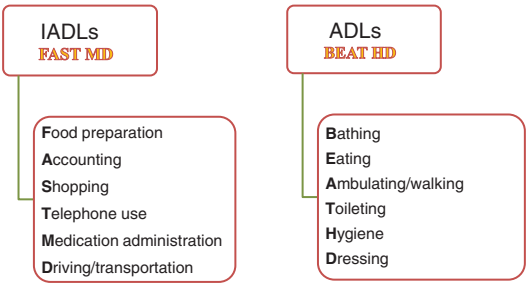


Fig. 9.2 Instrumental activities of daily living (IADLs) and basic activities of daily living (ADLs) [19]. From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

members, including aunts and uncles, have been affected by major neurocognitive disorders. Mrs. A quit smoking 20 years ago. She occasionally drinks alcohol. She was fairly active, exercised regularly, and used to have a busy social life until she became overwhelmed with the caregiver responsibilities for her mother at home. Now, she has resumed jogging and joined social groups since her mother moved to the long-term care facility. On this visit, her blood pressure is 145/90 mmHg (hypertension). She has been taking medication for hypertension for over 2 years. Her body mass index is 23 kg/m^2 (normal range). She eats a balanced diet with a daily intake of fruit and vegetables.

A. According to the 2017 Report from the Lancet Commission on Dementia Prevention, Intervention, and Care, What Are the Potentially Modifiable Risk Factors and Their Contribution to Global Major Neurocognitive Disorder (Dementia)? Specifically, What Risk Factors Do You Identify in Mrs. A's History?

In 2017, a comprehensive report from the Lancet Commission on Dementia Prevention, Intervention, and Care found that one-third of cases of global major neurocognitive disorders (dementia) may be preventable by addressing lifestyle factors that affect an individual's risk [43]. This report has addressed interventions and care strategies for patients with major neurocognitive disorders (dementia) and proposed the development of future international public health policy. The experts of this report have found that nine lifestyle factors together are responsible for 35% of cases of major neurocognitive disorders. Because the study did not include dietary factors, alcohol use, sleep, visual impairment, or air pollution due to the lack of data, the authors believed that contribution of lifestyle is probably more than 35%.

It is known that several genetic factors have been identified, especially in Alzheimer disease and frontotemporal neurocognitive disorder [44]. While this is non-modifiable, the apolipoprotein E epsilon4 (ApoE e4) allele is responsible for 7% increase in incidence of major neurocognitive disorder [43]. Although the ApoE4 status is unknown in Mrs. A, those individuals with ApoE4 gene should be doing everything they can to address these lifestyle factors which will potentially reduce their overall risk. Figure 9.3 shows the lifestyle risk factors according to data extracted from Livingston et al. [43], which include:

- *Early life*: not completing secondary education
- *Midlife*: hypertension, obesity, and hearing loss
- *Later life*: smoking, depression, physical inactivity, social isolation, and diabetes mellitus

Although this 2017 report has placed more emphasis on prevention based on epidemiological studies, they have also taken a broader view encompassing all types of major or mild neurocognitive disorder, not just due to Alzheimer disease.

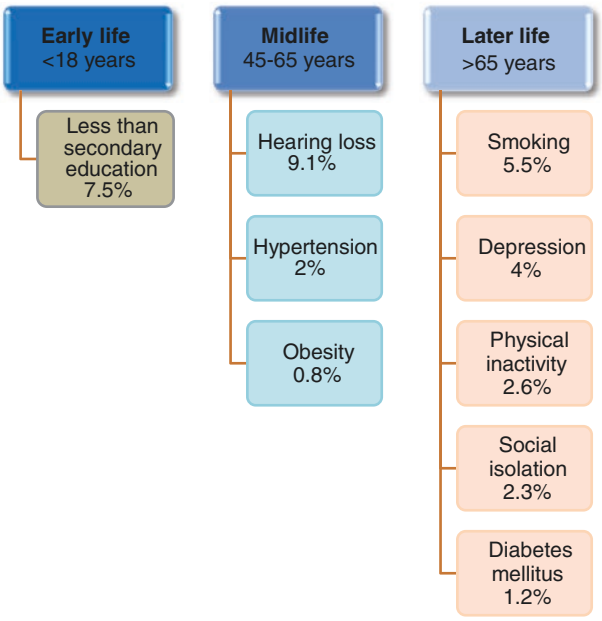


Fig. 9.3 Potentially modifiable risk factors and their individual contribution* (%) to global major neurocognitive disorder. *Data are %, which represent weighted population attributable fraction (i.e., the relative contribution of each risk factor to the overall population attributable fraction when adjusted for communality). Data extracted from [43]

The report has included many risk factors, including hearing impairment and social isolation, occurring through the entire life span, and how they interact with each other when several of them occur together. For example, hearing impairment doubled the risk of developing a major neurocognitive disorder 9–17 years later.

Fortunately, Mrs. A has increased her physical and social activation and ceased smoking. Her level of education does not constitute a risk factor. But she has the following risk factors for a major neurocognitive disorder: (1) a positive family history of major neurocognitive disorder due to Alzheimer disease, (2) a diagnosis of hypertension, and (3) a history of late-life depression.

B. How Would You Assess Mrs. A's Genetic Risk?

There has been no single causal genetic mutation identified for late-onset Alzheimer disease. Most cases are likely influenced by a combination of genetic risk factors (e.g., the APOE4 gene) and other risk factors such as hypertension and diabetes mellitus and probably many other factors not yet defined. The risk to a person who has a first-degree relative (parent or sibling) with late-onset Alzheimer disease is slightly higher than the risk in the general population (5%) but much lower than the risk to someone with a familial pedigree of early-onset disease. Early-onset Alzheimer disease (before age 65 years), which may have a significant genetic component, accounts for only 6–7% of all cases of Alzheimer disease, from which only 13% have an autosomal dominant transmission over more than one generation (grandparent, parent, and sibling) [45, 46]. The three known causative gene

mutations (amyloid precursor protein gene located on chromosome 21, presenilin-1 located on chromosome 14, and presenilin-2 located on chromosome 1) lead to the early-onset Alzheimer disease but are not known to be associated with late-onset or sporadic Alzheimer disease [47]. Sporadic cases of early-onset Alzheimer disease can occur with no family history or genetic mutations. Similarly, familial late-onset forms can occur with no responsible genetic mutations.

Therefore, in order to assess genetic risk in Mrs. A, it is critical to obtain an accurate family history with as much information as possible about the diagnosis of major neurocognitive disorder and age of onset in reportedly affected family member(s). To determine whether there is a causative gene in Mrs. A's family, the clinician must consider at what age did Mrs. A's mother first experience symptoms of Alzheimer disease (answer: age 78 years; therefore, suggestive of a late-onset Alzheimer disease), and are there any other biological family members with major neurocognitive disorders, and, if so, at what age was the onset? In this case, there is nothing in Mrs. A's reported family history to suggest autosomal dominant multigenerational transmission. Therefore, Mrs. A may need no further workup or assessment for the genetic aspect of her risk assessment.

C. What Should You Advise Mrs. A About Her Personal Risk of Developing a Major Neurocognitive Disorder?

If Mrs. A is physically inactive, has a systolic blood pressure above 140 mmHg, and continues to have symptoms of recurrent depressive disorder, her cumulative risk of major neurocognitive disorder by older adult age is about 9% (See Fig. 9.3), compared with baseline risk of 5% if she had no first-degree relative with Alzheimer disease. Because she is a first-degree relative of a patient with Alzheimer disease, based on an empirical estimation from epidemiologic data, Mrs. A's physician can inform her that her risk of Alzheimer disease by the age of 80 years is increased from 5% (baseline risk) to approximately 13%. This risk estimate is derived from data for offspring of Alzheimer disease patients in the context of the REVEAL study (Risk Evaluation and Education for Alzheimer's disease) [48]. Although the authors in this study have presented the methods for males, the risk estimates for other groups of individuals were reported as comparable [48].

D. What Should You Advise Mrs. A About Evidence-Based Strategies on Preventing, Delaying, or Slowing Her Risk of Developing a Major Neurocognitive Disorder?

For Mrs. A, and for all middle-aged and older patients concerned about memory impairment, the question is whether there are lifestyle factors that could be modified in an attempt to preserve memory function with aging. Although a healthy lifestyle should be recommended to all patients, the question is whether there is an evidence base to support specific recommendations to Mrs. A in order to preserve her memory.

Particular risk factors may predispose to certain types of major neurocognitive disorders while having insignificant influence on predicting the onset of other types. In recent years, a number of longitudinal studies have defined general (i.e., nongenetic) risk factors for global major neurocognitive disorder, especially caused by Alzheimer disease and vascular disease [49]. Lifestyle factors such as education level, smoking, diet, and alcohol, as well as vascular risk factors have been important predictors.

A number of studies have shown that elevated systolic blood pressure in midlife is associated with an increased risk of global major neurocognitive disorder including Alzheimer disease type; however, some studies have shown that a systolic blood pressure below 140 mmHg is also associated with an increased risk. In Mrs. A's case, aggressive treatment for hypertension will reduce her risk of cardiac disease and stroke and resultant neurocognitive disorder. Although there is evidence that smoking cessation will lessen her risk of Alzheimer disease, the possibility provides a reason to discourage Mrs. A from resuming smoking [43].

Another identified possible risk factor in this case is depression, which requires optimal treatment. Notably, depressive symptoms can also be part of the clinical presentation of a major neurocognitive disorder (see Question 9.4). It is biologically plausible that depression increases risk of neurocognitive disorder because it affects stress hormones, neuronal growth factors, and hippocampal volume. Mrs. A had been socially withdrawn during the caregiver period. Social isolation is also a risk factor for major neurocognitive disorder, and it increases the risk of depression, hypertension, coronary heart disease, and cognitive inactivity, which are linked to worsening cognitive impairment. All these are risk factors for major neurocognitive disorder themselves, which highlight the importance of addressing lifestyle factors.

Both total dietary fat intake and reduced levels of omega-3 fatty acids have been linked to an increased risk of major neurocognitive disorder in epidemiologic studies. However, a Mediterranean diet (i.e., consisting of a low intake of meat and dairy and high intake of fruit, vegetables, and fish) reduces blood glucose and insulin concentrations, insulin resistance, and markers of oxidative stress and inflammation and is associated with a decreased risk of Alzheimer disease [43]. Livingston et al. [43] believed that dietary factors and alcohol could be important, although they did not include these factors in their calculations due to lack of data. In the absence of evidence from randomized controlled trials, clinicians cannot offer unequivocal advice regarding diet for the primary prevention of major neurocognitive disorder. Having said that, in Mrs. A's case, it is reasonable to recommend a healthy diet given her stated risk factors.

Some other factors have been implicated. Although the US Institute of Medicine has concluded that moderate-to-severe traumatic brain injury is a risk factor for Alzheimer disease, non-repetitive traumatic brain injury may not predispose to global major neurocognitive disorder [43]. It is therefore appropriate to encourage Mrs. A to wear appropriate head protection should she engage in activities that could result in head injuries such as bicycling. Visual impairment, sleep disorders, bilingualism, and airborne particulate pollutants have also received some attention, but there is not enough consistent, high-quality evidence [43].

However, in a recent report, the National Academies of Sciences, Engineering, and Medicine committee has concluded that current evidence does not support a mass public education campaign to encourage people to adopt specific interventions to prevent neurocognitive disorders [50]. This committee reported however encouraging but inconclusive evidence for three specific types of interventions: (1) cognitive training, (2) blood pressure control for those with hypertension, and (3) increased physical activity.

Non-smoking, regular exercise, daily intake of fruit and vegetables, and low to moderate intake of alcohol may optimize her health during aging. Mrs. A should be advised of the potential benefits to prevent, delay, or slow the risk of developing a major neurocognitive disorder by following recommendations on diet, exercise, and level of social engagement, and treating her depressive disorder and hypertension, using evidence-based strategies. However, Mrs. A cannot be assured that these interventions will decrease her risk of Alzheimer disease despite other proven health benefits. In conclusion, Mrs. A should know that to date there are no high-quality clinical trials that have evaluated the effectiveness of modifying risk factors, and there are no proven therapies that will prevent major neurocognitive disorder.

Question 9.14

Major or mild vascular neurocognitive disorder is the second most common cause of neurocognitive disorders. The main criterion for the diagnosis is a temporal association between cerebrovascular disease and development of the neurocognitive disorder. The underlying cerebrovascular disease can include significant white matter hyperintensities, multiple strokes, or limited but strategic strokes.

A. What Are the DSM-5 Criteria for Major or Mild Vascular Neurocognitive Disorder?

Highlights of the DSM-5 diagnostic criteria for major or mild vascular neurocognitive disorder are presented in Table 9.10. For a complete review of the DSM-5 diagnostic criteria, the reader is referred to the DSM-5 manual [14]. Major or

Table 9.10 Major or mild vascular neurocognitive disorder: highlights of the DSM-5 diagnostic criteria [14]

DSM-5 criteria	Designation
The criteria are met for major or mild neurocognitive disorder Probable, ≥1 of the following: – Neuroimaging evidence of vascular disease – Temporal relationship between vascular disease and neurocognitive disorder – Both clinical and genetic evidence of vascular disease (e.g., CADASIL)	Major vascular neurocognitive disorder Mild vascular neurocognitive disorder Probable *or* possible *Specifiers:* with/without behavioral disturbance

mild vascular neurocognitive disorder commonly co-occurs with major or mild neurocognitive disorder due to Alzheimer disease, in which case they are both listed.

B. What Is the Association Between Late-Life Depression and Risk of Vascular Neurocognitive Disorder?

The development of late-life depressive symptoms, along with psychomotor retardation and executive dysfunction, is a common presentation among older adults with progressive small vessel ischemic disease (termed "vascular depressive disorder") and needs differentiation from vascular neurocognitive disorder [51]. This term is commonly used primarily in research settings only, because widely accepted diagnostic criteria are still lacking. In recent studies, magnetic resonance imaging techniques in patients with late-life depressive disorder have shown a variety of cerebrovascular lesions, including extensive white matter hyperintensities, subcortical microvascular lesions, lacunes, and microinfarcts, leading to the introduction of the term "MRI-defined vascular depression" [52]. These patients are important to be identified because vascular depressive disorder confers a greater risk to develop neurocognitive disorder, more likely related to vascular than to Alzheimer disease type ($P = 0.03$) [53].

C. What Are the Basic Treatment Recommendations of Vascular Neurocognitive Disorder? What Are the Risk Factors for Vascular Neurocognitive Disorders and Their Evidence-Based Potential for Modifiability?

Treatment of vascular neurocognitive disorder follows the same principles as for the treatment of other neurocognitive disorders and includes providing psychoeducation and support to the patient and family/caregivers, maintaining safety, and addressing unmet needs of the patient. Prevention of further vascular lesions is a core component of treating this neurocognitive disorder. Specific symptomatic treatment of vascular neurocognitive disorder is limited where some studies addressed cognition and some addressed behavioral symptoms. Modest cognitive improvement has been shown with off-label use of donepezil, galantamine, and memantine, although a positive impact on function is less clear, except in some cases of mixed Alzheimer and vascular neurocognitive disorder. The American Heart Association/American Stroke Association (AHA/ASA) stated that donepezil can be useful for cognitive enhancement in patients with vascular dementia (i.e., major vascular neurocognitive disorder); galantamine can be beneficial for patients with mixed vascular and Alzheimer neurocognitive disorder, whereas the benefit of rivastigmine and memantine is still not proven [54]. Table 9.11 lists the risk factors for vascular neurocognitive disorders, evidence-based recommendations regarding these factors, and potential for modifiability [55].

Table 9.11 Risk factors for vascular neurocognitive disorder, recommendations from AHA/ASA Scientific Statement and modifiability [55]

Risk factors	Recommendations	Comments
Demographics, ethnicity	Be aware of the risk, no recommendations	Unmodifiable
Education	Be aware of the risk, no recommendations	Unmodifiable, confounded by socioeconomic status
Lifestyle		
Mediterranean diet	Reasonable to recommend for primary prevention	Mainly from epidemiological data (e.g., fish, green leaves, nuts, olive oil)
Vitamins (B_6, B_{12}, D, E, other antioxidants)	No evidence of benefit for primary or secondary prevention	Modifiable and relatively safe (except for cost) but no evidence of benefit
Smoking	Recommend smoking cessation for secondary prevention, likely the same for primary prevention, although not specifically done	Modifiable, challenging, and need significant support to implement
Alcohol intake	Reasonable to recommend moderation in intake for secondary prevention	Modifiable, challenging, and need significant support to implement
Weight control	Reasonable to recommend for secondary prevention likely the same for primary prevention, although not specifically done	Modifiable, challenging, and need significant support to implement
Physical activity	Reasonable to recommend for primary and secondary prevention	Modifiable, challenging, and need significant support to implement
Physiological markers		
Hypertension	Definite recommendation to treat for secondary prevention, secondary prevention after stoke, reasonable as primary prevention in middle age and younger seniors but not in age >80 seniors	Modifiable, definite, adherence can be a challenge
Hyperglycemia	Reasonable to treat hyperglycemia for secondary prevention, uncertain benefit for primary prevention	Modifiable, secondary prevention is reasonable, adherence can be a challenge
Hyperlipidemia	Reasonable to treat hyperglycemia for secondary prevention, uncertain benefit for primary prevention	Modifiable, secondary prevention is reasonable, not clear if specific to cholesterol or include triglycerides, adherence can be a challenge
Anti-inflammatory	Uncertain	
Antiplatelets	Not recommended for primary prevention but can be a treatment of concomitant clinical vascular disease	
Concomitant clinical vascular disease	Recommend optimizing treatment, no specific evidence recommendation	Includes coronary artery disease, stroke, chronic kidney disease, atrial fibrillation, peripheral vascular disease, and low cardiac output

Abbreviation: *AHA/ASA* American Heart Association/American Stroke Association
From: Burhan AM, Moradizadeh M, Marlatt N. Major or mild vascular neurocognitive disorder. In: Hategan et al. (Eds.). Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

Table 9.12 Major or mild frontotemporal neurocognitive disorder: highlights of the DSM-5 diagnostic criteria [14]

DSM-5 criteria	Designation
The criteria are met for major or mild neurocognitive disorder Either (1) or (2): 1. Behavioral variant 2. Language variant	*Behavioral variant:* (a) ≥3 of: 1. Disinhibition 2. Apathy/inertia 3. Loss of sympathy/empathy 4. Perseverative/compulsive/ritualistic behavior 5. Hyperorality/dietary changes (b) Decline in social cognition and/or executive abilities *Language variant:* decline in speech production, word-finding, object naming, grammar, word comprehension

Question 9.15

Frontotemporal neurocognitive disorder is a heterogeneous disorder with distinct clinical phenotypes associated with multiple neuropathological entities.

A. What Are the Diagnostic Criteria of Frontotemporal Neurocognitive Disorder?

Frontotemporal neurocognitive disorder comprises clinical variants that include changes in behavior, language, executive control, and, often, motor symptoms. The core spectrum variants include behavioral variant of frontotemporal neurocognitive disorder and nonfluent/agrammatic, semantic, and logopenic variants of primary progressive aphasia [56]. Related disorders include frontotemporal neurocognitive disorder with motor neuron disease, progressive supranuclear palsy, and corticobasal degeneration [56]. Table 9.12 shows the highlights of the DSM-5 diagnostic criteria for variants of major or mild frontotemporal neurocognitive disorder [14]. For a full review of these criteria, the reader is referred to the DSM-5 [14].

B. List Common Screening Cognitive Tests That Specifically Assess Frontal Lobe Dysfunction, and Briefly Describe Them

- *Frontal Assessment Battery (FAB):* is a tool developed for frontotemporal neurocognitive disorder. It is a brief battery of six subsets including conceptualization, mental flexibility, motor programming, inhibitory control, sensitivity to interference, and environmental autonomy [57].
- *Frontal Behavioral Inventory (FBI):* is a 24-item questionnaire, developed for frontotemporal neurocognitive disorder; it is useful in early stages of disease. It involves asking caregivers about apathy, personal neglect, and loss of insight. It measures changes in behavior over time [58].

- *Middelheim Frontality Scale (MFS):* is a clinician-administered scale; it detects frontal lobe features scored on ten items, including initially spared memory and spatial abilities, personality and behavioral changes/impaired insight and judgment, disinhibition, dietary hyperactivity, changes in sexual behavior, stereotyped behavior, impaired control of emotions. Aspontaneity, speech disturbances, and restlessness [59].
- *Emotion Recognition Task (ERT):* emotion recognition impairment is a feature of behavioral-variant frontotemporal neurocognitive disorder. It can be helpful in differentiating frontotemporal neurocognitive disorder from Alzheimer disease type [60].
- *Montreal Cognitive Assessment (MoCA):* has a less ceiling effect than MMSE. It is poor at discriminating between frontotemporal and Alzheimer-related neurocognitive disorder, and usually more testing is required [61].

Question 9.16

Progressive cognitive decline is the central feature of major neurocognitive disorder with Lewy bodies.

What Are the Core Features and Suggestive or Supportive Features of This Illness? Define the Criteria for Probable Major Neurocognitive Disorder with Lewy Bodies as Compared to Possible Major Neurocognitive Disorder with Lewy Bodies

The consensus guidelines for the clinical diagnosis of *probable* and *possible* "dementia" with Lewy bodies (or major neurocognitive disorder with Lewy bodies) include the following features [14, 62, 63]:

1. Central feature
   - Progressive cognitive decline of sufficient magnitude to interfere with normal social and occupational function
2. Core features
   - Fluctuation of cognition
   - Recurrent visual hallucinations
   - Spontaneous features of parkinsonism
3. Supportive features
   - Repeated falls
   - Recurrent, unexplained syncope
   - Transient loss of consciousness
   - Severe antipsychotic sensitivity
   - Systematized delusions
   - Hallucinations of other modalities
   - Rapid eye movement (REM) sleep behavior disorder
   - Depression

4. Features less likely to be present
   - History of stroke
   - Any other physical illnesses or brain disorders sufficient enough to interfere with cognitive performance

According to the DSM-5 diagnostic criteria and the consortium criteria for dementia with Lewy bodies, a summary of these diagnostic criteria for neurocognitive disorder (dementia) with Lewy bodies is shown in Table 9.13 [14, 62, 63].

Question 9.17

The main types of major neurocognitive disorders include the following etiologies:

- Alzheimer disease
- Vascular disease

Table 9.13 Major neurocognitive disorder (dementia) with Lewy bodies (DLB): highlights of the diagnostic criteria [14, 62, 63]

DSM-5 criteria	DLB consortium criteria
The criteria are met for major neurocognitive disorder	Central feature must be present Memory impairment may not occur in early stages but is usually evident with progression Deficits on tests of attention, executive function, and visuospatial ability can be prominent
Core features Fluctuating cognition (variations in attention and alertness) Visual hallucinations (well-formed and detailed) Parkinsonism (onset after cognitive decline) *Suggestive features* REM sleep behavior disorder Antipsychotic sensitivity	*Core features* Fluctuating cognition (variations in attention and alertness) Recurrent visual hallucinations (well-formed and detailed) Spontaneous parkinsonism *Suggestive features* REM sleep behavior disorder Antipsychotic sensitivity Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET
Probable: ≥2 core features *or* ≥1 core + ≥1 suggestive features Possible: 1 core feature *or* ≥1 suggestive features	*Probable*: ≥2 core features *or* ≥1 core + ≥1 suggestive features *Possible*: 1 core feature *or* ≥1 suggestive features *Supportive features* (not proven to have diagnostic specificity): Falls, syncope, transient/unexplained loss of consciousness, autonomic dysfunction, nonvisual hallucinations, systematized delusions, depression, relative preservation of medial temporal lobe on CT/MRI
The disturbance is not attributable to cerebrovascular disease, systemic medical condition, another neuropsychiatric disorder, or substance use	A diagnosis is less likely if cerebrovascular disease is evident, if the disturbance can be attributable to another physical illness or brain disorder, and if parkinsonism appears for the first time at a stage of severe dementia

- Lewy body disease
- Frontotemporal lobar degeneration

A. Briefly Outline the Differentiating Characteristics Among the Four Main Types of Neurocognitive Disorders

Table 9.14 summarizes the typical characteristics of the main types of neurocognitive disorders [19].

B. What Are the Affected Cognitive Areas in Neurocognitive Disorder?

Figure 9.4 shows the six cognitive domains affected in neurocognitive disorders [14].

C. What Is the Differential Diagnosis of Episodic Memory and Associated Characteristics?

Table 9.15 outlines the differential diagnosis of episodic memory impairment and associated course of memory impairment [19].

Table 9.14 Typical characteristics of the main types of neurocognitive disorders [19]

Type of neurocognitive disorder	Characteristics
Alzheimer disease	Progressive cognitive and functional decline, early loss of insight Amnestic and non-amnestic phenotypes Cognitive changes and Alzheimer biomarker evidence required for diagnosis of probable Alzheimer disease
Lewy body disease	Spectrum of disorders with cognitive, movement, visual hallucinations, sleep disturbance, and autonomic changes Alpha-synuclein deposits present in neurons
Frontotemporal lobar degeneration	Focal atrophy of frontal/temporal lobes on MRI Personality and behavior/language changes Younger age at onset, strong familial component
Vascular cognitive impairment	Stepwise progression and focal neurological signs Complex attentional deficits, slowed processing speed, retrieval difficulties, dysexecutive syndrome, depression Mild motor signs in subcortical subtype Symptoms can overlap with Alzheimer disease

From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

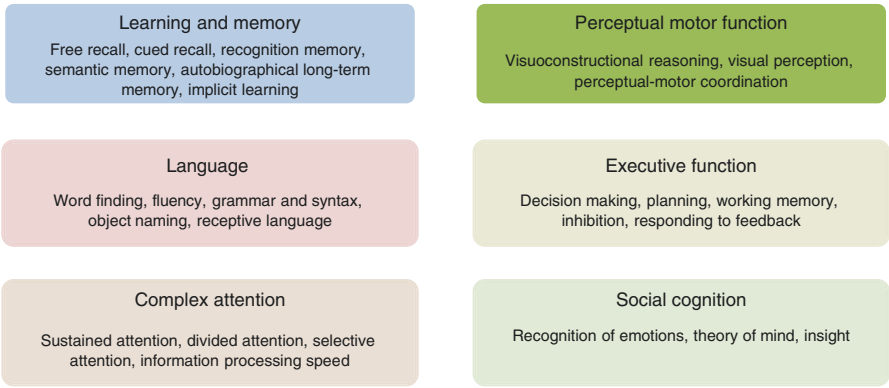


Fig. 9.4 Cognitive domains affected in neurocognitive disorder

Table 9.15 Differential diagnosis of episodic memory impairment [19]

Diagnostic entities	Course and progression of episodic memory
Alzheimer disease, Lewy body disease, frontotemporal neurocognitive disorder	Insidious onset and gradual progression
Vascular neurocognitive disorder, multiple sclerosis	Stepwise progression
Solitary stroke, space occupying lesion, traumatic brain injury, hypoxic or ischemic injury, encephalitis	Static pattern
Concussions, seizures, transient global amnesia	Transient pattern
Medications, hypoglycemia, tumors, Korsakoff syndrome	Variable time course pattern

From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

Question 9.18

A 79-year-old man has been followed up in your clinic with at least a 6-year history of major neurocognitive due to Alzheimer disease. He lives at home with his wife. Since his last follow-up visit, his wife reports that there has been a worsening of his cognition. He is resistant to care that is associated with hitting and grabbing at his wife and personal support worker. He also started to pace around the house at night and sleeps in the daytime.

Briefly Describe the Components of the "DICE" Approach to the Assessment and Management of His Neuropsychiatric Symptoms of Major Neurocognitive Disorder

Although this is further explored at Question 11.14, Topic 11, the DICE approach includes the following elements [64]:

1. ***Describe:*** the clinician should describe the symptoms by accurately characterizing the symptoms and the context in which they occur through discussion with

the caregiver and the patient with major neurocognitive disorder (if feasible). This includes identifying antecedents or triggers of the behavior. It is important to understand which aspects of the symptoms are most distressing or problematic to the patient and the caregiver, as well as their treatment goal.
2. ***I****nvestigate:* the clinician should examine, exclude, and identify possible underlying and modifiable causes.
3. ***C****reate:* the clinician, caregiver, patient (if feasible), and team should collaborate to create and implement a treatment plan. Treatments are medical, non-pharmacological (referred to as "behavioral and environmental modifications" which target the patient, caregiver, or environment (or a combination)), or pharmacological.
4. ***E****valuate:* the clinician should evaluate whether recommended strategies were attempted and implemented effectively, whether the target symptoms improved, whether the caregiver's distress was reduced, and whether there were any unintended side effects or consequences.

Once a symptom has resolved, ongoing monitoring for new behaviors, safety, caregiver distress, and ongoing use of the strategies learned during the DICE process for symptom management should continue.

Question 9.19

You see a patient in your office along with his daughter for agitation in the context of severe, major neurocognitive disorder due to Alzheimer disease. A year ago, a geriatrician started him on memantine, titrated to 20 mg daily, in addition to his donepezil 10 mg daily. On examination, he is irritable, agitated, and only able to use single words. His MMSE score is now 5 out of 30 (suggestive of severe disease stage), which indicated a decline of 6 points compared to a score from 12 months ago. He is incontinent of urine and requires assistance with bathing. He has lost significant weight due to anorexia since donepezil was started, has felt dizzy, had several falls, and experienced difficulties with swallowing his medications lately. The Global Deterioration Scale is 7 (i.e., very severe stage of disease).

A. The Patient's Daughter Wanted You to Address the Perceived Loss of Response to Treatment and She Wished Either to Switch or Discontinue Her Father's Cognitive Enhancers. What Are the Practical Issues to Consider in This Patient's Management and What Do you Advise the Family Member?

When prescribing cognitive enhancers, clinicians need to review with patients or their substitute decision maker the realistic treatment expectations, side effect profile, when to switch, and when to discontinue medications. It is essential to readjust the treatment expectations by reemphasizing that all available pharmacological treatments are symptomatic and, therefore, they do not alter the progression of neurocognitive disorder. Regarding reasonable options, the patient and his daughter need to know that all three cholinesterase inhibitors are modestly efficacious for mild-to-moderate stages, with donepezil being approved for mild to severe stages

of this disease. In mild-to-moderate stages of major neurocognitive disorder due to Alzheimer disease, patients show greatest improvement on cognitive measures usually at 6 months and cross baseline at 9–12 months [65]. On functional measures, patients may show stabilization that lasts for an average of 6 months. Cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) usually prevent new neuropsychiatric symptoms in those with mild-to-moderate disease stages (apathy, irritability, and agitation) but also may help improve some of these symptoms, especially in those with moderate-to-severe stages of disease. Memantine may be prescribed in moderate or severe stages of the disease, where cholinesterase inhibitors are contraindicated or ineffective in line with established clinical guidelines. In moderate-to-severe cases, memantine as monotherapy has been found to stabilize cognitive and functional manifestations of the disease for an average of 6 months [65]. Some evidence shows that in patients with moderate-to-severe major neurocognitive disorder, combination treatment with donepezil and memantine slowed the cognitive and functional decline, and these benefits were beyond those expected of cholinesterase inhibitor treatment alone, although the additive benefit of these two medications has been yet inconclusive [38]. Moreover, switching medications for loss of response after several years of treatment with a cholinesterase inhibitor is not recommended because this usually indicates the natural progression of the disease stage rather than loss of response [65]. In this patient's case, rather than switching to a second cholinesterase inhibitor, addition of memantine was a reasonable option. Because of this patient's course of progressive disease, the standard approach has been to offer him at least a trial of a cholinesterase inhibitor and, subsequently, memantine.

The clinicians need to provide information that discontinuing cognitive enhancers in patients with moderate-to-severe Alzheimer disease may lead to worsening of cognitive and functional impairment as compared to continued treatment, but this risk must be reconciled with the adverse events if treatment continues [38]. When a medication is discontinued because of a perceived lack of effectiveness, it is suggested that the dose be tapered to discontinuation, with monitoring over the following 1–3 months. If evidence of an observable decline, reinstating treatment may be considered if still feasible [38]. In this case, anorexia, weight loss, and dizziness were possible side effects from use of donepezil and memantine. His falls may have been either adverse events from use of cognitive enhancers or other plausible causes, including the progression of the disease. He had a rapid decline on MMSE score of 6 points during the previous 12 months, which may have suggested a lack of response to trial of memantine. Some clinicians use the Global Deterioration Scale to measure the progression of neurocognitive disorder [66]. This patient's disease has continued to advance (i.e., Global Deterioration Scale stage of 7, equivalent to severe disease) where there would be no clinically meaningful benefit for the patient to continue treatment with cognitive enhancers. Moreover, he already experienced dysphagia, which made continued use of oral treatment rather risky. After reviewing the treatment expectations, his daughter, now the patient's substitute decision maker, made the decision to taper and discontinue treatment of both cognitive enhancers. She will bring her father for a follow-up visit in 1-month time after treatment discontinuation to monitor his cognition and behavior. See Table 9.16 for some approaches to treatment discontinuation [65].

B. What Are Some Strategies for Gastrointestinal Side Effects in This Population Using Cholinesterase Inhibitors? What Are the Indications for Treatment Discontinuation of Cholinesterase Inhibitors?

Common strategies for gastrointestinal side effects of cholinesterase inhibitors and indications for treatment discontinuation of cholinesterase inhibitors are presented in Table 9.16 [65].

C. What Is the Main Side Effect Profile of Cognitive Enhancers? What Are the Main Contraindications and Precautions Used in the Assessment and Monitoring Prior to and After Initiating Cognitive Enhancers?

The main side effect profile of the three cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) is associated with their cholinergic activity (e.g., anorexia, nausea, vomiting, diarrhea, abdominal discomfort, fatigue, muscle cramps, dizziness), which is dose dependent. The NMDA (*N*-methyl-D-aspartate) receptor antagonist, memantine, is relatively well tolerated, and its side effects include dizziness, drowsiness, headache, vomiting, insomnia, agitation, anxiety, and hallucinations. Table 9.17 shows the contraindications and precautions used in the assessment and monitoring of patients prior to and after initiating cognitive enhancers [65, 67, 68].

Question 9.20

What Is the Titration Schedule and Total Daily Dose of Cognitive Enhancers?

The titration schedule and total daily dose of cognitive enhancers are shown in Fig. 9.5 [19].

Table 9.16 Strategies for GI side effects and treatment discontinuation of cholinesterase inhibitors [65]

Approach to GI side effects	Approach to treatment discontinuation
Await: GI side effects are more common at treatment initiation/dose increases, tend to be transient Slow titration rate by ≥4-week intervals Lower dose Ensure caregiver administration (if unintentional misuse by patient) Take with food Switch to rivastigmine transdermal (3 times fewer GI side effects) If intolerance: wait for complete resolution of GI side effects before switching to second drug Discontinue	Stop if: Patient experiences dysphagia Significant GI adverse events Rate of decline greater than before treatment (Global Deterioration Scale of 7 = very severe stage of disease) Patients/caregivers want to understand risks/benefits of stopping vs. continuing Do not stop if: Based on MMSE/MoCA score alone Patient is institutionalized Based on adverse events (e.g., falls) that may have other causes

Abbreviations: *GI* gastrointestinal, *MMSE* Mini-Mental State Examination, *MoCA* Montreal Cognitive Assessment

Table 9.17 Contraindications and precautions used in the assessment and monitoring prior to and after initiating cognitive enhancers [65, 67, 68]

Category	Cholinesterase inhibitors (donepezil, rivastigmine, galantamine)	Memantine
Cardiac system[a]	*Contraindications*: Second- or third-degree heart block in unpaced patient QTc prolongation (men >450 ms; women >470 ms)—avoid prescribing and seek advice Bradycardia of <50 bpm[b]	
	Used with caution with ongoing assessment and monitoring: Left bundle branch block Patients on concomitant rate-limiting drugs[c] (e.g., calcium channel blockers, beta blockers) Unexplained syncope	
	Cardiac monitoring[b,c,d] – Prior to starting the drug: monitoring the pulse rate is sufficient for most patients[d] – At 1 month post-starting the drug: recheck pulse rate and symptoms – If dose is to be titrated up: reassess pulse rate and symptoms after a further month – If pulse rate >60 bpm and asymptomatic: recheck at 6 months – If pulse remains satisfactory and patient is stable: recheck annually thereafter – If patient is unwell or develops symptoms: full assessment (including pulse and blood pressure) is required – If syncope or seizures occur: stop the drug, and refer for further investigations; if no causal relationship with the drug is found, or if a pacemaker is fitted, the drug may be resumed	
Renal system	Renal insufficiency (rivastigmine)	Creatinine clearance <30 mL/min: max daily dose <10 mg
Liver system	Liver disease (galantamine)	
Other organs systems	Peptic ulcer disease Chronic obstructive pulmonary disease (severe cases) Seizure disorder	
Medications	Rate-limiting drugs[c,d] (e.g., beta blockers, amiodarone, digoxin, diltiazem, verapamil) Anticholinergics (contraindication)	

[a]There are no established general guidelines for monitoring patients with cardiac disease and use of cholinesterase inhibitors

[b]In line with the accepted practice in many local memory clinics, Yorkshire and Humber Clinical Networks [67] raised the pulse rate threshold to 60 bpm. Further monitoring of patients on cholinesterase inhibitors is described in Table 9.16

[c]If rate-limiting calcium channel blockers or beta blockers are used to treat hypertension, alternative antihypertensive agents might be considered to facilitate the initiation of cholinesterase inhibitors

[d]Prescribe cautiously if pulse is 50–60 bpm and asymptomatic [68]

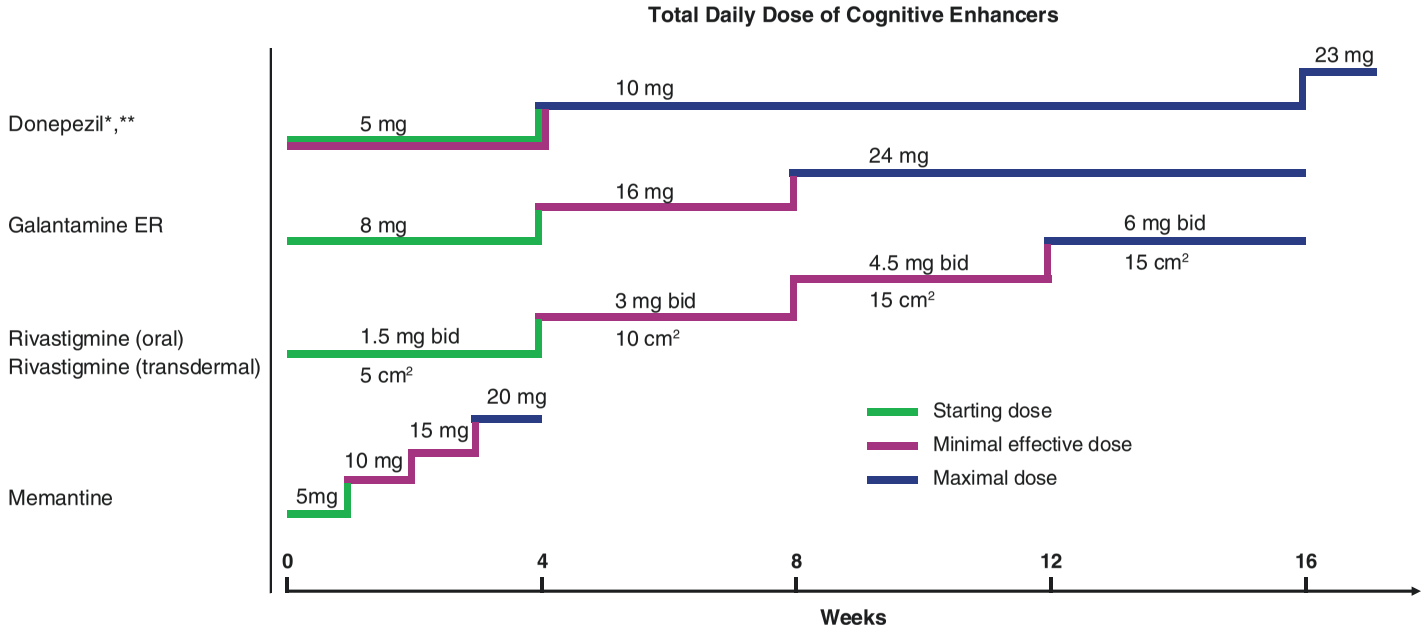


Fig. 9.5 Titration schedule and total daily dose of cognitive enhancers. *A dose of 10 mg daily is administered after a dose of 5 mg daily for 4–6 weeks; a dose of 23 mg daily is administered after a dose of 10 mg daily for at least 3 months. **US FDA approved a once-daily, sustained-release 23-mg tablet. From: Hategan A, Xiong GL. Major or mild neurocognitive disorder due to Alzheimer disease. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

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Topic 10: Other Major and Mild Neurocognitive Disorders: Parkinson Disease, Atypical Parkinsonism, and Traumatic Brain Injury Types

Question 10.1

A variety of neurological disorders can manifest with clinical features of Parkinson disease, in which the symptoms are caused not only by cell loss in the substantia nigra (the brain area most affected in typical Parkinson disease) but also by additional degeneration of cells in the parts of the central nervous system that normally contain dopamine receptors. In contrast to Parkinson disease, there are three atypical parkinsonian syndromes that manifest with parkinsonism, and include progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration, which can be associated with neurocognitive disorders. Neurocognitive disorder with Lewy bodies is often included in this group of atypical parkinsonian syndromes.

What Is Their Prevalence?

Parkinson disease affects 1–2 per 1000 persons at any time. Its prevalence is increasing with age and affects 1% of the population above age 60 [1]. Generally, the onset of Parkinson disease is between ages 55 and 65 years, with the likelihood of diagnosis increasing as patients reach age 80 years and above [2]. Neurocognitive disorder with Lewy bodies has a prevalence of 0.4% (400 cases per 100,000 persons) in older adults; progressive supranuclear palsy and multiple system atrophy both have a prevalence of 5–10 per 100,000 persons, whereas the prevalence of corticobasal degeneration is about 1 per 100,000 persons [3].

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_10

Question 10.2

The patient is a 65-year-old right-handed man presenting today with a chief complaint of sleep disturbance and excessive worries about his health. During the examination, he remarks, "I worry that my hand tremors are getting worse, even my handwriting is becoming difficult to read; this is getting in the way of my normal activities. I decided to retire due to this. What's wrong with me? Do I have Parkinson's?" The tremor worsens when he uses his hands for activities such as typing at his computer. His hand tremor has worsened over the past 2 years. His handwriting has become much smaller and is difficult to read. As a result of his tremor and the associated difficulties, he was resigned to retire 1 month ago after working as a teacher for many decades. Medications include an antihypertensive, a statin, and an antidepressant (citalopram 20 mg/day) started recently by his primary care physician for anxiety symptoms. Today his blood pressure is 120/60 mmHg. On physical examination, cranial nerves, sensation, muscle strength, and deep tendon reflexes are all normal. His face is hypomimic. There is no bradykinesia noted. Mild rigidity in the right upper extremity is noted. There is a mild hand tremor at rest, bilaterally, which is worse on the right than left side. His voice is somewhat soft and tremulous. Mental status examination reveals an anxious, otherwise euthymic, affect, and cognition is grossly intact (Montreal Cognitive Assessment score of 27/30). Routine laboratory data, including glucose, lipids, and thyroid-stimulating hormone, are all within normal limits.

What Are the Key Motor Symptoms of Parkinson Disease in This Patient?

Parkinson disease is a neurodegenerative disorder that affects movement. As in this case, it develops gradually, sometimes starting with a barely noticeable tremor in just one hand. But while a tremor may be the most well-known sign of Parkinson disease, the disease also commonly causes stiffness and/or slowing of movement. In early Parkinson disease, the patient's face may show little or no expression, arms may not swing during walking, and speech may become soft or slurred. Parkinson disease symptoms worsen as the condition progresses over time. Therefore, Parkinson disease is characterized by three cardinal motor features [4]:

- Tremor (i.e., involuntary, rhythmic, and alternating movements of one or more body parts)
- Rigidity (i.e., increased resistance of a joint to passive movements)
- Bradykinesia (i.e., slowness of voluntary and involuntary movements)

Tremor is the most noticeable cardinal symptom of Parkinson disease. It typically occurs at rest, during postural holding, or during voluntary movements; it can be seen in the hands, feet, or other body parts, and tremor frequency can vary

from low (4–5 Hz) to high (8–10 Hz) [5]. Although resting tremor is not necessarily disabling, it can stigmatize patients with Parkinson disease. Rigidity is associated with a feeling of stiffness with reduced ability to relax muscles. Bradykinesia is the most important feature and mainly contributes to the disability associated with disease progression [6]. In the case described, the patient presents with an early stage of Parkinson disease manifesting with progressive resting tremor and rigidity.

Question 10.3

Several major neurocognitive disorders manifest with parkinsonism, including Lewy body disease, Parkinson disease, and vascular parkinsonism. Patients with later stages of Alzheimer disease may develop extrapyramidal signs, which increase in frequency as the disease progresses.

How Do They Differ from Each Other?

Neurocognitive disorder due to Lewy bodies differs from Alzheimer disease in respect to the following features:

- Early parkinsonism is characteristic.
- Visuospatial deficits (as assessed by clock-drawing test) are prominent and occur at an early stage.
- Memory impairment (as assessed by Montreal Cognitive Assessment) can be relatively mild in early stages.
- Fluctuating cognitive performance is typical.
- Rapid eye movement (REM) sleep behavior disorder is often present.
- Atrophy of the medial temporal lobe including the hippocampus is mild in early stages.
- Early visual hallucinations are prominent and a characteristic feature.

Studies show that patients with Alzheimer disease can share a pattern of extrapyramidal signs similar to that seen in Parkinson disease, suggesting possible common pathogenic mechanisms across neurodegenerative diseases. However, the pattern of presentation in Alzheimer disease is different with increased frequency of motor symptoms as the disease progresses. In a study of 4284 subjects diagnosed with Alzheimer disease from the National Alzheimer's Coordinating Center (NACC) database, those with hallucinations, apathy, aberrant night behaviors, and more severe neurocognitive disorder showed higher axial (body bradykinesia) and limb bradykinesia scores. Limb bradykinesia was associated with a neuropathological diagnosis of Lewy body disease and axial component with reduced Alzheimer-type pathology [7].

Neurocognitive disorder due to Lewy bodies and neurocognitive disorder due to Parkinson disease form a spectrum lacking clear clinical and neuropathological delineation. The temporal sequence of symptom onset can help distinguish between the two disorders:

- If cognitive impairment precedes movement disorder by at least 12 months or occurs concomitantly with motor symptoms, the diagnosis of neurocognitive disorder with Lewy bodies is made.
- If motor symptoms occur before cognitive impairment, the condition is usually classified as neurocognitive disorder due to Parkinson disease [8].

Another common condition presenting with atypical parkinsonism is "vascular parkinsonism" caused by multiple, usually small, strokes. These patients usually have more neurological symptoms in the lower extremities (lower body parkinsonism) with resulting walking difficulties, balance problems, and falls.

Question 10.4

Aside from neurocognitive disorder with Lewy bodies, atypical parkinsonism comprises progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration.

A. What Are the Main Phenotypic Syndromes in These Three Atypical Parkinsonian Diseases?

Generally, progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration present with varied phenotypic syndromes. Among these, progressive supranuclear palsy is the most common atypical parkinsonian syndrome comprising two clinical subtypes:

1. Richardson syndrome, characterized by prominent postural instability, supranuclear vertical gaze palsy, and frontal dysfunction.
2. Progressive supranuclear palsy-parkinsonism, characterized by an asymmetric onset, tremor, and moderate initial therapeutic response to levodopa. The early clinical features of progressive supranuclear palsy-parkinsonism are often difficult to discern from Parkinson disease and other atypical parkinsonian syndromes, including multiple system atrophy and corticobasal syndrome.

Among these phenotypic syndromes, the most common are [9]:

- Progressive supranuclear palsy-Richardson syndrome
- Multiple system atrophy-parkinsonism
- Multiple system atrophy-cerebellar type
- Corticobasal syndrome

The differentiation between atypical parkinsonian syndromes and Parkinson disease is important because of the prognosis and treatment responses. Neuroimaging,

although currently of limited diagnostic value for early disease, may contribute valuable information in the differential diagnosis of atypical parkinsonism (see Question 10.6).

B. List the Main Nonmotor Features in Atypical Parkinsonism. What Is Their Clinical Significance?

In progressive supranuclear palsy and corticobasal degeneration, the most prominent nonmotor features are neuropsychiatric symptoms, including cognitive symptoms. In multiple system atrophy, the most prominent nonmotor feature is autonomic dysfunction, but sleep dysfunction, gastrointestinal symptoms, and pain can also be present. Nonmotor features in atypical parkinsonism assist in the differential diagnosis with Parkinson disease and have a significant impact on prognosis and quality of life of patients with atypical parkinsonism [9].

Question 10.5

Nonmotor symptoms of Parkinson disease are common, and identification is essential for appropriate management.

A. List the Main Nonmotor Symptoms in Parkinson Disease

Nonmotor symptoms in Parkinson disease include the following [10]:

- Neuropsychiatric domain
- Autonomic domain
- Sensory domain

Nonmotor symptoms occur in up to 88% of cases of parkinsonism. Nonmotor neuropsychiatric and autonomic symptoms include depression, anxiety, hallucinations, cognitive symptoms, rapid eye movement (REM) sleep behavior disorder, orthostatic hypotension, sexual dysfunction, and constipation [11]. Nonmotor sensory symptoms include pain, numbness, paresthesia/dysesthesia, akathisia, restless legs syndrome, dyspnea, and internal tremor [10].

B. Describe the Neuropsychiatric Symptoms in Parkinson Disease. What Are the Prodromal Symptoms in Parkinson Disease?

Nonmotor symptoms of Parkinson disease include neuropsychiatric symptoms such as depression, anxiety, apathy, psychosis, impulse control disorders, sleep disorders, and cognitive impairment and occur in the majority of these patients [12].

Depression alone occurs in approximately 45% of cases [13]. Depression tends to be underdiagnosed and undertreated and reduces quality of life independent of

motor symptoms [13]. The etiology of depression in Parkinson disease has been associated with injury to the noradrenergic, serotonergic, and dopaminergic pathways in the brain [13]. Hypomimia and reduction of voluntary movements are overlapping manifestations in both Parkinson disease and major depressive disorder, which may confuse the diagnosis. However, diagnosis of depression in patients with Parkinson disease is essentially based on subjectively experienced anhedonia and feeling of emptiness [13]. Other typical signs and symptoms of depression in Parkinson disease include a dysphoric affect and irritability, pessimism about future, and a sense of guilt [6]. Depression may precede motor symptoms of Parkinson disease by several years.

Anxiety is also common in Parkinson disease. Anxiety can be present as panic attacks, phobias, or generalized anxiety disorder and can be related to parkinsonian-induced motor fluctuations [12]. Studies suggest that depression and anxiety may be early symptoms during the prodromal phase of Parkinson disease [14].

Virtually all patients with Parkinson disease develop sleep disturbance, and there is evidence that the process usually begins early in the course of the disease [15]. Sleep disorders include insomnia, restless legs syndrome, periodic limb movements of sleep, rapid eye movement (REM) sleep behavior disorder, sleep fragmentation, and excessive daytime sleepiness [16]. The etiology of sleep disturbance in Parkinson disease is probably multifactorial, including degeneration of central sleep regulation centers in the brainstem and thalamocortical pathways. Sleep disturbance, like other nonmotor features of Parkinson disease, is known to predate the onset of motor symptoms [16]. REM sleep behavior disorder and depression can precede the expression of motor features by more than a decade [16]. Sleep disorders, and REM sleep behavior disorder in particular, are often seen in synucleinopathies such as Parkinson disease, but also in multiple system atrophy and Lewy body neurocognitive disorder [17]. The pooled prevalence of REM sleep behavior disorder in Parkinson disease and control group is 23.6% vs. 3.4%, and the patients who had symptoms of Parkinson disease carried a 3.6- to 9-fold increased risk for developing this sleep disturbance compared to healthy controls [18]. Excessive daytime sleepiness may also be a pre-motor marker of Parkinson disease [16]; its etiology is probably multifactorial, including a combination of the disease process, the effect of nocturnal sleep deprivation, and antiparkinsonian medication side effects.

C. How to Identify and Manage Nonmotor Symptoms of Parkinson Disease?

Identification of nonmotor symptoms of Parkinson disease is essential for appropriate management. This includes screening for neuropsychiatric symptoms and starting treatment as required. Depression has the single largest effect on the quality of life of patients with Parkinson disease [11, 19]. However, physician recognition of depression is low (only up to 30%) in Parkinson disease cases [20]. Table 10.1 illustrates the distinct and overlapping clinical features of major depressive disorder and Parkinson disease. The Beck Depression Inventory, Hamilton Depression Rating

Table 10.1 Distinct and overlapping clinical features of major depressive disorder and Parkinson disease

Clinical features	Major depressive disorder	Parkinson disease
Distinct clinical features		
Motor and affective manifestations	Psychomotor retardation, restricted/depressed affect, agitation	Bradykinesia, stooped posture, masked face/hypomimia, tremor
Overlapping clinical features		
Other physical manifestations	Muscle tension, gastrointestinal symptoms, sexual dysfunction	
Vegetative changes	Decreased energy, fatigue, sleep difficulties, appetite changes	
Cognitive manifestation	Impaired concentration, memory, and problem-solving	

Scale, and Montgomery Asberg Depression Rating Scale should be considered to screen for depression in Parkinson disease. Relative to placebo, efficacy of antidepressants has been demonstrated for nortriptyline, desipramine, citalopram, and paroxetine, although the time course of the antidepressant response has differed [21]. However, a randomized, double-blind, placebo-controlled trial of antidepressants in Parkinson disease has demonstrated the efficacy of serotonin norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs) [22]. Concerns that SSRIs may worsen parkinsonism have not been proven [21]. Starting doses of antidepressants should be low to avoid aggravation of anxiety [21].

Dopaminergic therapy increases dopamine levels in the brain and helps to improve motor and nonmotor symptoms, but it can cause side effects including delirium and psychotic symptoms. These medications should be used cautiously in patients with a history of psychosis due to the risk of exacerbation. It is unclear whether Parkinson disease-related psychosis is due to the disease itself, dopaminergic treatment, or a combination of both. For psychosis due to Parkinson disease, antipsychotics are the treatment of choice. Therefore, clozapine should be considered, quetiapine may be considered, but olanzapine, risperidone, or haloperidol should not be considered. The antipsychotic medication class received a black box warning by the regulatory drug agencies including Food and Drug Administration (FDA) and Health Canada for increased risk of death in older patients with major neurocognitive disorder (dementia) and related psychosis. Pimavanserin, a non-dopaminergic atypical antipsychotic, was approved in 2016 by the FDA to treat psychosis (hallucinations and delusions) experienced by patients with Parkinson disease [23]. There are no widely used, validated tools for psychosis screening in Parkinson disease.

The Montreal Cognitive Assessment (MoCA) and the Cambridge Cognitive Examination should be considered to screen for neurocognitive disorder due to Parkinson disease. None of the three cognitive enhancers (donepezil, galantamine, rivastigmine) has been approved for treatment of mild neurocognitive disorder, irrespective of etiology. Rivastigmine (oral and transdermal system) is FDA and Health Canada approved for the treatment of mild-to-moderate stages of major neurocognitive disorder (dementia) due to Parkinson disease. Rivastigmine and

donepezil have been used for neurocognitive disorder with Lewy bodies, but improvement is modest, and motor side effects may occur. Rivastigmine is available in a patch (4.6 mg/24 h, 9.5 mg/24 h, and 13.3 mg/24 h) for patients unwilling or unable to take by mouth. For transdermal treatment interruption longer than 3 days, there is a need to retitrate dosage starting at 4.6 mg/24 h. Consider dose adjustments in patients with mild-to-moderate hepatic impairment and low (<50 kg) body weight.

D. What Are the American Academy of Neurology Guidelines on the Treatment of Nonmotor Symptoms of Parkinson Disease?

The 2010 American Academy of Neurology guidelines on the treatment of nonmotor symptoms of Parkinson disease recommends the following [20]:

- Sildenafil may be considered for erectile dysfunction.
- Polyethylene glycol may be considered for constipation.
- Modafinil may be considered for patients with subjective perception of excessive daytime somnolence.
- Methylphenidate may be considered for fatigue (but cautious use is recommended because of potential for misuse).
- For insomnia, evidence is insufficient to support or refute the benefit of levodopa on objective sleep parameters that are not affected by motor symptoms; evidence is also insufficient to support or refute the use of melatonin for poor sleep quality.
- Levodopa/carbidopa should be considered to treat periodic limb movements of sleep in Parkinson disease.
- Evidence is insufficient to support or refute the benefit of levodopa for anxiety.
- Evidence is insufficient to support or refute the treatment of REM sleep behavior disorder.
- Evidence is insufficient to support or refute specific treatments for urinary incontinence and orthostatic hypotension.

Question 10.6

How Can Neuroimaging Be Useful to Monitor Progression in Parkinson Disease?

The progression of motor symptoms of Parkinson disease depends upon the nigrostriatal dopaminergic damage [24]. This can be monitored by functional neuroimaging techniques, such as single-photon emission tomography (SPECT) and positron emission tomography (PET). Neuroimaging studies have shown that nearly 50% reduction in dopaminergic nigrostriatal cells is required before clinical expression of the motor

symptoms [25]. A study on sequential SPECT scans in patients with Parkinson disease has demonstrated a decline in striatal uptake of approximately 11.2% annually from the baseline scan, compared with 0.8% annually in the healthy controls ($p < 0.001$). Although striatal uptake in these patients was correlated with clinical severity, the annual percentage loss of striatal uptake did not correlate with the annual loss in measures of clinical function [25]. Therefore, neuroimaging can provide a quantitative biomarker for the progressive nigrostriatal dopaminergic degeneration and an objective endpoint for new therapeutic trials in Parkinson disease.

Question 10.7

What Are the Key Neuropathological Signatures in Parkinson Disease and Atypical Parkinsonism?

The typical and atypical parkinsonian syndromes are synucleinopathies and tauopathies (i.e., disorders characterized by the abnormal deposition of the proteins α-synuclein and tau). The site of deposition is correlated with the clinical features [3].

The motor symptoms of Parkinson disease (bradykinesia, muscular rigidity, and tremor) depend upon degeneration of the dopaminergic neurons in the substantia nigra pars compacta. However, neuropathological studies show that alterations outside the substantia nigra (e.g., ascending involvement from medulla oblongata to neocortex) also occur and are strongly correlated with the nonmotor symptoms of Parkinson disease [6]. A major component of Lewy bodies and glial cytoplasmic inclusions, assumed to be etiologically involved in Parkinson disease and multiple system atrophy, is α-synuclein [26]. The quantitative status of brain α-synuclein in different parkinsonian syndromes is still unclear, and it is uncertain whether α-synuclein accumulation is restricted to regions of pathology [26]. Like progressive supranuclear palsy, corticobasal degeneration is associated with accumulation of aggregates containing the four-repeat isoforms of tau. Houlden et al. [27] have shown that progressive supranuclear palsy and corticobasal degeneration may share a similar cause, although the pathogenic mechanism behind the two diseases leads to a different clinical and pathologic phenotype.

In summary:

- Parkinson disease is considered a synucleinopathy, in which alpha-synuclein may play a role in the development of both (rare) familial and (more common) sporadic cases of Parkinson disease.
- Neurocognitive disorder with Lewy bodies and multiple system atrophy are α-synucleinopathies.
- In neurocognitive disorder with Lewy bodies, α-synuclein is primarily deposited in neocortical neurons, with some brain stem involvement as well. The main clinical features are cognitive impairment and, later on, parkinsonism.

- In multiple system atrophy, α-synuclein is deposited in oligodendrocytes, primarily in the cerebellum but also in the brain stem. The main clinical features are autonomic dysfunction, parkinsonism, and cerebellar ataxia.
- Synucleinopathies often impair REM (rapid eye movement) sleep.
- Progressive supranuclear palsy and corticobasal degeneration are primary tauopathies.
- Progressive supranuclear palsy typically presents with supranuclear vertical gaze palsy, early postural instability, and falls, with parkinsonism or frontotemporal neurocognitive disorder as its most prominent feature.
- Corticobasal degeneration typically presents with markedly asymmetrical parkinsonism, asymmetric hand clumsiness or apraxia, or cortical sensory disturbance.

Question 10.8

What Are the Red Flags Differentiating Atypical Parkinsonism from Parkinson Disease?

Common red flags suggestive of atypical parkinsonism are summarized in Table 10.2 [28].

Question 10.9

To date, there is no proven neuroprotective or disease-modifying therapy for Parkinson disease and atypical parkinsonism, and treatment remains symptomatic.

Table 10.2 Features predictive of atypical parkinsonism [28]

Key Features	Additional Features
• Rapid disease progression • Absence or paucity of tremor • Early gait instability, falls • Irregular jerky tremor, myoclonus • Poor response to levodopa • Early, positive "applause sign" (i.e., continued applauding in response to instructions to clap three times)	• Supranuclear gaze palsy (progressive supranuclear palsy) • Dysautonomia (multiple system atrophy) • Severe dysarthria, dysphonia, stridor (multiple system atrophy) • Pyramidal tract/cerebellar signs (multiple system atrophy) • Apraxia, alien limb, myoclonus (corticobasal syndrome) • Early, prominent cognitive impairment (neurocognitive disorder with Lewy bodies, progressive supranuclear palsy, corticobasal syndrome)

A. What Is the Symptomatic Treatment for Parkinson Disease and Atypical Parkinsonism?

Studies show that a patient's quality of life worsens significantly if treatment is not instituted at or shortly after diagnosis [29]. Available medications for motor symptoms include levodopa, dopamine receptor agonists, anticholinergics, and antiglutamatergics. Levodopa, coupled with carbidopa, remains the gold standard of symptomatic treatment for Parkinson disease. Levodopa provides the greatest antiparkinsonian benefit for motor symptoms (specifically bradykinesia and rigidity), but its long-term use is associated with the development of motor fluctuations ("wearing-off") and dyskinesia, which can be difficult to manage. Levodopa may provide some improvement in parkinsonism associated with progressive supranuclear palsy and corticobasal degeneration; however, benefits are often minimal and transient [30]. In fact, a "poor" response to levodopa is one of the criteria for the diagnosis of progressive supranuclear palsy and corticobasal degeneration [30].

Monoamine oxidase B inhibitors (e.g., selegiline) are one option for the early treatment of Parkinson disease, although they have weaker symptomatic effects than levodopa and dopamine agonists, but fewer significant adverse effects than dopamine agonists [31]. Dopamine agonists (e.g., ropinirole, pramipexole) offer moderate symptomatic benefit and delay the development of dyskinesia compared with levodopa. Their adverse events include drowsiness, sudden-onset sleep, hallucinations, and impulse control disorders (e.g., hypersexuality; hoarding; pathologic gambling, shopping, and Internet use) [32].

There is some evidence that botulinum toxin and baclofen are helpful in reducing dystonia, including blepharospasm, and problematic sialorrhea [30]. Benzodiazepines may be useful to treat dystonia and myoclonus [30].

Cholinesterase inhibitors and *N*-methyl-D-aspartate receptor antagonists have been used off-label in progressive supranuclear palsy, corticobasal degeneration, and other tauopathies with the aim of improving cognition; however, there is limited evidence that they are effective and adverse effects may outweigh benefits [30].

The use of atypical antipsychotics for behavioral disturbance is not recommended in older adults with associated conditions such as major neurocognitive disorder because of increased risks of mortality. Additionally, most antipsychotics will worsen parkinsonism. Antidepressants may be useful for behavioral symptoms and depression but monitoring for adverse effects is necessary [30].

With treatment, disability progresses with advanced disease and many patients with Parkinson disease develop long-term motor complications, including fluctuations and dyskinesia. Postural instability and major neurocognitive disorder (dementia) add to the disability of advanced stage of Parkinson disease. Therefore, symptomatic therapy for advanced disease requires different strategies. For patients who have motor fluctuations and dyskinesia that cannot be adequately managed with medication, surgical option with deep brain stimulation is considered. Levodopa/carbidopa enteral infusion is an option available in some countries and provides improvement that rivals that seen with deep brain stimulation [33].

This treatment is a valuable option in patients with advanced fluctuating Parkinson disease, especially those who do not have access to or are not candidates for deep brain stimulation or who have failed this surgical therapy [33].

B. What Are the Practice Guidelines for the Treatment of Movement Disorder in Neurocognitive Disorder Due to Lewy Bodies?

The treatment of neurocognitive disorder due to Lewy bodies usually needs to address all three domains of the syndrome: cognitive symptoms, neuropsychiatric symptoms, but also movement disorder [8]. A particular problem is posed by the fact that treatment with levodopa may improve the parkinsonian symptoms, especially in early stage, but may worsen the neuropsychiatric symptoms. Dopamine agonists should not be used for treating movement disorder in neurocognitive disorder due to Lewy bodies (see Question A). Moreover, patients with neurocognitive disorder due to Lewy bodies are particularly sensitive to the motor adverse effects of antipsychotics so that extreme caution should be used.

C. What Is the Multidisciplinary Approach to Treatment for Parkinson Disease and Atypical Parkinsonism?

In the absence of an effective drug treatment to target the underlying cause of these diseases, management should focus on optimizing quality of life, relieving symptoms, and assisting patients with their activities of daily living. A multidisciplinary approach should include neurologists, psychiatrists, physiotherapists, occupational therapists, speech and language therapists, dieticians, ophthalmologists, and palliative care specialists [30].

Question 10.10

What Are the Behavioral Adverse Effects of Dopaminergic Treatments in Parkinson Disease? How Are These Behaviors Managed?

Dopamine replacement treatment (especially with dopamine agonists) can cause impulse control disorders and compulsive reward-seeking activities, which worsen patient quality of life. The risk factors implicated in these adverse effects include [32]:

- Young age at disease onset
- Male sex
- Underlying personality traits characterized by high impulsivity and novelty seeking
- Personal or family history of addictive disorders

In predisposed individuals, dopamine replacement treatment leads to dopamine receptor overactivation within the mesocorticolimbic pathways resulting in compulsive medication intake and impulse control disorders [32]. Compulsive medication intake is commonly associated with motor fluctuations in advanced disease, while impulse control disorders can occur in early disease and with normal-range medication dosages.

Reduction of dopaminergic medication dose along with psychosocial support is often required. Use of selective serotonin reuptake inhibitors may help, while atypical antipsychotics may have a limited benefit. Deep brain stimulation should be considered with caution in these patients. Given the potentially medicolegal consequences of these behaviors, clinicians should discuss risks with patients before treatment is initiated. Prevention is based on the identification of at-risk individuals and monitoring [32].

Question 10.11

What Are the Main Predictors of Survival in Atypical Parkinsonian Syndromes?

A 2017 systematic review and meta-analysis has shown that in progressive supranuclear palsy-Richardson syndrome, early dysphagia and early cognitive symptoms are unfavorable predictors of survival [34]. In multiple system atrophy, severe dysautonomia and early development of motor features are associated with shorter survival. In progressive supranuclear palsy and multiple system atrophy, survival was predicted by early falls [34].

Question 10.12

A 65-year-old man is admitted to a psychiatric unit for an index episode of depressive symptoms. He has become apathetic, withdrawn, and had sleep difficulties. He was diagnosed with Parkinson disease 2 years ago, but had noticed onset of a mild left resting hand tremor 2 years earlier and progressive slowing of gait and rigidity of his left arm. Initially, he was started on carbidopa/levodopa 25/100 mg twice daily with positive response. However, his illness has progressed with gait instability, onset of falls, slurred speech, and mild dysphagia. Now, he complains that his mood and enjoyment in life are low, his memory has declined, and his family noticed that he appears to stare more and rarely initiates conversation.

On physical examination, he is fully oriented. His speech is soft and dysarthric, language is intact, but delayed recall is impaired (on MoCA he recalled 2 out of 5 words with no cue). His facial expression reveals hypomimia (masked facies). Vertical saccades (upgaze and downgaze) are reduced, and horizontal saccades are slowed. Prior to trial of carbidopa/levodopa, he had moderate bradykinesia of hand movements, abnormal finger tapping (i.e., the patient is asked to finger tap for abound 10–15 s for as quickly and widely as they can; slowing of speed, loss of

amplitude, and pauses in finger taps are consistent with bradykinesia). He had rigidity in extremities, on the left more than the right. He had marked neck rigidity. He stood without assistance, his gait was slow, and his stance was narrowed and unstable with a tendency to hold onto walls. An MRI of his brain from 2 years previously was notable for age-related cerebral atrophy and mild prominence of basal cisterns. Now, the MRI shows atrophy extending to midbrain and superior cerebellar peduncles.

Further increase in carbidopa/levodopa dose proves to be unhelpful. Over the past 2 years, he has continued to slow down in all of his movements, his dysarthria has worsened, and his vertical gaze palsy has become more apparent.

A. What Is the Diagnosis?

This case depicts clinical features suggestive of progressive supranuclear palsy. As in this case, progressive supranuclear palsy mainly occurs in individuals over the age of 60, although it occasionally affects younger people. Early in the disease course, the patient's features were typical of Parkinson disease, including resting hand tremor, asymmetric rigid bradykinesia, and response to levodopa. Later, he developed oculomotor abnormalities, bulbar features with dysarthria and dysphagia, increased postural instability, and diminishing levodopa response. Atrophy of the midbrain and superior cerebellar peduncles correlates with disease progression in progressive supranuclear palsy. Table 10.3 shows the comparative demographics, clinical, and neuropathological features among atypical parkinsonian syndromes [3, 35–37].

The patient had problems with his memory and speed of thinking. Patients with progressive supranuclear palsy typically retain insight about what is going on around them. In most cases, such patients are more likely to be described as experiencing "cognitive impairment" (or mild neurocognitive disorder) rather than having a major neurocognitive disorder. However, a small proportion of patients with major frontotemporal neurocognitive disorder also develop progressive supranuclear palsy, and monitoring for progression is required [9].

B. What Neuropsychiatric Disturbances of Progressive Supranuclear Palsy Are Present in This Patient?

The patient presented with apathy, depression, and cognitive and sleep disturbances. Patients with progressive supranuclear palsy typically present with a range of neuropsychiatric disturbances including cognitive and functional decline. In a study of 154 patients with progressive supranuclear palsy, behavior domains and total frequency scores of the Neuropsychiatric Inventory (NPI) have shown that more than half had apathy, depression, and sleep difficulties, and approximately one-third had agitation, irritability, disinhibition, and eating problems [38]. Therefore, these patients may frequently be seen in psychiatric services for

Table 10.3 Demographic, clinical, and neuropathological features in atypical parkinsonian syndromes [3, 35–37]

	NCD with Lewy bodies	Multiple system atrophy	Progressive supranuclear palsy	Corticobasal degeneration
Onset	Age 50–80; males > females; duration < 8 years	Age > 40; duration < 10 years; males = females	Onset in 60 s; males = females; duration < 8 years	Age 50–70; duration < 8 years
Neuropathology	α-Synuclein in neuronal somata and processes with distribution in neocortex and brain stem	α-Synuclein in cytoplasm of oligodendrocytes and neurons with distribution in cerebellum, pons, and basal ganglia	Tau in astrocytes, oligodendrocytes, and neurons with distribution in basal ganglia and brainstem	Tau in astrocytes, oligodendrocytes, and neurons with distribution in neocortex and basal ganglia
MRI pattern	Normal medial temporal lobes (unlike Alzheimer disease)	Atrophy of putamen, middle cerebellar peduncle, pons, cerebellum	Atrophy of dentate nucleus, globus pallidus, striatum, midbrain, cerebellum, frontal lobe atrophy	Parietal lobe atrophy: focal, mostly asymmetric
Basic diagnostic evaluation	Cognitive and functioning impairment ≥1 of 3 key characteristics: – Spontaneous parkinsonism – Fluctuations in attention and alertness – Recurrent visual hallucinations Early visuospatial impairment (clock-drawing test, figure copying test), impaired speech (naming, verbal fluency), executive dysfunction, and memory impairment may occur at a later stage. MoCA and FAB are used	Poor response to levodopa, orthostatic hypotension after 3 min of standing from supine position (≥20 mmHg systolic or ≥10 mmHg diastolic), erectile dysfunction, urinary incontinence	Poor response to levodopa; oculomotor dysfunction (slowed, hypometric vertical saccades, frequent square wave jerks Apathy, psychomotor retardation, reduced verbal fluency (<9 words in 1 min), executive dysfunction (<6 correct successive Luria sequences) 4 clinical predictor domains: – Oculomotor dysfunction – Postural instability – Akinesia – Cognitive dysfunction	Poor response to levodopa Apraxia, abnormal FAB, reduced verbal fluency (<9 words in 1 min), executive dysfunction (<6 correct successive Luria sequences) Subtypes: Corticobasal syndrome (25%) Frontal behavioral-spatial syndrome (10%) Richardson syndrome (40%) Progressive nonfluent aphasia (<5%)

(continued)

Table 10.3 (continued)

	NCD with Lewy bodies	Multiple system atrophy	Progressive supranuclear palsy	Corticobasal degeneration
Extended diagnostic evaluation	SPECT/FDG-PET (striatal dopaminergic denervation, occipital hypometabolism), sleep laboratory (REM sleep behavior disorder)	SPECT/FDG-PET (symmetric striatal dopaminergic denervation, hypometabolism in putamen, brainstem, or cerebellum), sleep laboratory (REM sleep behavior disorder)	SPECT/FDG-PET (symmetric striatal dopaminergic denervation, hypometabolism in frontal lobe and midbrain, symmetric postsynaptic striatal degeneration)	SPECT/FDG-PET (asymmetric striatal dopaminergic denervation, asymmetric hypometabolism in striatum and parietal cortex, asymmetric postsynaptic striatal degeneration)
Symptomatic treatment	Cholinesterase inhibitors (rivastigmine 6–12 mg/d, donepezil 5–10 mg/d) for NCD Memantine (5–20 mg/d) for behavioral symptoms Levodopa (100–200 mg/d) for akinetic/rigid symptoms Second-generation antipsychotics (clozapine 6.25–100 mg/d, quetiapine 25–100 mg/d) for psychosis	Levodopa (100–200 mg/d), amantadine (100–200 mg/d): mild/moderate improvement of motor symptoms Midodrine (5–10 mg/d), fludrocortisone (0.1 mg/d): positive effects on orthostatic hypotension Desmopressin: positive effect on nocturia	Levodopa (100–200 mg/d), amantadine (100–200 mg/d): mild/moderate improvement of motor symptoms Zolpidem (5–10 mg/d): for impaired sleep, short-term benefit in voluntary saccades Coenzyme Q10: mild improvement of motor/ neuropsychiatric symptoms Botulinum toxin A: good improvement of focal dystonia SSRIs, SNRIs: for depression/ anxiety. Cholinesterase inhibitors (rivastigmine 6–12 mg/d, donepezil 5–10 mg/d) for NCD Dextromethorphan plus quinidine: for pseudobulbar affect	Levodopa (100–200 mg/d): mild/moderate improvement of motor symptoms Botulinum toxin A: good improvement of focal dystonia Baclofen (max 40 mg/d): mild/moderate improvement of dystonia Clonazepam (2–6 mg/d): moderate improvement of myoclonus Propranolol (80–120 mg/d): moderate improvement in postural tremor

FAB frontal assessment battery, *FDG* fluorodeoxyglucose, *MoCA* Montreal Cognitive Assessment, *NCD* neurocognitive disorder, *MRI* magnetic resonance imaging, *PET* positron emission tomography, *REM* rapid eye movement, *SPECT* single-photon emission computed tomography, *SSRIs* selective serotonin reuptake inhibitors, *SNRIs* serotonin norepinephrine reuptake inhibitors

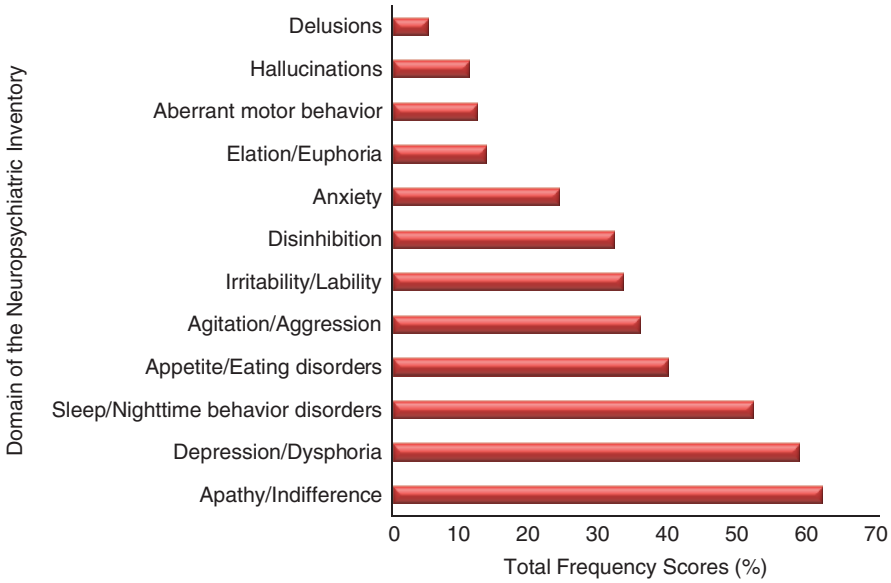


Fig. 10.1 Neuropsychiatric profile and frequencies in progressive supranuclear palsy. Data derived from [38]

symptom management. Figure 10.1 shows the common neuropsychiatric profile and frequencies in progressive supranuclear palsy based on data derived from Gerstenecker et al. [38].

Question 10.13

A 67-year-old man is being referred to an outpatient psychiatric clinic for depression, anxiety, and sleep difficulties with dream enactment. He also presents with a 5-year history of progressive bilateral upper extremity tremor, bradykinesia, gait difficulty with freezing and recurrent falls, myoclonus, dysarthric speech, dysphagia, urinary incontinence, constipation, and erectile dysfunction. Over the past year, he has been treated with a high dose of carbidopa/levodopa titrated to effect. Compared to prior to carbidopa/levodopa trial, he reported little change in symptoms except a mild decrease in tremor.

On examination, the patient has a facial hypomimia, reduced vertical saccades, dysarthric speech, and mild tremulousness. Jerky tremor is apparent with intention and sustained posture. He has bradykinesia, axial and bilateral limb rigidity, and slow gait with freezing. The MRI of his brain shows moderate cerebral atrophy and bilateral hyperintensities in the putamen.

What Is the Diagnosis?

This case illustrates features of a phenotypic syndrome of multiple system atrophy-parkinsonism including rapid progression, early gait and postural instability, dysarthria, dysphagia, atypical tremor, axial and limb rigidity, generally symmetric bradykinesia, dysautonomia with urinary incontinence, gastrointestinal dysmotility, erectile dysfunction, neuropsychiatric symptoms, and rapid eye movement (REM) sleep behavior disorder (See Table 10.3). The rapid progression despite partial response to high-dose dopaminergic treatment within 5 years of disease onset is a red flag for atypical parkinsonism [3].

Question 10.14

An 81-year-old man with a history of hypertension, prostatic hypertrophy, and heart failure presents with symptoms of progressive gait difficulty, falls, tremulousness, fatigue, and right-hand dysfunction that he had experienced over the past year. His life partner reported that his gait and movement have slowed over the course of past several years, but have recently worsened further in the setting of bilateral leg edema. More recently, he has begun dragging his right leg more. He noticed increasing stiffness in his right arm, tendency to hold his right arm flexed at his side. He believes his symptoms are now spreading to his left side as well. He has symptoms of micrographia (he is left handed). He has a slowed speech, decreased facial expression, and mild swallowing difficulty. He reports that swallowing pills has become difficult. The patient denies changes in memory or mood, but his interests and enjoyment in life have decreased. He was previously diagnosed with parkinsonism and treated with a dopamine agonist (ropinirole) with some subjective motor benefit. However, the addition of carbidopa/levodopa did not produce supplemental benefit.

On examination, the patient was fully oriented, he displayed a mild disorganized thought process, and his cognition was otherwise intact. He was noted for mild hypophonia and dysarthria, mild facial hypomimia, reduced vertical saccades, and slowed optokinetic nystagmus. His right upper extremity tone was rigid, and he tended to hold the right arm flexed at his side, but there was no neglect. He had no tremor. He had ideomotor apraxia (i.e., impaired performance of skilled motor acts despite intact sensory, motor, and language function); e.g., he displayed an inability to pretend to brush his hair. He had impaired graphesthesia in his right hand, evidenced by an inability to recognize writing on his skin solely by the sensation of touch. His gait was slow and stiff with his right leg dragged. His brain MRI shows asymmetric cerebral atrophy predominantly on the left and atrophy of the rostral midbrain.

After the initial presentation, his symptoms rapidly progressed with increasing symptoms of vertical gaze palsy, right-sided rigidity, and alien limb phenomenon

(i.e., involuntary motor activity of the limb in conjunction with the feeling of estrangement from that limb). He has developed limb-kinetic apraxia and cortical sensory deficits. He now requires a wheelchair and assistance with basic activities of daily living. His speech remains mildly dysarthric. His thought content reveals some grandiosity and his cognition shows short-term memory decline. He has remained on a dopamine agonist (due to subjective benefit over carbidopa/levodopa) and receives botulinum toxin injections for right upper extremity dystonia.

What Is the Diagnosis?

This case demonstrates progressive rigid bradykinesia, dystonia, apraxia, cortical sensory deficits, and asymmetric limb dysfunction consistent with a diagnosis of corticobasal degeneration (See Table 10.3). Later progression of his axial rigidity, falls, supranuclear gaze palsy, and psychiatric symptoms including cognitive deficits raise the possibility of a phenotypic syndrome of corticobasal-progressive supranuclear palsy [3, 28, 39].

Question 10.15

Traumatic brain injury (TBI) constitutes a spectrum of focal or diffuse cerebral insults that result from sudden impact, penetrating wounds, hypoxic and toxic metabolic insults, and cerebrovascular injuries. The consequences of TBIs occur in two phases: primary injury (arising from the aforementioned etiologies) and secondary injury (arising from the pathophysiological brain changes caused by the primary injury, including excitotoxicity and energy failure, ischemia, edema, inflammation, and cell death). Following TBI, significant neuropsychiatric complications may occur.

A. What Are the Associated Neuropsychiatric Symptoms of Mild TBI?

Mild TBI, or concussion, constitutes the majority (70–90%) of these injuries [40], although this may be underestimated because not all patients receive treatment. In mild TBI, depression, anxiety and irritability, impaired cognitive function, headaches, and fatigue are common [41]. For milder cases, these complaints usually lessen with time. Studies suggest that repeated mild injuries may cause cumulative damage to the brain, resulting in long-term cognitive dysfunction and major neurocognitive disorder [42].

B. What Are the Long-Term Implications of a Single Mild TBI?

Studies show that 58% of mild TBI patients manifest symptoms at 1 month after TBI [43], but a widely cited figure in the literature suggests that only about 15% of single mild TBI individuals will experience post-concussion syndrome and concomitant long-term cognitive impairment at 1 year [44]. However, a recent review by McInnes et al. [41] shows that approximately half of individuals with a single mild TBI demonstrate long-term cognitive impairment. Future prospective, longitudinal studies are required.

Question 10.16

What Is the Relationship of Traumatic Brain Injury (TBI) to Major Neurocognitive Disorder?

The association of TBI with the development of major neurocognitive disorder has a long history. A recent summary on the relationship between TBI and major neurocognitive disorder includes the following research points [45]:

- Increasing severity of a single moderate-to-severe TBI increases the risk of subsequent Alzheimer disease.
- Repetitive, mild TBIs increase the risk for chronic traumatic encephalopathy (a degenerative neuropathology).
- TBI may be a risk factor for other neurodegenerative disorders that can be associated with major neurocognitive disorders.
- TBI appears to lower the age of onset of neurocognitive disorder.
- Specific risk factors for TBI-associated neurocognitive disorder are:
  - Any blast or blunt physical force to the head that produces violent head displacement
  - Decreased cognitive and/or neuronal reserve and the related variable of older age at time of TBI
  - The presence of apolipoprotein E ε4 allele (a genetic risk factor for Alzheimer disease)
- Neuropathological features associating TBI with neurocognitive disorder include:
  - Neurodegenerative amyloidopathies and other proteinopathies
  - Chronic traumatic encephalopathy
  - White matter tract and neural network disruptions

These findings suggest that dose-dependent effects of violent TBI in vulnerable brains predispose to major neurocognitive disorder; among several potential mechanisms is the propagation of abnormal proteins along damaged white matter networks, although further research is needed [45].

Question 10.17

A 79-year-old male who is not on any anticoagulants is brought to the local emergency department by his family member after a mechanical fall from standing. He is amnestic to the event and mildly confused and has some mild dizziness when he stands, but otherwise has no neurological deficits. His brain CT scan reveals mild chronic microangiopathic changes. He has a Glasgow Coma Scale of 14 and has suffered a mild traumatic brain injury (TBI).

A. What Is the Immediate Management in the Emergency Department?

In the emergency department, the first priority is to stabilize and resuscitate, to manage the airway if needed, and to evaluate for any other trauma in the patient. Falls in older adults are multifactorial, including gait instability and polypharmacy, which need evaluation. The diagnosis of mild TBI can be challenging in the emergency department if the patient's baseline cognitive function is unknown. It is important to obtain collateral information from family members or caregivers who know the patient in order to establish whether the patient is usually oriented to time, place, person, and circumstances before you can determine whether there is a cognitive change or not. Because the brain CT is relatively negative in this case, symptom and functional assessment should be done. He may be able to be discharged home with follow-up for physiotherapy and early reevaluation, provided that he is able to ambulate easily and has a family member or caregiver who can assist him if needed. If he is medically unstable, or is too confused to manage his activities of daily living, then other options (e.g., admission, referral to a rehab or skilled nursing home) should be considered.

B. What Should the Clinician Know About Mild TBI in Older Adults?

Older adults have more prolonged courses following TBI, with slower recovery rates [46]. They are at high risk of adverse outcomes such as skin breakdown due to decreased mobility. Even with a mild TBI and without abnormal CT, patients can experience high mortality rates and significant long-term sequelae, including [47]:

- Sleep difficulties
- Depression or behavioral changes
- Worse or new cognitive impairment
- Hearing or vision changes
- Headaches
- Vestibular dysfunction/dizziness or vertigo
- Fatigue

C. If the Patient Is Stable, What Should You Tell the Patient and His Family to Expect?

Even if his CT scan is negative in the context of TBI symptoms (e.g., dizziness, worse or new cognitive impairment), inform the patient that he has suffered a concussion and set expectations that the symptoms may resolve quickly but can sometimes become long term. If the patient is stable, the clinician should encourage early follow-up for reevaluation.

Question 10.18

In older adults, falls are the most common cause for TBI.

A. What Are the Mechanisms for TBI and Their Frequencies?

In older adults, falls are the leading known external cause of TBI, representing almost two-thirds of the total number. Other mechanisms for TBI include motor vehicle accident (8%), struck by/against objects (6%), assault (1%), and unknown (25%) [48].

B. What Is the Course of Recovery from TBI?

The course of recovery from TBI is variable and depends on the patient's age, prior history of brain injury or substance abuse, and the specifics of the brain injury. The severity of a TBI is rated at the time of injury and initial assessment as mild (loss of consciousness <30 min; posttraumatic amnesia <24 h), moderate (loss of consciousness 30 min–24 h; posttraumatic amnesia 24 h–7 days), or severe (loss of consciousness >24 h; posttraumatic amnesia >7 days) [49]. However, the severity rating of the TBI does not necessarily correspond to the severity of the resulting neurocognitive disorder. For example, in older adults with decreased cognitive reserve, mild TBI is more likely to result in partial recoveries. Moreover, repeated mild TBI may be associated with persisting neurocognitive disorder [49].

Question 10.19

The Mayo Classification System for TBI Severity allows using clinical descriptions instead of relying on Glasgow Coma Scale (GCS) alone.

Describe the Mayo Classification System for Mild (Probable) and Symptomatic (Possible) TBI

There are several classification systems for TBI. For patients with GCS recorded, TBI is categorized as mild (GCS 13–15), moderate (GCS 9–12), and severe (GCS 3–8) [50]. However, the Mayo TBI scale takes into account symptoms as well as neuroimaging findings [51]. The Mayo system classifies mild (probable) TBI if one or more of the following criteria apply [52, 53]:

- Loss of consciousness of momentary to <30 min
- Posttraumatic amnesia of momentary to <24 h
- Depressed, basilar, or linear skull fracture (with dura intact)

Symptomatic (possible) TBI is classified if one or more of the following features apply:

- Blurred vision
- Confusion
- Dazed
- Headache
- Dizziness
- Focal neurologic symptoms
- Nausea

Question 10.20

Aside from major or mild neurocognitive disorder, major depressive disorder after traumatic brain injury (TBI) is highly prevalent and associated with increased comorbidity and disability.

A. What Is the Prevalence of Major Depressive Disorder After TBI?

The development of depression as a secondary condition is frequent after TBI, with a prevalence of 10–42% within the first 2 years of injury [54]. Bombardier et al. [55] found that the prevalence of major depressive disorder during the first year after TBI was 53%; however, risk of post-TBI depression probably persists beyond 1 year.

B. What Are the Predictors of Major Depressive Disorder After TBI? What Are the Clinical Outcomes After TBI?

Predictors of major depressive disorder after TBI include the following [55]:

- Age 60 years or older
- History of depression at the time of TBI

- History of depression prior to TBI
- Lifetime alcohol dependence

Severity of TBI as a predictor of major depressive disorder has been controversial. Other biological markers such as genetic polymorphisms, neurotransmitter and neuroendocrine changes, and psychosocial risk factors need future elucidation [55].

Depression after TBI has been associated with comorbid anxiety and poorer functional outcomes in multiple domains at 1 year after injury. Depression after TBI is a significant predictor of poorer self-reported health and lower quality of life [55].

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Topic 11: Neuropsychiatric Symptoms Due to Major and Mild Neurocognitive Disorders

Question 11.1

The clinical management of major and mild neurocognitive disorders is often complicated by neuropsychiatric symptoms, also referred to as behavioral and psychological symptoms of dementia (BPSD). These symptoms may include depression, anxiety, agitation, aggression, delusions, hallucinations, wandering, apathy, disinhibition, resistance to care, hoarding, rummaging, and sleep disturbances.

What Is the Prevalence of Neuropsychiatric Symptoms in Major and Mild Neurocognitive Disorders?

Neuropsychiatric symptoms occur frequently in neurocognitive disorders. If left untreated, these symptoms can have serious adverse consequences, leading to greater impairment in activities of daily living and worsened quality of living [1]. Depending on the method of study, estimates of neuropsychiatric symptoms range from 61 to 75% [2] in older adults with major neurocognitive disorders. The prevalence is slightly lower in those with mild neurocognitive disorders, 31–51% [2]. Despite memory and other cognitive deficits being the defining criteria for neurocognitive disorders, it is usually the neuropsychiatric symptoms that lead to clinical presentation [3, 4]. Thus, management of patients with major and mild neurocognitive disorders will typically involve assessment and treatment of these symptoms.

Question 11.2

Depending on the studies and scales used to profile the neuropsychiatric symptoms, they can be clustered and grouped in different ways. Commonly used scales such as the Neuropsychiatric Inventory (NPI) and the Cohen-Mansfield Agitation Inventory (CMAI) have been used to quantify behavioral symptoms.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_11

A. The Neuropsychiatric Inventory (NPI) Is an Instrument Used to Measure and Quantify Behavioral Symptoms in Neurocognitive Disorders. This Scale Is Administered by a Clinician to the Caregiver/Family Member and Is Commonly Used in Clinical Studies. List the Behavioral Domains That Are Assessed by the NPI

The NPI assesses behaviors that are common in patients suffering from major neurocognitive disorders. The domains include [5]:

- Hallucinations
- Delusions
- Agitation/aggression
- Dysphoria/depression
- Anxiety
- Irritability
- Disinhibition
- Euphoria
- Apathy
- Aberrant motor behavior
- Sleep and nighttime behavior change
- Appetite and eating change

B. Another Commonly Used Scale to Quantify Behavioral Symptoms Is the Cohen-Mansfield Agitation Inventory (CMAI). Briefly Describe This Scale

This 29-item scale is used to assess agitated behaviors in older adults and was developed for use in nursing homes. The CMAI classifies agitation into four main categories [6]:

- Physically nonaggressive behaviors
- Physically aggressive behaviors
- Verbally nonaggressive behaviors
- Verbally aggressive behaviors

C. What Other Scales Can Be Used to Quantify Neuropsychiatric Symptoms of Major Neurocognitive Disorder?

The Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) scale is a clinical rating scale published in 1987 [7]. This scale consists of two parts: the first part is concentrating on symptomatology and the second part is a global rating of the symptoms based on severity. The domains covered include paranoid and delusional

ideation, hallucinations, activity disturbances, aggression, diurnal variation, mood, anxiety and phobias [8]. Since then, a potentially more sensitive BEHAVE-AD Frequency-Weighted Severity Scale (BEHAVE-AD-FW) has been published, which adds a frequency weighting to severity weightings of the traditional BEHAVE-AD measure [7]. Both these instruments are informant-based instruments. Another newer validated version, the empirical BEHAVE-AD (E-BEHAVE-AD) scale, is a 12-item scale scored on a four-point severity scale that is clinician interview based [7].

Question 11.3

In patients with major neurocognitive disorder due to Alzheimer disease, there are many factors that may affect the prevalence of neuropsychiatric symptoms. These factors include disease duration, age, education level, population demographics, and the severity of cognitive impairment [3]. Up to 80–97% of patients with Alzheimer disease are affected by neuropsychiatric symptoms at some point during the course of their illness [9].

A. What Is the Most Frequent Neuropsychiatric Symptom Experienced by Those with Major Neurocognitive Disorder Due to Alzheimer Disease?

In a meta-analysis of 48 published studies, the most frequent neuropsychiatric symptom was found to be apathy, followed closely by depression and aggression [3]. The prevalence of various neuropsychiatric symptoms is illustrated in Fig. 11.1. Apathy has been defined as the absence of motivation not attributable to depressive

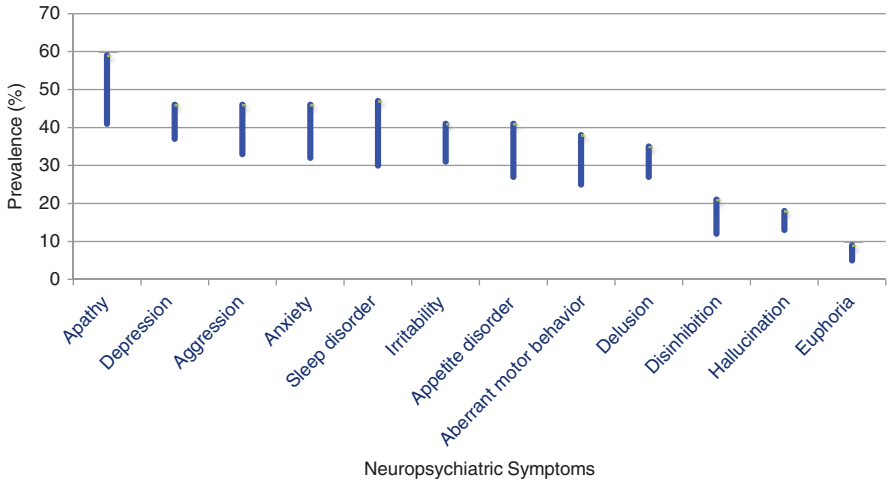


Fig. 11.1 Prevalence range of neuropsychiatric symptoms in Alzheimer disease [3]

disorder/emotional distress, intellectual impairment, or decreased level of consciousness [10]. Unfortunately, despite apathy being a common symptom and complaint in neurocognitive disorders, there is also limited evidence of efficiency of pharmacotherapy for its treatment. Some studies have noted benefits with the use of acetylcholinesterase inhibitors and memantine [11]. There has also been a small randomized, double-blind, placebo-controlled trial that showed promise with the use of methylphenidate in treating apathetic patients [12]. There has been case studies supporting the use of modafinil, but it did not improve apathy in a randomized controlled study [13]. There is still insufficient evidence that pharmacological intervention will improve apathy in patients with neurocognitive disorders. Further large-scale, placebo-controlled, randomized studies are still needed to establish the potential benefit of using pharmacological agents in the treatment of apathy.

B. How Does the Prevalence of Neuropsychiatric Symptoms Differ Between Major Neurocognitive Disorders Due to Alzheimer Disease Versus That Due to Lewy Body Disease?

In major neurocognitive disorder due to Lewy body disease, depression and anxiety seem to be much more prevalent than in Alzheimer disease [14]. As well, the frequencies and severities of neuropsychiatric symptoms at the early stage of major neurocognitive disorder were found to be higher in patients with Lewy body disease compared to those with Alzheimer disease [15]. Not surprisingly, in patients with early stage of major neurocognitive disorder due to Lewy bodies, the most prevalent neuropsychiatric symptom was hallucinations [14]. As disease progresses, apathy becomes more frequent than hallucinations. Other common neuropsychiatric symptoms in major neurocognitive disorder due to Lewy body disease include delusions, sleep disturbances, and aberrant motor behaviors [15]. Figure 11.1 illustrates the prevalence of neuropsychiatric symptoms in major neurocognitive disorder due to Alzheimer disease [3].

Question 11.4

Dr. Keen, a local primary care physician whom you have shared patients with in the past, calls your office today asking for advice in regard to one of his patients. He tells you that Mr. C is a 71-year-old man who lives in the community with his wife. Dr. Keen recently diagnosed Mr. C with a mild neurocognitive disorder as Mr. C has a 2-year history of worsening short-term memory concerns (he would not be able to remember a conversation he had a day ago). Neither the patient nor his wife has noted any issues with his function thus far. In the past 3–4 weeks, Mr. C started having concerns that someone has been breaking into the house and stealing his things. He believes that his neighbors may be the ones breaking in as he had an argument in the past with his next-door neighbor about their dog urinating on their lawn. He believes his neighbor is now retaliating and doing things to scare him so he and Mrs. C will move out of their house. Dr. Keen initially thought it could be an episode of delirium and ordered some basic metabolic panel, a urinalysis and an

electrocardiogram. All the results are normal. Physical exam was also normal with no specific neurological symptoms. Dr. Keen wonders if the delusions could be related to Mr. C's memory impairment or whether he should be considering a diagnosis of a possible independent psychotic disorder.

What Are the Common Neuropsychiatric Symptoms Observed in Those with Mild Neurocognitive Disorders? Identify the Neuropsychiatric Symptoms in the Case Described

Neuropsychiatric symptoms are quite common in mild neurocognitive disorders, occurring in 31–51% of patients [2]. Similar to the case with major neurocognitive disorders, a recent review found apathy to be one of the most common symptoms observed, occurring in approximately 30–40% of individuals with mild neurocognitive disorders [16]. In fact, in cognitively normal older adults, the presence of apathy itself is a predictor of subsequent onset of both amnestic and non-amnestic mild neurocognitive disorder [17]. Depressive and anxiety symptoms are also quite prevalent, with some studies suggesting a prevalence range of 40–50% [16]. Other common neuropsychiatric symptoms seen include psychosis (prevalence of 3–14%) and agitation and disinhibition (prevalence of 4–35%) [16]. The wide range of prevalence for agitation is due to the variability in the definition and assessment of agitation.

In Mr. C's case, his paranoid delusions are consistent with the common paranoid themes that someone with a neurocognitive disorder would have. If there are no other symptoms of disorganization or other mood symptoms, then the most likely differential for Mr. C's delusions would be mild neurocognitive disorder with neuropsychiatric symptoms (in this case, delusions), and less likely would be a comorbid delusional disorder.

Question 11.5

While there are many studies looking into how and why neuropsychiatric symptoms occur in neurocognitive disorders, the underlying mechanism of neuropsychiatric symptoms is still not well understood. Different neurobiological systems have been implicated in the pathogenesis of cognitive decline and development of behaviors in major neurocognitive disorder. Answers to the how and why questions may help clinicians better understand and manage these symptoms.

A. What Are Some Neuroimaging Findings of Apathy in Major Neurocognitive Disorder Due to Alzheimer Disease?

In an MRI study looking at patients with major neurocognitive disorder due to Alzheimer disease with apathy, there seems to be a significant association between apathy and larger white matter hyperintensities in the frontal lobes [17]. The loss of white matter integrity in the left anterior cingulum, left posterior cingulum, right

superior longitudinal fasciculus, splenium body and genu of the corpus callosum, and bilateral uncinate fasciculus has also been implicated in apathy [18]. SPECT studies suggest that there is a relationship between hypoperfusion in the right temporoparietal, prefrontal, and anterior parietal areas and apathy [19].

B. How Do These Findings Compare with That of Apathy in Frontotemporal Neurocognitive Disorder?

In those with frontotemporal neurocognitive disorder, apathy seems to be associated with glucose hypometabolism in the dorsolateral and frontal medial areas [20]. Data from PET scans also suggest impaired metabolic activity in the anterior cingulate, ventromedial and orbital prefrontal cortex, the dorsolateral prefrontal cortex, and the left anterior insula [21].

Question 11.6

Mrs. P is a 69-year-old married female, living at home with her 78-year-old spouse. You saw Mrs. P initially about 2 years ago and diagnosed her with a major vascular neurocognitive disorder. You have been seeing her for follow-up every 6 months and have noted that over the past year, her cognition has declined more precipitously. Her Montreal Cognitive Assessment (MoCA) score was 13/30 when you saw her 6 months ago, and it was previously 21/30 when you first saw her for consultation 2 years ago. Mr. P has had to take over more of the household chores such as cooking and cleaning. In the last month, Mr. P has noted more issues with confusion and agitation, especially in the evenings. There have been occasions in the recent weeks where Mrs. P would approach Mr. P and ask him where her husband was, thinking that she needs to go home to him. Mr. and Mrs. P came to your office today for follow-up. Mr. P asked for the opportunity to speak with you alone and tells you that Mrs. P actually struck out at him 3 days ago. Apparently, Mrs. P thought that Mr. P was a burglar in the home and wanted him to leave the house. She tried to push him out the door, hit him in the chest a few times, and then threatened to grab her kitchen knife if he did not leave. Mr. P was able to calm Mrs. P down by telling her that he was a repairman there to fix their bathroom sink. Mrs. P accepted that explanation and resumed watching television. When Mr. P approached her 30 min later, she had no recollection of the episode and was once again able to recognize him as her husband. He is quite concerned about what to do if something similar should occur again.

What Do You Advise Mr. P In Terms of Something Like This Occurring Again in the Future?

While Mrs. P may have been in the early stages of her disease 2 years ago, she has since progressed to a moderate stage now. Studies seem to suggest that as major vascular neurocognitive disorder progresses in severity, the frequency and severity

of neuropsychiatric symptoms also increase [15]. This would then translate to a high likelihood that Mrs. P could become physically aggressive again in the future if she becomes agitated. Psychoeducation should be provided to Mr. P in regard to how to deal with aggressive behaviors. He should be made aware that aggression can sometimes occur unprovoked and that there are both pharmacological and non-pharmacological interventions for dealing with aggressive behaviors in major neurocognitive disorders. Non-pharmacological strategies should be employed as first-line management, and only when these interventions fail should one consider pharmacological treatment.

Question 11.7

Given that neuropsychiatric symptoms are a frequent occurrence in both mild and major neurocognitive disorders, assessment and treatment of these symptoms are both important parts of managing neurocognitive disorders. However, there are no medications that have been approved by Health Canada or the U.S. Food and Drug Administration, except for risperidone in Canada for "the short-term symptomatic management of aggression or psychotic symptoms in patients with severe dementia of the Alzheimer type unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others." Hence, when other medications are used in managing behavioral disturbances, these drugs are being used off-label. It is extremely important to consider the risks and benefits in making the decision to initiate medications.

What Are Some Pharmacological Interventions That One Would Consider for Neuropsychiatric Symptoms?

The major classes of medications that are often used in managing behavioral symptoms include antipsychotics, antidepressants, cognitive enhancers, benzodiazepines, and mood stabilizers. Table 11.1 shows some examples of commonly used medications. Antipsychotic medications and their use for neuropsychiatric symptoms have been studied in a number of randomized controlled studies. Meta-analysis shows that the efficacy for these agents is modest, but significant, compared to placebo [22]. In particular, risperidone, olanzapine, and aripiprazole are the recommended antipsychotics for severe agitation, aggression, and psychosis [23].

Table 11.1 Commonly used psychotropics to manage agitation and behavioral symptoms

Antipsychotics	Antidepressants	Cognitive enhancers	Benzodiazepines	Mood stabilizers
Olanzapine	Escitalopram	Donepezil	Lorazepam	Carbamazepine
Risperidone	Citalopram	Galantamine	Clonazepam	Valproic acid
Aripiprazole	Sertraline	Rivastigmine	Diazepam	Lamotrigine
Olanzapine	Duloxetine	Memantine	Alprazolam	Gabapentin
Haloperidol	Trazodone			
	Mirtazapine			

Similarly, there seems to be evidence from meta-analyses that would suggest that antidepressants may help with agitation when compared with placebo, with two studies favoring sertraline and citalopram [24]. The cognitive enhancers, which include the cholinesterase inhibitors and memantine, are often used to delay the progression of Alzheimer disease. But the efficacy of their use in managing behaviors seems to be modest at best [23, 25]. Benzodiazepines, given their many risks and potential side effects in the older population, are generally only used for short term as on-demand, PRN medications. There has also been a lot of interest in the use of mood stabilizers or anticonvulsants in treatment of behaviors. However, in a systematic review that included carbamazepine, valproic acid, gabapentin, lamotrigine, topiramate, and oxcarbazepine, carbamazepine was the only medication that showed efficacy but was noted to be associated with significant adverse effects [26].

Question 11.8

What Are the Risks and Adverse Events Associated with the Use of Second- and Third-Generation Antipsychotic Medications in Older Adults with Major Neurocognitive Disorders?

In the early 2000s, both Canada and the USA issued warnings in using antipsychotic medications in patients with major neurocognitive disorder with the concern being that of increased risk of cerebrovascular adverse events. Since then, further studies have confirmed that the use of second- and third-generation antipsychotics is associated with the increased risk of death compared with placebo [27, 28]. This risk also extends to the use of first-generation antipsychotics [28]. Other common adverse events with antipsychotic use are listed in Table 11.2.

Table 11.2 Adverse events associated with antipsychotic use

Antipsychotic-related adverse events	Cerebrovascular accident or transient ischemic attack
	Parkinsonism or extrapyramidal signs
	Motor disturbance or dyskinesia
	Gait disturbance
	Sedation
	Cognitive disturbance
	Dizziness
	Headache
	Seizures
	Agitation or aggression
	Sleep disturbance
	Fatigue or weakness
	Falls
	Weight gain
	QT prolongation

Question 11.9

What Are Some Risks and Side Effects Associated with Antidepressant Use in Older Adults with Neuropsychiatric Symptoms Due to Neurocognitive Disorders?

While antidepressants such as selective serotonin reuptake inhibitors have been traditionally considered as "safe" medications, they are not without their risks and side effects. Common side effects of antidepressants include nausea, headache, increased appetite/weight gain, loss of libido and other sexual problems, insomnia, dry mouth, blurred vision, constipation, syndrome of inappropriate antidiuretic hormone secretion, and possibly delirium. Antidepressant use in older adults has been associated with suicide, gastrointestinal bleeds, falls, and bone loss leading to fracture risk [29]. However, a large meta-analysis specifically examining suicide in antidepressant clinical trials also found a protective effect in those aged 65 and over [30]; thus, this risk is still to be further substantiated. The increased risk of falls in a population that is already at risk due to other medical conditions and polypharmacy is something that needs to be carefully considered when weighing the risks and benefits of antidepressant use.

Question 11.10

Mr. P is a 72-year-old widower who comes into your office for assessment for behavioral symptoms in context of his major neurocognitive disorder—moderate severity. He is accompanied by his daughter K, who is his primary caregiver. You have been trying a number of different medications to treat Mr. P's agitation and restlessness. In the past year, you have tried citalopram, sertraline, trazodone, risperidone, and olanzapine. K tells you that the last trial of quetiapine (up to 50 mg/day) has been ineffective. Mr. P continues to pace restlessly at home, particularly in the evenings, getting even more upset if K tries to distract him with a different activity. K recently had a discussion with the personal support worker who comes twice a week to help Mr. P with bathing. The worker mentioned that her neighbor, who has Alzheimer disease and had been having issues with agitation, was recently put on valproic acid which seems to have helped. K wants to know if Mr. P could be put on valproic acid.

Would You Try Valproic Acid in This Patient?

There has been mixed evidence for the use of valproic acid in the treatment of neuropsychiatric symptoms. While there have been positive studies showing efficacy, there have also been just as many negative studies showing its ineffectiveness in behavioral symptoms [31]. In fact, a more recent Cochrane review corroborates the ineffectiveness of valproate preparations in treating agitation in major

neurocognitive disorder [32]. Given the significant adverse effects including sedation, falls, infection, and gastrointestinal side effects, the review did not recommend the use of valproic acid in the management of agitation in major neurocognitive disorder [32]. For Mr. P, as there are still other potential pharmacologic interventions that have not been tried (i.e., carbamazepine, aripiprazole), use of valproic acid is not recommended, unless the patient has a comorbid diagnosis of bipolar disorder. You should explain the pros and cons of the use of valproic acid to Mr. P and K and discuss other possible alternatives to help K guide in her decision making for her father.

Question 11.11

Ms. L is a 91-year-old single female who lives in an independent unit in a retirement home. You had diagnosed her about a year ago with an early stage major vascular neurocognitive disorder. She has been referred back to you by her neurologist who is now concerned about some depressive symptoms. Ms. L tells you today that her mood has been low for the past few months. She denied any specific triggering event, but that over the past year, she has been feeling increasingly hopeless due to her physical decline and limited mobility (her stroke from 2 years ago left her with significant right-sided weakness and she ambulates now with a walker) as well as her declining memory. Due to her extremely poor vision from her macular degeneration, she is no longer able to draw and paint, which is how she has always coped with stress in the past. She also does not have many visitors anymore, as her niece, the only family member she has, left recently and moved to France for a job opportunity. Many of her friends have passed away or have significant health issues of their own. While Ms. L has some acquaintances at the retirement home, she has not made the effort to try and make a deeper connection with anyone there. Ms. L really has no interest in having to build a friendship. In fact, she has been staying mostly in her unit at the retirement home as she just does not want to talk with anyone. At the same time, she complains of feeling lonely. Her sleep has worsened lately as well; her sleep has never been normal as she has struggled with restless legs for years, but over the past 2 months, it would take her 2–3 h to actually fall asleep as she would lay in bed thinking of all the things that she never had a chance to accomplish. She admits to you that she feels hopeless; while she reports that she would never take her own life, she would not mind if she passed away in her sleep.

Ms. L has a previous history of depressive symptoms about 8 years ago when her husband passed away. At the time, she had a hard time accepting his death and recalls "being in a funk" for a few months before being able to come to terms with it. She had a short trial of sertraline at the time but discontinued it after 1 week because of side effects (she cannot recall the specific problem). She ended up attending grief counseling and found it to be helpful. The "funk" eventually resolved on its own.

Her current medications include donepezil 10 mg daily, ramipril 5 mg daily, pantoprazole 40 mg daily, clonazepam 0.5 mg qhs, acetaminophen 325 mg TID, atorvastatin 10 mg qhs, carbidopa/levodopa 25/100 mg QID, levothyroxine 75 mcg

qam, and escitalopram 10 mg qam (this was initiated by her neurologist, and she has been on the current dose for 2 months but she has not noticed any benefits).

What Is Your Management Plan?

The first step would be to rule out any systemic medical illnesses that may be contributing to her depressive symptoms. Basic blood work should be done including metabolic panel, liver-associated enzymes, thyroid function (to ensure she is adequately treated on her levothyroxine), and vitamin B_{12} (low levels can contribute to depressive symptoms and worsen cognitive impairment). An electrocardiogram should also be done to monitor her QT interval as she was recently started on escitalopram, which has a risk of QT prolongation.

After acute systemic medical illnesses have been ruled out, then consideration should be given to treat the depressive symptoms. As she has not had any benefits with escitalopram, this can be tapered and discontinued. A retrial of sertraline would be reasonable if she agrees. Sertraline can be started at 25 mg daily for 1 week and then, if well tolerated, further increased to 50 mg daily. The dose can be titrated up as needed. If she is reluctant to try sertraline because of the history of issues with side effects, the use of mirtazapine can be considered. Mirtazapine may be helpful for her initial insomnia. Mirtazapine can be started at 15 mg qhs. If that is well tolerated, the dose can be further titrated slowly up to 30 mg qhs.

Ms. L is also quite isolative and inactive now. In looking at psychotherapy as a potential treatment option, cognitive behavioral therapy may help activate her, although adaptation to her current cognitive status is necessary. Interpersonal therapy with a focus on loss (loss of mobility, loss of eyesight) is another alternative. Encouragement should be given to get Ms. L to participate more in the activities offered by the retirement home. For a long-term goal, her clonazepam should be tapered and discontinued given its risks in the geriatric population.

Question 11.12

Because there are significant risks and side effects associated with various pharmacological interventions in treating neuropsychiatric symptoms due to major neurocognitive disorder, the recommendation is to try non-pharmacological interventions before using medications.

What Is the Evidence for the Use of Non-pharmacological Interventions in Neurocognitive Disorders?

In a systematic review looking at the efficacy of non-pharmacological therapies in Alzheimer disease, these interventions showed a positive result not only in improving behaviors but also in delaying institutionalization, and improving cognition,

activities of daily living, behavior, and quality of life [33]. In another recent systematic review of 20 studies, the authors looked specifically at non-pharmacological interventions in neuropsychiatric symptoms. They found that these interventions show significant efficacy at reducing agitation, psychotic symptoms, and apathy [34], thus, supporting the notion that non-pharmacological interventions are safer, more effective alternatives in treating neuropsychiatric symptoms.

Question 11.13

Mrs. M is an 89-year-old widowed female who has been living at a retirement home for the past 2 years. Mrs. M was previously diagnosed with mild cognitive impairment by her primary care physician about 3 years ago. You are being asked to see her for a consult at retirement home because the nursing staff and patient's family have noted some symptoms of anxiety and agitation in Mrs. M in the past 4–5 months. You saw Mrs. M earlier this morning and she seemed quite calm and pleasant. She was able to respond appropriately to your questions and tells you that she has only been getting upset lately because there is a new male co-resident that has moved into the home that Mrs. M has been "having some issues with." She tells you that this resident has significant issues with his memory and keeps coming into her room uninvited. She does not know why he "targets" her as he does not go into anyone else's room. She is worried that he will rummage through her things and steal her belongings. So she has started to stay in her room more often to make sure she does not leave her room unattended (she is not able to lock her door). She denies worrying that he will hurt her, just that she does "not like him very much." When the retirement home staff tries to get her to leave her room for meals or activities, she often does not want to go and that is when she admits she can become a bit irritable. Mood is reported to be fairly good other than the issues arising from her conflict with this co-resident. She denies any other issues or concerns. Mrs. M admits that her memory is not good, but does not think it is any worse in the past year. Physically, she is relatively healthy with no ongoing medical issues. The only medication she is taking is ramipril 2.5 mg qam.

You were able to complete a Montreal Cognitive Assessment test with her and she scored 17/30. She was not able to do the Trail Making Test Part B (could not understand your instructions) and was not able to draw the cube. She did draw the clock contour and numbers correctly but placed the hands incorrectly (hands pointed at "10" and "11" for requested time of "ten past eleven"). She was able to name all three animals. She repeated the numbers forward and backward and tapped to the letter A appropriately. She scored two out of three on serial sevens subtraction. She was able to repeat one sentence correctly and named ten "F" words in 1 min. She was able to get one out of two on abstraction but lost all five points in delayed recall. She only knew the city in orientation.

You were able to talk with her son J for additional collateral information, and he tells you that Mrs. M's short-term memory has continued to decline over the years. She would have trouble remembering things that were said 15–20 min ago. She seems to

focus a lot on the past; e.g., often telling the same stories of when she was dating her husband in her 20s. He was not able to notice any changes in her daily routine, although he did admit that the staff at the retirement home do everything for her as they look after her meals, her medications, and cleaning of the room and laundry. She has been a bit more isolative as she stopped playing cards with a few of the other ladies in the home. The son tells you that although there was a gentleman who accidentally wandered into her room a few months ago, this only happened one time and he has since moved to a different floor, so he is not sure why Mrs. M is still so concerned about this co-resident. He has noticed that she seems to get more anxious and agitated in the evenings, often looking out her door to watch for this co-resident. She would not be able to concentrate on anything she is doing as she is convinced that he will barge in at any moment. She ends up pacing back and forth in her room for most of the evening. The retirement home staff members are having more difficulty convincing her to eat in the dining room, so most of her meals are brought to her room now. He asks you today if you could start her on lorazepam to help her with "her nerves."

A. Do You Start Her on Lorazepam?

Given the potential risks and side effects of lorazepam (or any benzodiazepines), this would not be indicated. As well, while Mrs. M may be agitated, the underlying reason for her agitation seems to be related to her paranoid delusions around this co-resident whom she feels is targeting her for some reason. Even if lorazepam is able to decrease her agitation/anxiety, it is unlikely that this medication will resolve her delusional thinking. Also, as Mrs. M has no history of paranoia prior to the past few months, other medical contributors should be ruled out. Thus, a full workup should be requested if it has not been done already (i.e., blood work to rule out any electrolyte imbalance, tests to rule out any sources of infection, and head imaging if there are neurological signs) to rule out possibility of a delirium. If the investigations are normal, it is possible that Mrs. M has progressed from a mild neurocognitive disorder to a major neurocognitive disorder. Even though there are no explicit changes in her daily function, this is difficult to ascertain as the retirement home has been doing many tasks for her. Her son has noted a decline in her memory, and that she has become more isolative. Along with the presence of delusions (and the absence of any medical findings), it is likely she has progressed further into her cognitive difficulties, likely reaching the threshold of a major neurocognitive disorder.

B. What Are Some Suggestions That You Can Give to the Retirement Home Staff and Family to Help Decrease Her Agitation?

As nothing has been tried yet to ameliorate her agitation or delusional symptoms, the first step would be to try non-pharmacological interventions. There is some evidence to suggest that behavioral interventions can help reduce agitation, with fewer adverse

events compared to haloperidol or trazodone [33]. Behavioral interventions may include looking at analyzing and modifying the antecedents and consequences of behavior, possibly using distraction techniques to avoid a distressful outcome. There is also evidence for education and training of staff, to improve knowledge of major neurocognitive disorder, communication techniques, and behavior management [33]. Other promising therapies for agitation include music therapy and aromatherapy [34].

Question 11.14

In assessing behaviors, it is important to have a framework that allows for a systematic approach to guide caregivers through a process to give context to and better understand the possible causes of the behavior. A validated model that has been developed to facilitate this process is the "DICE" (Describe, Investigate, Create, Evaluate) model. It is suggested that neuropsychiatric symptoms are caused by underlying illnesses, unmet needs, caregiver factors, environmental factors, or a combination of those factors [35]. Once there is a better understanding of why the behaviors are occurring, then caregivers can better target the underlying causes of the behavior and develop appropriate strategies to manage these behaviors.

Describe the Sequential Steps in the DICE Approach

The sequential steps in the DICE approach include describe, investigate, create, and evaluate [36]. In the first step of "describe," details are elicited about the behavior from the patient and caregivers. The antecedents of the behavior, the specifics of the behavior itself, and the consequences of the behavior are identified. It is also helpful to understand the most distressing or problematic aspect of the symptom (to the patient and caregiver) and his/her treatment goal.

The next step is "investigate." In this step, the factors that may have contributed to the behavior are identified. These factors may be patient driven (see Table 11.3) due to unmet needs, acute medical illness, or sensory deficits; caregiver driven, caregiver burnout/depression, lack of knowledge/skills, or communication issues; or environmentally driven, over/under-stimulation, lack of routines or pleasurable activities, or safety factors.

Table 11.3 Patient considerations in the "investigate" step

Unmet needs	Acute medical illness	Sensory deficits
Poor sleep Hunger Toileting Boredom Too cold/ hot	Urinary tract infection Dehydration Constipation Depressive or anxiety disorder Medication side effects Pain	Visual impairment (poor vision or lack of proper eyeglasses) Hearing impairment (hearing loss or lack of working hearing aids)

In the step "create," a collaborative treatment plan is developed to address the underlying causes and the behaviors. This may involve identifying non-pharmacological interventions targeted at the patient and their behavior and/or pharmacological intervention when a comorbid process has been identified (e.g., antibiotics for a urinary tract infection or pain medications for pain concerns).

The final step of "evaluate" is to assess whether the treatment plan has been implemented effectively, whether the neuropsychiatric symptoms improved, and whether the caregiver's distress was reduced. As symptoms change over time and course of the disease process, it is important to monitor the behaviors and remove or change the interventions if they are no longer considered appropriate.

Question 11.15

Mrs. L is a 50-year-old married female, living at home with her husband, her two children (aged 22 and 24), and her parents. She comes to her primary care physician's office today complaining of feeling stressed. Mrs. L's parents moved into her home 6 months ago, as her father was no longer able to manage care for her mother, who was diagnosed with a major neurocognitive disorder 5 years ago. Her mother's cognition and function have worsened in the past few months. Now, in addition to her full-time job as paralegal, Mrs. L is providing personal care to her mother, cooking all the meals for everyone in the house, and dealing with some health issues of her own as she was recently diagnosed with diabetes mellitus. Mrs. L breaks down crying in the office and tells her family physician that she has not been sleeping well—her mother often wanders around the house in the middle of the night, rummaging and taking things out of drawers. Mrs. L no longer has time to meet up with her girlfriends and, thus, has not been able to access her friends to "vent." She admits she is tired all the time and just does not seem to have the energy to even smile anymore. She often feels like she is not doing a good job at work or at home, as she is constantly just running from place to place, trying to stay on top of everything. She tells you that sometimes, she just wants to run away and have a prolonged break from her responsibilities.

What Are Some Non-pharmacological Interventions That Can Have Positive Mood Benefits in Caregivers?

A systematic review of non-pharmacological strategies supports the intervention of providing caregiver education for coping skills, adding problem-solving, cognitive restructuring techniques, and offering emotional support, provided in either group or individual sessions seem to have a positive effect on caregiver mood [33]. In addition, the use of computer or telephone systems providing information and support also seems to improve caregiver mood after 6–12 months of use [33]. In Mrs. L's case, it would also be important to remind her that she should be asking other family members to help and pitch in, to alleviate some of her responsibilities (e.g.,

she can ask her two children to be in charge of cooking the meals a few times a week). If she continues to feel overwhelmed, this could have a negative impact on her control of diabetes mellitus, which would then further add to her stress.

The presence of neuropsychiatric symptoms in the patient is the most predictive factor for caregiver burden and depression [37]. This in turn creates a further burden in healthcare costs. Unless caregivers are properly supported, the burden on the healthcare system will escalate as the population ages.

Question 11.16

You are seeing Mrs. A for consultation today at her nursing home at the request of the house physician. Mrs. A, who has a pre-existing diagnosis of major neurocognitive disorder with Lewy bodies, in the moderate-to-severe stage, has not been sleeping well at night for the past 3 months. She will often wake up in the middle of the night and start wandering around the nursing home. On numerous occasions, she has wandered into other co-residents' rooms and will wake them up, disturbing their sleep. Mrs. A has also been napping more often during the daytime, leading to her missing many of the activities that she previously enjoyed. Mrs. A recently had a fall when she woke up in the middle of the night and wandered down the hallway without her walker, sustaining a bruised hip. The nursing home staff are concerned that she is at increased falls risk and further injuries, if she keeps wandering at night.

What Are Some Interventions for Sleep Disturbances?

Sleep disorders are very common behavioral symptoms noted in those with major neurocognitive disorder, occurring in 30–47% of those with Alzheimer disease [3]. Sleep disturbances can include excessive daytime sleep, increased sleep latency, and sleep fragmentation at night. These disturbances are believed to be due to a progressive deterioration and decrease in the number of neurons in the suprachiasmatic nucleus, which is part of the central sleep and circadian regulation centers [38]. Sleep disturbances are also highly prevalent in those with Parkinson disease and Lewy body disease, including prolonged sleep latency, increased sleep fragmentation, nightmares, and early morning awakenings [38]. These symptoms can lead to increased caregiver stress (especially if the patient is up and wandering in the middle of the night, which in turn also causes poor sleep for the caregiver) and can have a further negative impact on the patient's cognition and behaviors.

In considering pharmacologic treatments, benzodiazepines are commonly used for sleep disturbances. However, while they may help to decrease sleep latency and increase total sleep time, they have little effect on sleep maintenance [39]. In addition, their significant potential side effects of sedation, confusion, daytime sleepiness, and rebound insomnia make them a poor choice for treatment. Antihistamines, which are found in many over-the-counter sleep aids, also have significant risks of sedation, cognitive impairment, daytime sleepiness, and other anticholinergic side

effects. While there was much hope for the use of melatonin in treating sleep disturbances in patients with major neurocognitive disorders, the results of a number of studies have not been positive [40, 41].

Non-pharmacological interventions have been found to be helpful with sleep disorders. There are a number of studies suggesting that the use of light therapy to entrain the biological clock may be beneficial by increasing total nighttime sleep and decreasing daytime sleep [38, 39]. A number of randomized control studies also supported that cognitive behavioral therapy for insomnia was helpful in improving sleep efficiency in older adults [42].

Unfortunately, there is no easy solution for Mrs. A and her sleep difficulties. The staff at the nursing home could try light therapy with her, as that would have few side effects. Cognitive behavioral therapy is likely not an option given her limited cognitive abilities. The nursing home staff should also try and engage her in daytime activities to limit her napping, as that would further add to the nighttime sleep management. If pharmacologic interventions were needed, the aim would be short-term use with the goal of tapering these medications once her normal sleep pattern can be reestablished.

Question 11.17

It has been suggested that behavioral symptoms can have a more negative impact on the patient and caregivers than the cognitive decline including memory loss itself [43].

What Are Some Consequences of Neuropsychiatric Symptoms?

Neuropsychiatric symptoms are associated with earlier institutionalization in nursing homes, increased emergency room visits and hospitalizations, and increased healthcare costs and can predict a faster rate of deterioration [44, 45]. Caregivers of patients with neuropsychiatric symptoms are more prone to developing depressive symptoms compared to caregivers not having to manage behavioral symptoms [43]. Evidence suggests that agitation, dysphoria, irritability, delusions, and apathy were the behavioral symptoms that caregivers find to be severely distressing [46]. Given these potential consequences, clinical management of these symptoms is important at limiting disability not only in the patients themselves but also their caregivers.

Question 11.18

It is generally accepted that the presence of neuropsychiatric symptoms in mild neurocognitive disorder is associated with a higher risk of progression to major neurocognitive disorder and that its presence is linked to a higher likelihood of progression from mild-to-severe major neurocognitive disorder [47]. In a study looking

for symptoms that may increase risk for conversion from mild neurocognitive disorder to major neurocognitive disorder, three symptom clusters were identified [48]:

- Severe cluster
- Affective cluster
- Asymptomatic cluster

Symptoms in the severe cluster, consisting of agitation, anxiety, apathy, nighttime behaviors, and inhibition, have a twofold higher risk to major neurocognitive disorder in those with mild neurocognitive disorder, and symptoms in the affective cluster, consisting of depression, anxiety, irritability, and nighttime behavior, have a 1.5-fold risk compared to the asymptomatic cluster [48].

In Cognitively Intact Individuals, What Is the Implication of the Presence of Neuropsychiatric Symptoms?

Studies suggest that the presence of later-life onset of neuropsychiatric symptoms in cognitively normal individuals is associated with an increased risk of developing neurocognitive changes [16, 49]. Symptoms of agitation, anxiety, apathy, irritability, and depression have been linked to the increased risk of developing mild cognitive impairment in cognitively healthy individuals compared to the cognitively healthy without neuropsychiatric symptoms [49]. The concept of mild behavioral impairment (MBI) has been proposed to identify patients who may or may not have cognitive symptoms, with an increased risk of developing major neurocognitive disorder. (For further details on MBI, please refer to Question 9.2, at Topic 9, Common Major and Mild Neurocognitive Disorders.) The MBI checklist, developed to detect MBI, consists of questions aimed at five symptom domains: apathy/drive/motivation, mood/anxiety, impulse control/agitation/reward, social appropriateness, and thoughts/perception (see Table 11.4). With the notion that neuropsychiatric symptoms can manifest in advance of cognitive impairment, the observation of behavioral or personality changes for the first time later in life should increase suspicion for an underlying neurocognitive disorder.

Question 11.19

In a culture where physicians often value a patient's participation in medical decisions, the concept of capacity to consent to treatment is very important. Consent and capacity can often be a confusing issue, especially in psychiatry, as it is not always straightforward. Consent and capacity in those with major neurocognitive disorders, especially if neuropsychiatric symptoms are present, can complicate this even further. As major neurocognitive disorder is a progressive disease, while a patient may be capable at one point to consent to treatment, he or she may no longer be capable 3 months later. Also, while a patient may be deemed capable to make one specific

Table 11.4 Mild behavioral impairment checklist domains and question topics

Domains	Topics of questions in each domain
Interest/drive/motivation	Loss of interest in friends/family/home Less spontaneous and active Loss of motivation to act on obligations or interests Less affectionate
Mood/anxiety	Presence of sadness and tearfulness Ability to experience pleasure Feelings of being a failure/burden Increase in anxiety/worries Presence of panic symptoms
Impulse control	Presence of agitation/aggression Sexual disinhibition or intrusive behaviors Increasing levels of frustration/impatience Lack of judgment Changes in eating behaviors Presence of repetitive behaviors
Social inappropriateness	Insensitivity to others Inappropriate disclosure of private information Lack of social judgment
Thoughts/perception	Presence of paranoia/suspiciousness Presence of grandiosity Presence of auditory and visual hallucinations

medical decision, he or she may not be capable to make a different treatment decision at the same time period as capacity to consent is specific to the decision at hand. Patients with major neurocognitive disorder cannot be assumed incapable, as patients with mild-to-moderate disease can often still evaluate and analyze the information around their treatment decision.

What Are the Components in Capacity to Consent to Treatment in Patients with Major Neurocognitive Disorder?

While the legal definition of capacity to consent to treatment may vary in different countries, there are some common basic principles:

- The person must be able to communicate his/her choice.
- The person must understand the information that is relevant to making a decision about the treatment.
- The person must appreciate the reasonably foreseeable consequences of a decision or the lack of a decision.
- The person must be able to reason about the treatment choices.

In a patient with major neurocognitive disorder, the person must have the cognitive ability to understand and remember the information that is given regarding the proposed treatment. He or she must also be able to weigh the information in context

of his or her life circumstances. The ability to reason and make decisions must also be intact. The neurocognitive disease process may impair all of these abilities. It is up to the clinician to assess whether the patient is at a point in his/her disease where these abilities are still intact.

Question 11.20

Geriatric psychiatrists are often asked to assess and treat patients with a major neurocognitive disorder who present with behavioral symptoms. It is important to recognize that the behavioral symptoms themselves may also affect the person's capacity to consent to treatment. In the instance where the patient's decision for a particular treatment differs from the patient's caregiver, whose decision should the clinician follow? The answer to that question depends on whether the clinician believes if the patient is capable of making that decision.

How Does the Presence of Neuropsychiatric Symptom Due to Major Neurocognitive Disorder Impact on Capacity to Consent to Treatment?

As decisional capacity can be affected by the presence of psychosis or mood symptoms in a cognitively intact patient, it would be reasonable to draw the conclusion that the presence of neuropsychiatric symptoms due to major neurocognitive disorder would potentially impair medical decision-making capacity. In a recent study looking at the relationship between behavioral disturbance and decision making in major neurocognitive disorder due to Alzheimer disease, the presence of delusions and apathy impaired the expression of choice compared with those without these symptoms, and the presence of mania impaired the reasoning aspect in capacity [50]. There were no significant differences between those patients with hallucinations, agitation/aggression, anxiety, irritability, disinhibition, and aberrant motor behavior compared to those without these symptoms [50].

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Topic 12: Sleep-Wake Disorders in Late Life

Question 12.1

Age-related physiological changes and age-related increases in pathology prevalence are underlying mechanisms associated with sleep difficulties in older adults.

What Are the Common Age-Related Sleep Changes?

The sleep architecture changes with aging. The common age-related physiological changes in the sleep-wake cycle are summarized in Fig. 12.1 [1, 2].

Question 12.2

What Are the Adverse Consequences of Age-Related Sleep Changes?

The adverse consequences of sleep disturbances include the following [1, 3–5]:

- Increased use of healthcare resources
- Impaired quality of life
- Increased risk of motor vehicle accidents
- Increased risk of placement into long-term care facilities
- Increased incidence of primary sleep disorders
- Decline in health status and physical function

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_12

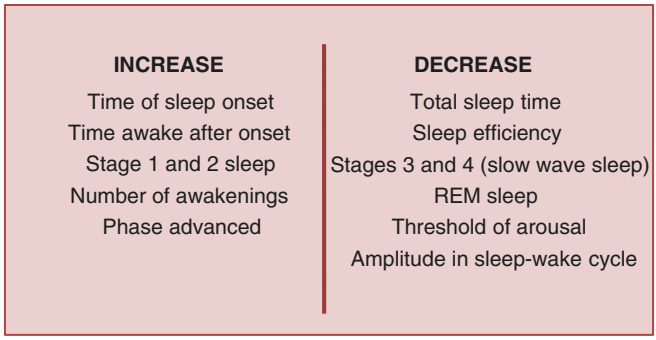


Fig. 12.1 Normal age-related sleep-wake cycle changes [1, 2]

Question 12.3

List Some Sleep-Wake Disorders That Are Closely Associated with Age-Related Sleep Changes

The sleep-wake disorders that have been closely associated with age-related sleep changes are the following:

- Circadian rhythm sleep-wake disorders
- Rapid eye movement (REM) sleep behavior disorder
- Breathing-related sleep disorders (e.g., obstructive sleep apnea)

Notably, the criteria for sleep-wake disorders in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) are based on symptoms which include difficulties in sleep onset and maintenance, early morning awakenings, and non-restorative sleep [3].

Question 12.4

A. What Are the Common Sleep-Wake Disorders Encountered in Older Adults?

The most common sleep-wake disorders encountered in older adults are summarized in Table 12.1 [3]. Of note, the utilization of biomarkers such as polysomnography results, where indicated (e.g., for the diagnosis of breathing-related sleep disorders and periodic limb movements during sleep, which both often coexist with restless legs syndrome), has been included in the DSM-5 classification system for sleep-wake disorders [1, 3].

Table 12.1 Summary of the DSM-5 diagnostic criteria for common sleep-wake disorders in the elderly [3]

Sleep-wake disorder	Diagnosis	Criteria
Specifiers for all disorders: – Episodic/recurrent/ persistent – Acute/subacute/ persistent *Severity:* mild/ moderate/severe	Insomnia disorder	Dissatisfaction with sleep quantity/quality and one (or more) of: – Difficulty initiating sleep – Difficulty maintaining sleep – Early morning awakening Frequency in nights/week: 3 (or more) Duration in months: 3 (or more)
Circadian rhythm sleep-wake disorders	Advanced sleep phase type	Advanced sleep onset and awakening times
	Delayed sleep phase type	Delayed sleep onset and awakening times
	Irregular sleep-wake type	Disorganized sleep-wake pattern throughout the 24-h period
Breathing-related sleep disorders	Obstructive sleep apnea hypopnea	Either (1) or (2) on polysomnography: 1. 5 (or more) obstructive apneas/hypopneas/hour of sleep, and (a) Nocturnal breathing disturbances and/or (b) Daytime sleepiness, fatigue, unrefreshing sleep 2. 15 (or more) obstructive apneas/hypopneas/hour of sleep
	Central sleep apnea	Evidence on polysomnography: 5 (or more) central apneas/hour of sleep
Parasomnias	REM sleep behavior disorder	Repeated arousals during REM sleep, with vocalization and/or complex motor behaviors. Either (1) or (2): 1. REM sleep without atonia on polysomnography 2. History suggestive of this sleep disorder and an established synucleinopathy diagnosis
	Restless legs syndrome	Urge to move legs during periods of rest/inactivity (partially/totally relieved by movement); it occurs/ worsens in the evening or at night Frequency per week: 3 times (or more) Duration in months: 3 (or more)

B. What Does a Clinical Diagnosis of Sleep-Wake Disorder Require?

A clinical diagnosis of sleep-wake disorder requires the determination of two factors [1]:

- The duration for the complaint of sleep dissatisfaction
- The resulting daytime symptoms of drowsiness

C. How Is Drowsiness Determined?

Drowsiness is often determined by self-reporting napping behavior or by the Epworth Sleepiness Scale. The Epworth Sleepiness Scale is a brief self-administrated questionnaire with scores ranging from 0 to 24, with higher scores denoting greater drowsiness [6].

Question 12.5

Is Sleep Disturbance Part of a Prodrome of Neuropsychiatric Disorders, an Actual Manifestation of Neuropsychiatric Disorders, or a Risk Factor for Neuropsychiatric Disorders?

Sleep disturbances can be common symptoms in depressive, anxiety, and neurocognitive disorders. However, sleep difficulties can also represent risk factors for the subsequent development of neuropsychiatric disorders; as well, they can be a prodromal phase of a neuropsychiatric disorder [7]. Many systemic medical conditions in late life (e.g., osteoarthritis, chronic obstructive pulmonary disease, congestive heart failure) can coexist with a host of neurological disorders (e.g., Parkinson disease, Alzheimer disease, Lewy body disease), which all could disturb sleep and also themselves may be worsened during sleep (e.g., confusional arousals occurring in patients with Alzheimer disease) [3]. Moreover, REM sleep behavior disorder is often an early indicator of alpha synucleinopathies such as Parkinson disease and Lewy body disease [8].

Question 12.6

Whereas physiological changes in sleep architecture are expected to occur with aging, they do not account for most of the disturbed sleep in the geriatric population; however, primary sleep disorders as well as systemic medical and psychiatric comorbidities are more common contributors to disturbed sleep in older adults.

What Are the Most Common Primary Sleep Disorders in Late Life? Describe Each Disorder

Primary sleep disorders are sleep-wake disorders that cannot be attributed to systemic medical or psychiatric disorders or to the influence of medications or other substances. The most common primary sleep disorders in older adults are [3]:

- Restless legs syndrome
- Periodic limb movement disorder
- REM sleep behavior disorder
- Breathing-related sleep disorders

Restless legs syndrome is a feeling of discomfort in the lower extremities associated with the urge to move, with a diurnal variation of symptoms worsening in the evening and bedtime, with resulting distress related to insomnia as one of its most significant complaints. Patients experience difficulty with falling asleep and staying still during sedentary activities [9]. Differential diagnosis of restless legs syndrome includes anxiety disorders, tic disorders, peripheral neuropathy, and akathisia.

Periodic leg movements in sleep are motor symptoms occurring in up to 90% of patients with restless legs syndrome, and their combined presence supports a diagnosis of restless legs syndrome [10]. Periodic limb movements in sleep are repetitive, stereotypical contractions of the legs, which occur in clusters, lasting up to 5 s [11]. Periodic limb movements in sleep are different from periodic leg movement disorder; they are not usually noticed by the patient and can only be diagnosed by polysomnography [11]. Periodic limb movement disorder is defined as periodic limb movements in sleep occurring in patients with unexplained sleep disturbance or other functional impairment and when the frequency of limb movements is greater than 15 per hour [11, 12].

REM sleep behavior disorder is characterized by the loss of normal atonia that occurs during REM sleep, with resulting dream acting out [3]. REM sleep behavior disorder can be idiopathic or associated with antidepressant use (e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors) or with lesions in pontomedullary areas [8, 13]. Idiopathic REM sleep behavior disorder is often associated with one of the synuclein-mediated neurodegenerative diseases (e.g., Parkinson disease, Lewy body disease, multiple system atrophy), but it is also associated with non-neurodegenerative disorders (e.g., narcolepsy, multiple sclerosis, Guillain-Barre syndrome, amyotrophic lateral sclerosis), as well as the use of certain pharmacological agents [8, 13].

REM sleep behavior disorder occurs in up to 50% of patients with Parkinson disease and is considered a nonmotor manifestation of Parkinson disease [14]. For this reason, REM sleep behavior disorder is an important and clinically relevant predictor (or a prodromal marker) of Parkinson disease and other synucleinopathies [8].

Sleep-disordered breathing includes obstructive sleep apnea which increases with age and is the predominant type of sleep apnea in older adults [15]. Abnormal respiratory patterns can range from significant snoring to episodes of complete airway obstruction where breathing ceases for a period of 10 s or more [16]. The severity of obstructive sleep apnea depends on the frequency of respiratory events and level of daytime sleepiness. Sleep-disordered breathing is diagnosed by polysomnography. Obstructive sleep apnea is also associated with an increased risk for systemic medical conditions, such as hypertension, heart disease, stroke, and neurocognitive disorders.

Question 12.7

A higher prevalence of insomnia in older adults compared with younger patients has been demonstrated in epidemiological studies.

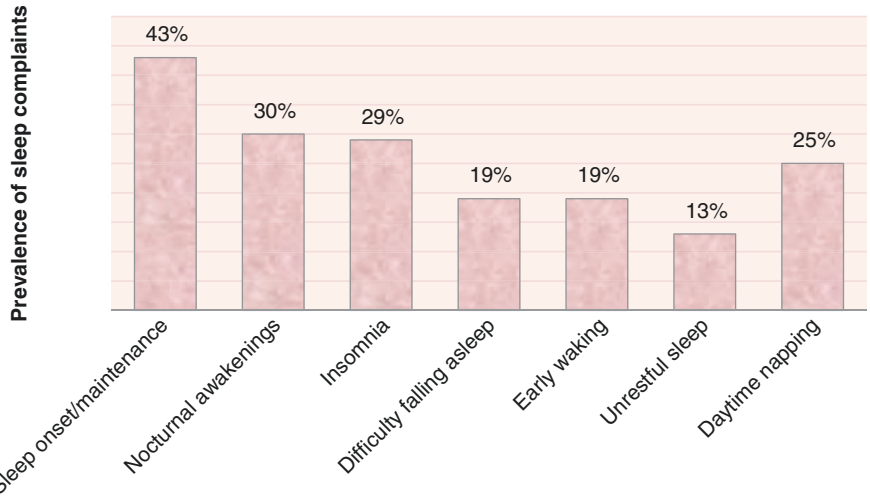


Fig. 12.2 Prevalence of sleep complaints in community-based epidemiological studies. Data extracted from [18, 19]

What Is the Prevalence of Sleep Difficulties in Older Adults?

Approximately 40% of adults aged 60 or older may experience sleep difficulties including insomnia and frequent awakenings [17]. In a community-based epidemiological study of sleep complaints in late life (mean age, 74 years), 57% of subjects reported chronic sleep disruption, with the prevalence rates of the sleep complaints as illustrated in Fig. 12.2 [18, 19]. Similar to this study, the Established Populations for Epidemiologic Studies of the Elderly (EPESE) reported that 43% of patients aged 65 or older had difficulties in sleep onset or maintenance, and 25% reported daytime napping [19].

Question 12.8

What Is the Treatment for Restless Legs Syndrome, Periodic Limb Movement Disorder, REM Sleep Behavior Disorder, and Obstructive Sleep Apnea?

Restless legs syndrome and periodic limb movement disorder are treated with dopaminergic agents (e.g., ropinirole, pramipexole), which are considered first-line treatment, followed by opioid and benzodiazepine agents. In older adults, medications must be prescribed judiciously due to side effects, most notably the development of sleep apnea, delirium, falls, and fractures with opioids, benzodiazepines, and

hypnotics [11]. REM sleep behavior disorder is treated with clonazepam 0.5–2 mg qhs or melatonin 3–12 mg qhs as the most common treatment options [20]. Obstructive sleep apnea with clinical symptoms is treated with continuous positive airway pressure (CPAP). CPAP keeps the upper airways open using air pressure, thereby improving symptoms by decreasing hypoxemia and sleep fragmentation [13]. CPAP has been shown to improve episodic memory, sustained attention, and some aspects of executive function [13].

Question 12.9

What Is the Non-pharmacological and Pharmacological Treatment of Insomnia?

Pharmacotherapy should only be used for insomnia when non-pharmacological strategies have been exhausted (see Box 12.1 for non-pharmacological approaches) [21]. The five general principles to consider when using medications to treat insomnia in older adults are illustrated in Fig. 12.3 [7, 22].

Box 12.1 Non-pharmacological Approaches to Chronic Insomnia in Older Adults [21]

Avoid/minimize the use of caffeine, cigarettes, alcohol, and stimulating medication before bedtime
Exercise daily, but not close to bedtime
Avoid frequent napping; limit naps to one per day, less than 30 min
During the day, increase exposure to natural and bright light
Maintain bedtime ritual: bedroom is used for sleep; room is comfortable, with minimal light exposure
Avoid heavy meals and liquids before bedtime
Avoid the use of electronics (especially with bright screens) 1–2 h before bedtime

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Benzodiazepines and benzodiazepine receptor agonists (the "Z" drugs) are frequently prescribed in patients with insomnia due to their sedative properties and effectiveness in sleep initiation. However, in older adults, these medications can cause impaired cognition (including increasing delirium risk), impaired coordination and motor function, and daytime sleepiness, which can result in falls, motor vehicle accidents, and poor quality of life [23].

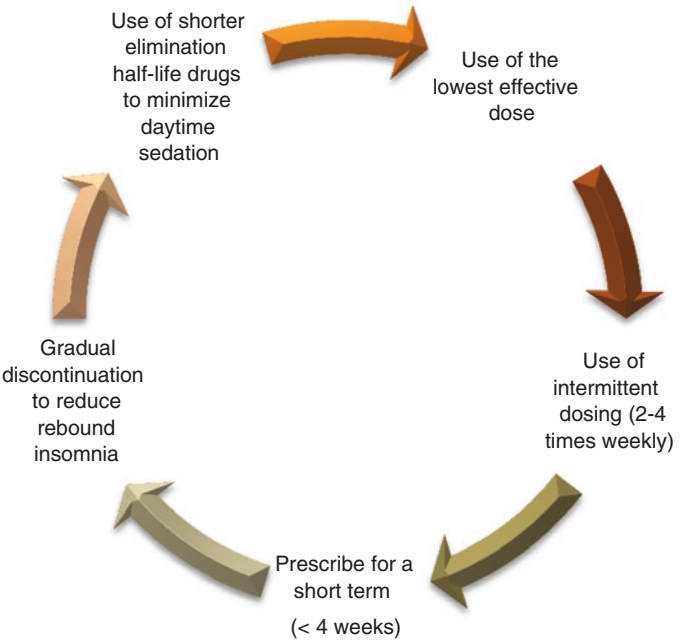


Fig. 12.3 The general principles of using medications to treat insomnia in older adults [7, 22]

Although the only Health Canada and US Food and Drug Administration-approved antidepressant for insomnia is the tricyclic doxepin (small dose of 3–6 mg qhs), many antidepressants are frequently prescribed off-label to treat disturbed sleep in patients, even without depressive disorder [24]. Caution is required for those with glaucoma who are treated with tricyclic antidepressants because of their anticholinergic side effects. Trazodone and mirtazapine are two of the most clinically useful antidepressants for treating insomnia. However, trazodone causes daytime drowsiness and dizziness, which can lead to falls and functional impairment, and has rare cases of priapism [25]. Table 12.2 summarizes the pharmacological treatment options for insomnia in older adults [21].

Question 12.10

The patient is a 75-year-old male with dyslipidemia, being treated with rosuvastatin 20 mg daily. He has had a recent history of major depressive disorder being successfully treated with citalopram 20 mg daily as indicated by a significant improvement in his Hamilton Rating Scale for Depression scores from 24 (severe) down now to 6 (no depression). However, at a psychiatric follow-up visit, he still complains of persistent fatigue. There are no over-the-counter medications taken. There is no history of substance use. He drinks one caffeinated beverage per day prior to noontime. He reports that he goes to bed at 10:30 PM, falls asleep within 30 min, and wakes up at 6:30 AM. He takes daytime naps because of his fatigue. His wife, who accompanied

Table 12.2 Pharmacological treatment of insomnia in older adults [21]

Drug class	Medication/dosage[a] (at bedtime)	Adverse effects	Drug interactions	Comments
Benzodiazepines[b,c]	Lorazepam 0.5–1 mg (insomnia not official indication but widely used)	Sedation, depression, irritability, delirium risk, memory impairment, dizziness, headache, weakness, dose-dependent ataxia, falls/fracture risk, behavioral changes, rebound insomnia, daytime anxiety	Additive sedation with CNS depressants CYP3A4 substrates	2015 Beers Criteria: *All benzodiazepines* should be used with caution or avoided as potentially inappropriate in older adults Benzodiazepines should be used in older adults only with specific approved indications; monitor for cognitive status. Risk of tolerance and dependence. More rebound insomnia with lorazepam *Flurazepam*: not recommended (potential for accumulation leading to delirium risk and cognitive impairment) *Triazolam*: should be avoided in older adults, especially doses >0.125 mg *Clonazepam*: given in REM sleep behavior disorder
	Temazepam 15–30 mg (max dose 7.5 mg for older adults)			
	Nitrazepam 5–20 mg (max dose 5 mg for older adults)			
	Flurazepam 15–30 mg (max dose 15 mg for older adults)			
	Triazolam 0.125–0.25 mg (max dose 0.125 mg for older adults)			
	Clonazepam 0.25–2 mg			
Melatonin[d]	Melatonin 0.3–12 mg (max dose 5 mg for older adults)	Dizziness, headache, nausea, somnolence, tachycardia, pruritus, nightmares	Warfarin, nifedipine, fluvoxamine	To be given 30–90 min pre-bedtime. Appears to be safe when used for ≤3 months. Used with REM sleep behavior disorder. Not well studied in older adults
Ramelteon[b] (melatonin agonist)	Ramelteon 8 mg (available in USA and Japan)	Headache, somnolence, sore throat		No behavioral impairment; no abuse potential; no restriction on duration of use. Contraindicated in patients taking fluvoxamine, liver disease

(continued)

Table 12.2 (continued)

Drug class	Medication/dosage[a] (at bedtime)	Adverse effects	Drug interactions	Comments
Z-Drugs[b,c]	Zaleplon 10–20 mg (max dose 10 mg for older adults) (discontinued in Canada)	Dizziness, somnolence, gastrointestinal disturbances, ataxia, falls/fracture risk, rebound insomnia, morning hangover effect, transient global amnesia, anterograde amnesia, delirium risk, nighttime acting out, sleepwalking, bitter/metallic taste	CYP3A4 substrate	*All Z-drugs* should be used with caution and for <90 days in older adults *All Z-drugs* interact with CNS depressants and CNS active drugs. Caution to be exercised when used
	Zolpidem 5 mg SL (available in USA) Zolpidem ER 6.25–12.5 mg (max dose 6.25 mg for older adults) (available in USA)		CYP3A4, 1A2, 2C9 substrate; erythromycin, ketoconazole, rifampin	Should be avoided in patients with cognitive impairment
	Eszopiclone 1–3 mg (max dose 2 mg for older adults) (available in USA)		CYP3A4, 2C1 substrate	Less chance of morning hangover effect, rapid onset, allow 8-h sleep, complex sleep-related behaviors induced, risk of tolerance/dependence
	Zopiclone 3.75–7.5 mg (max dose 5 mg for older adults) (available in Canada)		CYP3A4, 2C8 substrate	Does not accumulate, less rebound with discontinuation
Tryptophan[d]	Tryptophan 500 mg–2 g	Weight loss, dizziness, xerostomia, headache, nausea, improper sexual behavior, serotonin syndrome (alone and with serotonergic agents)		Given 20 min before bedtime. Erratic response

Sedating antidepressants (use in comorbid depression, anxiety, other comorbid indications)	Trazodone 25–100 mg	Orthostatic hypotension, cardiac conduction problems, dizziness, somnolence, xerostomia, dry eyes, weight gain, priapism		Does not depress respiration (safe in obstructive sleep apnea); less risk of morning hangover, tolerance/dependence. Used in agitated behavior affecting sleep in major neurocognitive disorder—"sundowning"
	Mirtazapine 7.5–15 mg	Sedation, constipation, xerostomia, increased appetite, weight gain		Used with comorbid condition; not approved for insomnia
	Doxepin 3–6 mg Nortriptyline 10–50 mg	Sedation, weight gain, urinary retention, constipation, orthostatic hypotension, QTc prolongation, delirium, lethal in overdose		Sedating tricyclic antidepressants (TCAs) can moderately reduce sleep latency and increase total sleep time. Use only low dose; avoid tertiary TCAs in older adults (e.g., amitriptyline, imipramine, doxepin >6 mg/day) as highly anticholinergic. Contraindicated in those with glaucoma, urinary retention. Use requires ECG monitoring *Doxepin:* only Health Canada-/FDA-approved antidepressant for insomnia *Nortriptyline*: used with chronic pain
Antipsychotics	Quetiapine 12.5–100 mg Olanzapine 2.5–10 mg Risperidone 0.25–1 mg Ziprasidone 20–80 mg	Orthostatic hypotension, QTc prolongation, increased appetite, hyperglycemia, hyperprolactinemia, dyslipidemia, hematologic effects, rash		Use primarily when comorbid psychotic disorders and psychotic symptoms associated with other illnesses (e.g., bipolar disorder, depressive disorder, neurocognitive disorders) do not respond to other treatments. Use with caution in older adults, especially when comorbid major neurocognitive disorders are not associated with psychotic symptoms. Increased risk of stroke and sudden cardiac death. Use requires metabolic and ECG monitoring

(continued)

Table 12.2 (continued)

Drug class	Medication/dosage[a] (at bedtime)	Adverse effects	Drug interactions	Comments
Suvorexant[b] (oral dual orexin receptor antagonist)	Suvorexant 10–20 mg (no doses available for older adults) (not available in Canada)	Somnolence, sedation, muscle weakness, abnormal dreams, headache	CNS depressants; CYP3A4 substrates	Given 30 min before bedtime. Caution in obstructive sleep apnea
Dopamine agonists	Ropinirole 0.25–4 mg	Nausea, somnolence, symptomatic hypotension, syncope, hallucinations; augmentation and rebound are rare; application site reaction with transdermal patch	Interact with dopamine antagonists	First-line treatment in restless legs syndrome and periodic limb movement disorder disrupting sleep; effective and well tolerated
	Pramipexole 0.125–0.75 mg			
	Rotigotine (transdermal patch) 1–3 mg/24 h			
Antihistamines (over-the-counter)	Dimenhydrinate 25–50 mg	Daytime somnolence, xerostomia, blurred vision, urinary retention		Use not recommended in older adults due to lack of efficacy and safety data. Highly anticholinergic; clearance reduced with advanced age; tolerance develops rapidly (i.e., within a few days)
	Diphenhydramine 25–50 mg			
	Hydroxyzine 25–100 mg			
	Doxylamine 25–50 mg			
Valerian[d]	Valerian 450 mg (no doses available for older adults)	Morning somnolence, headache, gastrointestinal effects, anxiety, hepatotoxicity		Not well studied in older adults

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[a]Older adult doses were available

[b]FDA-approved for the treatment of insomnia in older adults

[c]Health Canada-approved for the treatment of insomnia in older adults

[d]Evidence supporting efficacy variable and insufficient

the patient for his follow-up visit, reported that she noticed loud snoring, somniloquy (i.e., sleep talking), and some movements during his sleep but stated that he was not bothered by these movements and they did not last very long. There is no history of somnambulism (i.e., sleep walking), falling asleep while driving, or car accidents. He also complains of some difficulty remembering things during the day but attributes this to his fatigue and resulting poor concentration. He has no allergies. His family history reveals heart disease and an unspecified anxiety disorder.

Physical exam shows that he is overweight and has a neck circumference of 19 inches (48.3 cm) (normal in men, <17 inches (<43.2 cm); normal in women, <15 inches (<38.1 cm)). His vital signs are normal. At this visit, the Montreal Cognitive Assessment (MoCA) is 23/30 (4 points lost on delayed recall task and 3 points lost on attention task).

Due to the reported movements during his sleep, he is subsequently referred for a polysomnography, which reveals a diagnosis of severe obstructive sleep apnea, decreased sleep efficiency, and severe periodic limb movements with sleep arousals.

A. What Are the Disorders That Can Present with Insomnia in This Case?

There are a number of factors that may be contributing to his insomnia. His depressive disorder appears to be the most obvious factor. The insomnia may have preceded his depressive disorder, and thus contributing to its onset, it may have been a symptom of the depressive disorder or may be unrelated to the depressive disorder altogether. However, given his history of depressive disorder, treating his residual insomnia can be of greater importance in order to prevent a relapse of depressive symptoms.

Another cause could be restless legs syndrome. Restless legs syndrome commonly occurs with periodic limb movements in sleep, as was likely in this case, with restless legs syndrome being clinically diagnosed by history. This may explain the daytime fatigue and his subjective experience of sleeping well during the night. Screening for medical contributors to restless legs syndrome and periodic limb movement disorder may help narrow down diagnoses (e.g., iron deficiency, low ferritin levels, diabetes mellitus) and assist in treatment.

B. How Would You Manage This Patient's Insomnia at This Time?

The main medical disorders possibly contributing to his complaint of insomnia are major depressive disorder, obstructive sleep apnea, and periodic limb movement disorder. However, his major depressive disorder has been reported to be successfully treated, and it is plausible that his sleep and cognitive symptoms are unrelated to the major depressive disorder but to his sleep apnea. Therefore, the first step in management would be to address his obstructive sleep apnea.

There is a bidirectional relationship between depressive disorder and obstructive sleep apnea [26]. Moreover, in patients with sleep apnea, comorbid depressive disorder has been found to contribute to the severity of daytime fatigue. This patient has several risk factors for sleep apnea including dyslipidemia, increased neck circumference, and increased body mass index. A diagnosis of obstructive sleep apnea on polysomnography could explain both his daytime sleepiness and mild cognitive impairment. As in this case, treatment of obstructive sleep apnea with CPAP may lead to improvement in depressive disorder as well as cognitive impairment and could prevent further cognitive decline [13, 27].

While the periodic limb movement disorder was not a priority at this point, the patient will need to continue with his CPAP treatment and follow up with his physician in 3 months. If symptoms persisted or recurred, a dopamine agonist may be trialed.

C. Generally, What Other Factors Can Disturb Sleep?

A number of chronic illnesses, medications, and other substances can contribute to insomnia in older adults (see Table 12.3 and Box 12.2) [21].

Table 12.3 Chronic illnesses associated with disturbances of sleep [21]

Illness group	Examples
Acute or chronic pain	Arthritis, fibromyalgia, neuropathic pain, cancer, chronic headaches
Cardiac disease	Nocturnal angina, congestive heart failure (nocturnal hypoxemia, nocturia)
Respiratory disease	COPD, nocturnal bronchospasm, sleep-related laryngospasm
Endocrine disease	Hypothyroidism-associated central sleep apnea, diabetes mellitus (nocturia, neuropathic pain)
Genitourinary problems	Incontinence and resulting nocturia
Neurological disorders	Stroke (difficulty changing positions, aspiration), major neurocognitive disorders, nocturnal seizures, neuromuscular degenerative disorders

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Box 12.2 Medications and Other Substances That Can Contribute to Insomnia in Older Adults [21]

Caffeine
Nicotine
Antidepressants
Psychostimulants
Diuretics
ACE inhibitors
Alpha blockers
Beta blockers
Dopamine agonists
Theophylline
Bronchodilators
Corticosteroids
Statins
Cholinesterase inhibitors
H_1 antagonists

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D. What Is the General Approach to the Treatment of Insomnia in Older Patients?

The management of sleep-wake disorders in older adults includes the assessment of sleep complaints and the multiple risk factors including medical and psychosocial problems and the therapeutic plan. Assessing and treating sleep-wake disorders are challenging in older adults because of their increased rates of polypharmacy which can interfere with sleep, increased vulnerability to commonly prescribed sleep aids, and increased comorbidity including cognitive impairment interfering with history taking. A decision tree approach to the assessment and management of insomnia is presented in Fig. 12.4 [21].

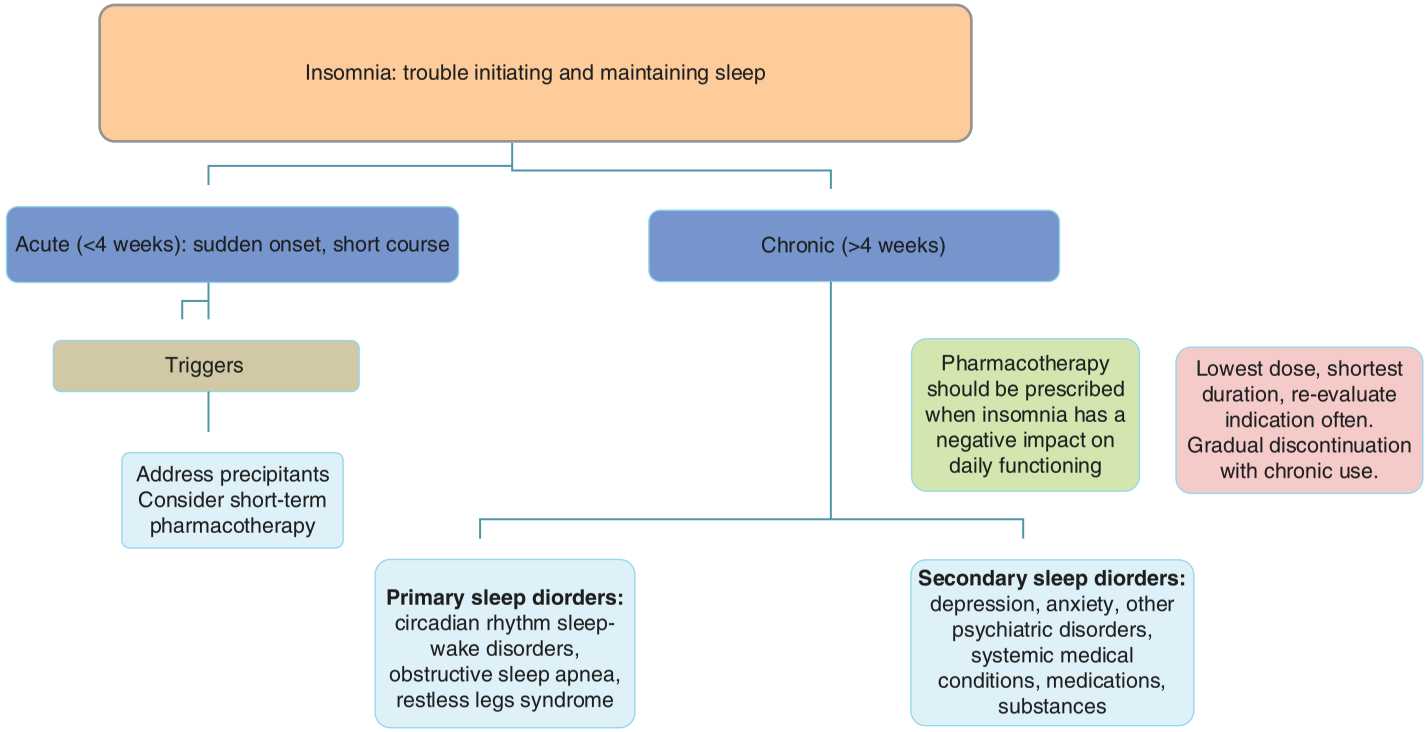


Fig. 12.4 Decision tree approach to assessment and treatment of insomnia [21]. From: Meghji Z, Hategan H, Amoako-Tuffour A. Pharmacological treatment of insomnia in older adults. In Hategan et al., eds. Geriatric Psychiatry: A Case-Based Textbook. Springer, 2018. Used with permission from Springer

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Topic 13: Personality Disorders in Late Life

Question 13.1

Personality disorders are associated with significant impairment in physical, emotional, and social functioning in later life [1]. The few studies of personality disorders in older adults have been limited to assessing the applicability of personality tests, scales, and inventories [2]. Recognizing the dearth of empirical research regarding personality disorders in late life, researchers have increasingly investigated the course of these disorders over the life span and analyzed personality traits that could predict or protect against the development of functionally impairing neurocognitive and other psychiatric disorders later in life [3–5].

A. What Are Two Broad Approaches for Conceptualizing Personality Disorders?

One type is *categorical* which views personality as including qualitatively distinct clinical syndromes, as is reflected in the current *Diagnostic and Statistical Manual of Mental Disorders*, *5th edition* (DSM-5) diagnostic categories [6]. For example, personality disorders are divided into three clusters (A, odd-eccentric; B, dramatic-emotional; and C, anxious-fearful). The categorical perspective can be considered more of a "medical" viewpoint in which individuals are diagnosed once they meet specific diagnostic criteria. The DSM-5 currently uses this categorical approach because it reflects current clinical practice while acknowledging that the categorical approach is problematic in some ways. For example, some patients meet criteria for more than just one personality disorder.

The DSM-5 presents the *dimensional* model as an alternative approach that views personality as a continuum of "normal" to maladaptive variants of various

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_13

personality functioning and pathological personality traits. The proposed dimensional model includes diagnostic criteria of "moderate or greater impairment in personality functioning" and "one or more pathological personality traits."

Personality dysfunctions occur in the *self* (identity and self-direction) and *interpersonal functioning* (in terms of empathy and intimacy). The personality traits are categorized into five broad domains:

- Negative affectivity (versus emotional stability)
- Detachment (versus extraversion)
- Antagonism (versus agreeableness)
- Disinhibition (versus conscientiousness)
- Psychoticism (versus lucidity)

B. What Is the Hallmark of "Normal" Personality?

Normal personality involves flexibility, or adaptability, in thinking, feeling, and behaving, as opposed to rigidity, which may lead to psychopathology. With a dimensional perspective, "normal" personality would include adequate personality functioning in terms of the self and interpersonally [6].

Question 13.2

A. According to the DSM-5, What Are the Criteria for a Personality Disorder?

The DSM-5 defines a personality disorder as "an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment" [6].

B. What Are the Characteristics of the Three Clusters of Personalities According to the DSM-5?

The DSM-5 categorizes personality disorders in the following three clusters [6]:

- *Cluster A* is characterized by impaired social integration, may appear odd or eccentric, and includes paranoid, schizoid, and schizotypal personality disorder.
- *Cluster B* is characterized by a relative lack of concern for others; may appear dramatic, emotional, or erratic, and includes antisocial, borderline, histrionic, and narcissistic personality disorder.

Table 13.1 Classification of personality disorders based on current DSM-5 model, with general definition and each ten personality disorders, with the minimum number criteria that must be met for each and their specific patterns of dysfunction [7]

Personality disorders	
General definition: An enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture. The pattern is manifested in two or more of the following: (1) cognition, (2) affectivity, (3) interpersonal functioning, and (4) impulse control	
Cluster A –Paranoid (4/7): Distrust (others' motives are interpreted as malevolent) –Schizoid (4/7): Social and emotional detachment –Schizotypal (5/9): Discomfort in close relations, distortions, eccentricities	Cluster C –Avoidant (4/7): Social inhibition and hypersensitivity to negative evaluation –Dependent (5/8): Excessive need to be taken care of leading to submissiveness –Obsessive-compulsive (4/8): Preoccupation with perfection and control
Cluster B –Antisocial (3/7): Disregard for rights of others; empathy deficits –Borderline (5/9): Instability in relationships and affects –Histrionic (5/8): Excessive emotionality, attention-seeking –Narcissistic (5/9): Grandiosity, need for admiration, vulnerability to shame	Other personality disorders –Personality change due to another medical condition: For instance, secondary to a frontal lobe lesion (specifiers: labile, disinhibited, aggressive, apathetic, paranoid, other, combined, unspecified) –Other specified personality disorder: The general criteria are met, and: (1) traits from several personality disorders are present, but criteria for any specific personality disorder do not meet the threshold (also formerly called "mixed" or "personality disorder NOS" in DSM-IV), or (2) the individual has a personality disorder that is not included in the DSM-5 classification (e.g., passive-aggressive) –Unspecified personality disorder: Clinical situation not meeting criteria for any of the above categories (also formerly "personality disorder NOS" in DSM-IV)

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- *Cluster C* is characterized by a negative affect, may appear anxious or fearful, and includes avoidant, dependent, and obsessive-compulsive personality disorder. Refer to Table 13.1 for a more detailed description of these clusters [7].

Question 13.3

A. What Is the Estimated Prevalence of Personality Disorder in Older Adults?

An analysis of the National Epidemiologic Survey on Alcohol and Related Conditions found that 8% of American adults aged 65 years and older met criteria

for at least one personality disorder, with the most prevalent being obsessive-compulsive personality disorder [1].

B. How Stable Are Personality Disorders over the Life Span?

Historically, the cardinal feature of a personality disorder has been the stable nature of symptoms throughout the life span, with words such as "enduring," "pervasive," and "inflexible" in the current DSM-5 definition of a personality disorder [6]. However, cross-sectional studies have generally found that the prevalence of personality disorders decreases with age [3, 8–11]. Furthermore, longitudinal data suggest that the prevalence and severity of some personality disorders—particularly Cluster B personality disorders—decrease over time [4, 12–16], while obsessive-compulsive and schizoid personality disorders increase [17, 18].

Even "normal" personality traits appear to change over time, with Roberts and DelVecchio finding that personality traits do not stabilize until after the age of 50 [19] and even fluctuate throughout life [19, 20].

Question 13.4

What Are Some Challenges in Diagnosing Older Adults with Personality Disorders?

Some of the challenges in diagnosing older adults with personality disorders include:

- The heterogeneity of the geriatric population. Due to cultural and environmental factors, there may be large differences in the coping styles and worldview of older adults, depending on their age, which can range from youngest old (65–74 years) to oldest old (85 years and over) [21]. For example, someone in the oldest old age category in 2018 may have grown up during the Great Depression and then lived through World War II, while an individual in the youngest old group may have lived through the Vietnam War and the "hippy" and "free love" era.
- Clinician biases and misconceptions regarding the geriatric population that may preclude a valid diagnostic process (see Table 13.2) [7].
- Current personality disorder diagnostic criteria do not reflect the lifestyle and experiences of older adults, leading to measurement errors [21, 22].
- Current diagnostic criteria for a personality disorder require that functionally impairing personality traits emerged during adolescence or young adulthood [6]. This would require an individual to recount memories of their emotional states and reactions at least 50 years in the past. In addition, it is possible that symptoms of personality disorder that had been quiescent, and well-compensated for by various social and other supports, emerge in older age as these stabilizing factors go away (e.g., via death or disability).

Table 13.2 Misconceptions constituting barriers to diagnose personality disorder in older adults [7]

Potential bias to the evaluation of personality disorder in older adults
Older people spend little money
Older people do not have sex
Older people are dependent
Older people are less active
Older people have a depressed mood that is "normal"

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- Onset of major neurocognitive disorders (dementia), which in of themselves can lead to personality changes [23].
- Declining physical health.

Question 13.5

In contrast to the younger adult population, Cluster B personality disorders seem to be rare among the geriatric population [1].

What Are Some Reasons for This?

- Researchers have speculated that lower rates of these disorders are due to the attrition at younger ages of this group that is more prone than others to substance use disorders, risky behavior, impulsivity, and self-injurious behaviors, leading to more traumatic deaths from injuries and completed suicides [1, 22, 24].
- Some features of personality disorders may have faded away over time [25]. Those with Cluster B personality disorders during their younger years "slowed down," improved their impulse control with accumulated life experience, or are simply less physically able—or have less opportunity—to engage in high-risk behaviors.
- Inadequate diagnostic criteria and diagnostic or rating instruments for borderline personality disorder and antisocial personality disorder in older patients [26, 27].

Question 13.6

A. What Is the Five-Factor Model of Personality?

The five-factor model is a hierarchical organization of personality traits that includes five broad domains of personality in the general population [28]. After decades of proposing various theoretical frameworks of reference, in the 1960s, "five factorists" came to a consensus on the following terms to describe the following five broad domains of personality: openness to experiences, conscientiousness,

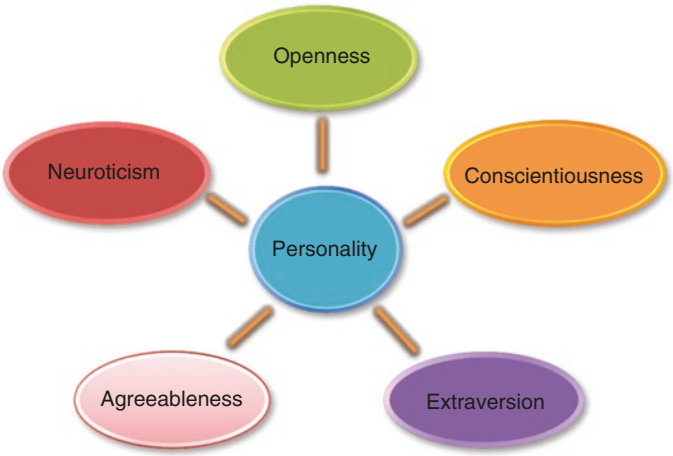


Fig. 13.1 The five-factor model of personality. Data extracted from [28]

extraversion, agreeableness, and neuroticism (see Fig. 13.1) [28]. Studies based on the five-factor model continue to be used to this day and have been validated cross-culturally and in adults of all ages [29].

The characteristics of the five domains of personality are presented below [28]:

- *Openness to experiences*—imaginative, esthetically reactive, creative, wide breadth of interests, original, curious, introspective, and liberal (open minded)
- *Conscientiousness*—efficient, reliable, deliberate, dutiful, responsible, organized, and able to delay gratification
- *Extraversion*—outgoing, energetic, facially expressive, affectionate, talkative, gregarious, fun-loving, and passionate
- *Agreeableness*—softhearted, trusting, generous, acquiescent, lenient, and good-natured
- *Neuroticism*—worry excessively, temperamental (fluctuating moods), self-consciousness, vulnerable, and self-pitying

B. What Personality Traits as Defined in the Five-Factor Model Are Associated with Increased, and Decreased, Risk of Developing Major Neurocognitive Disorders?

- *Neuroticism* has been associated with worse performance on various cognitive measures such as memory and global cognitive status [23, 29–31].
- *Higher conscientiousness and openness* have been associated with better memory performance and less decline over time [23].
- *Lower conscientiousness* has been associated with an increased risk of major neurocognitive disorder.

Question 13.7

What Are Some General Outcomes in Older Patients with Patients with Personality Disorders?

Older adults diagnosed with personality disorders tend to have [31]:

- A lower self-perceived quality of life and general health
- A decreased physical, social, and cognitive functioning
- Lower levels of self-esteem, life satisfaction, and sense of well-being
- Fewer social supports
- Increased risk of comorbid psychiatric disorders

Question 13.8

A 75-year-old Caucasian female ("Carol"), with no previous medical history, presents with a 1-week history of arthralgias, fatigue, and swelling on the left side of her head. Carol awakens one morning with decreased vision in her left eye. Assuming that she needs a new prescription for glasses, Carol's husband ("Ben") schedules a same-day appointment with Carol's optometrist. The optometrist diagnoses Carol with ischemic optic neuropathy, and she is sent to the emergency department (ED) for prompt evaluation by neuro-ophthalmology, neurology, and internal medicine. Full workup leads to a diagnosis of giant cell arteritis, or temporal arteritis. A temporal artery biopsy confirms the diagnosis.

Carol is admitted to the hospital and started on IV dexamethasone 25 mg per day (the equivalent of prednisone 100 mg per day). Three days later, you are called by the internal medicine resident: "We want to switch Carol from IV to high-dose oral prednisone, but she keeps spitting out the pills. She is claiming that we are trying to hurt her. She has hardly slept since admission, talks nonstop, and has been flirting with the attending. This morning, she slapped a young male nurse's rear end and winked at him! She is agitated and sleeping poorly."

A. What Are the Likely Diagnoses at This Time?

Acute onset mania at age 75 is *not* classic bipolar disorder. The first consideration is delirium, but a manic or psychotic episode from her rheumatologic disease and/or its treatment is equally, if not more, likely.

Case continued: You go to see her. Her husband, Ben, is sitting beside Carol, quietly holding her hand. As soon as you introduce yourself, Carol dramatically rolls her eyes, throws off Ben's hand, hops out of bed, and says loudly and tersely, "*Oh, great.* Now my so-called doctor is calling me *crazy*. Well, that kid-doctor is clueless."

Carol paces restlessly, complaining that as a daughter of the former Board of Directors of the hospital, she deserves to be treated with respect. Carol targets her anger at you but then suddenly turns her attention to a staff member who attempted to unobtrusively pick up Carol's empty lunch tray. Carol complains loudly and bitterly that the hospital is trying to poison her by feeding her "tasteless pig feed" and that she is "starving." Carol said she will not take the methylprednisolone pills and prefers to stay in the hospital for IV infusions, even if she has to stay in the hospital "forever."

You redirect Carol's attention back to you, after which she refuses to participate in completing the Montreal Cognitive Assessment (MoCA). "It is a waste of time for someone like me. I am a retired professor, after all." She refuses to answer routine interview questions. She cannot tell you any of her medications or why she is taking them.

Ben, whom you initially thought was Carol's son, tells you privately that Carol has never had any outpatient or inpatient psychiatric history. Carol drank alcohol heavily for all of her adult life until she achieved sobriety 15 years ago via Alcoholics Anonymous (AA), where Ben and Carol met.

You learn that Ben is 20 years younger than Carol, whom he says he "adores… Carol's the love of my life! She's the only family I have. I would be dead without her," Ben explains. Since being laid off from his job as a bus driver 6 months ago, he spends his days doting on Carol. Calling her "My Queen," Ben says he's "scared to death" of losing Carol and anxiously peppers you with questions about Carol's systemic medical and psychiatric diagnoses. He repeatedly tells you that you can call him at "all hours of the night…Really, I know everything about Carol!" and points to an overstuffed folder with copies of Carol's medical records.

B. What Is the Likely Explanation?

While rheumatologic illness itself can be associated with comorbid psychiatric illness, the likely explanation is psychotic/manic episode induced by high-dose corticosteroids [32–34]. Corticosteroids, especially at a daily dose exceeding 40 mg of prednisone or the equivalent (her dexamethasone dose is equivalent to 100 mg of prednisone/24 h), are at high risk to induce multiple psychiatric symptoms, which may or not be frank delirium per se.

C. What Do You Do Now?

Anterior ischemic optic neuropathy is a vision-threatening emergency. Currently, the recommended treatment for patients with giant cell arteritis with acute visual changes includes 3 days of high-dose IV methylprednisolone, followed by high-dose oral prednisolone for 4 weeks, and a tapering dose over the next 12–16 weeks [35]. Nonadherence to treatment risks permanent blindness. Carol said she prefers to stay in the hospital indefinitely, which is obviously not an option in this era of limited hospital lengths of stay.

The psychiatrist's role in this situation is to provide recommendations to the treatment team to stabilize the patient's mood as soon as possible to promote medication adherence to oral methylprednisolone and ultimately to expedite the patient's discharge from the acute, to an outpatient, setting. Adherence in this case is particularly crucial given the potentially dire consequence of nonadherence (i.e., blindness), as well as the extended period of time that Carol will need to take the medication.

D. What Are Your Medication Options?

Even though Carol meets criteria for an acute manic episode, lithium is not indicated. The potential medical risks associated with lithium (e.g., renal insufficiency, hyperparathyroidism, hypothyroidism, increased risk for delirium) exceed the potential benefits of lithium in medically unstable patients, especially when less risky medication options are available. Better options include an atypical antipsychotic or anticonvulsant (e.g., valproate given either orally or intravenously can be administered in the ICU or ward).

Case continued: Carol is started on a regimen of valproic acid intravenously and risperidone intramuscularly. Two days after starting valproic acid and risperidone, Carol's mood has improved so much that she has agreed to start taking all of her medications, including methylprednisolone, by mouth.

You go to see her, and as usual, Ben is sitting attentively by Carol's side. Carol is pleasant, coherent, and apologetic for her behavior toward you and other staff earlier in the week. Carol has been sleeping through the night. She effusively expresses gratitude for the "wonderful" care she has received. She reports good tolerance to oral doses of methylprednisolone, valproic acid, and risperidone.

E. The Internal Medicine Resident Informs You That Carol Will Probably Be Discharged Home Tomorrow. What Do You Recommend?

Carol will be on oral methylprednisolone for up 16 weeks. To ensure that Carol's mental status remains stable as she continues to take corticosteroids, you recommend that she continue taking both valproic acid at the current dose of 1500 mg/day (may switch to a longer-acting formulation for simpler dosing, such as extended-release divalproex sodium 1500 mg at bedtime) and to continue her current dose of risperidone, which is now 2 mg twice a day. It is possible that Carol will require gradually decreasing doses of the psychotropic medications as dose of methylprednisolone is tapered. You schedule an appointment to see Carol in clinic in 1 month and sign off on the case.

Case continued: The next morning, you get an urgent call from the nurse, who states that ever since you left, Carol has been sobbing uncontrollably, very irritable, and refusing to take all of her medications. You evaluate the patient, who reports that

she is "fine," and wonders what all the fuss is about. Ben is sitting by her side, holding Carol's hand. He angrily asks why Carol's doctors "want to kick Carol out of the hospital so quickly," stating, "It's obvious that she's not ready to be discharged! This is malpractice." The patient is sitting up in bed, smiling, calm, and coherent. Carol explains that she was just having a "bad night" last night and that nothing is wrong.

At your request, Ben reluctantly leaves the room so that you can speak with Carol privately. As Ben leaves the room, Carol and Ben blow each other kisses. Immediately after the door closes shut, Carol starts sobbing, hysterically saying that she is not ready to be discharged, and plans to kill herself by overdosing on all her medications if forced to go home to "that big fat slob. He drives me insane!" and states that she wants a divorce. She then says that she is going to sue the hospital because of how poorly they have treated her. Carol then turns to you, stating, "I thought I could trust you. But now, you're like everyone else in my life whom I've trusted. .. Just take your fancy, know-it-all degree and dump me like everyone else!"

Carol denies that Ben abuses her physically or sexually—"Oh my God, it makes me wanna throw up just thinking about having him touch me"—but that he "abuses" her by hoarding piles of junk in their home. She denied having a history of outpatient or inpatient psychiatric treatment. Carol confirms that she has been abstinent from alcohol for the past 15 years and that she and Ben indeed met in AA. When asked if she has ever attempted suicide, she said "Maybe" and refused to elaborate. She then stated that she has changed her mind and wants to be discharged right away.

F. What Do You Recommend?

You recommend involuntary inpatient psychiatric admission until further suicide risk assessment.

Case continued: Meanwhile, you speak to Ben, who expresses outrage and surprise that Carol needs to be admitted to a psychiatric unit. Ben tells you that Carol's mood has been "great" in the past few days and describes their relationship as "perfect." Ben argues that he is fully capable of caring for Carol at home, will keep her "safe" by hiding her medications, and begs you not to admit Carol to the psychiatric unit.

When you explain to him why she will be transferred to the psychiatric unit under an involuntary commitment, Ben is then resigned to the fact that Carol will be transferred. Expecting that he will be allowed to stay with Carol on the psychiatric unit, he tells you he will be up to the unit shortly. When you inform him that the psychiatric unit is a locked unit and that visitors are only allowed during set visiting hours, Ben becomes angry and walks away.

You catch a glimpse of Carol as she is wheeled off the medical floor. She is smiling and joking with the psychiatric technician who is escorting her to the psychiatric unit.

Carol is admitted involuntarily to the psychiatric unit, and you see her in the morning. Methylprednisolone, divalproex sodium, and risperidone are all resumed.

The inpatient psychiatric nurse reports that Carol's mood has appeared euthymic since admission, explaining, "She seems pretty happy here…a real social butterfly…smiling and talking to the staff and other patients." Carol has been taking her medications and enthusiastically participating in all groups and other unit activities.

The nurse seems annoyed when she explains that last night, Carol had her husband bring a suitcase full of belongings from home. In the middle of the night, Carol insisted that she have her room changed because unlike herself, her roommate was "crazy." The overnight staff observed Carol calling her husband multiple times to request things like her favorite lavender-scented shampoo, conditioner, and body lotion. According to the overnight staff, Carol "threw a fit" when informed that she would not be allowed to store a personal blow dryer and curling iron on the psychiatric unit.

When Ben visited Carol during visiting hours, the staff noted that the couple held hands, gazing into each other's eyes intently for 2 h. As Ben left, they blew each other kisses. The staff thought this was strange, since just before Ben came, she complained to one of the nurses about what a "total slob" her husband was.

G. What Psychiatric Diagnoses Are Now on Your Differential?

In addition to corticosteroid-induced psychosis and mania that is now under control with medications, you suspect a Cluster B personality disorder. Thus far, there has been no evidence of any antisocial personality disorder. However, even after a resolution of corticosteroid-induced manic symptoms, Carol exhibited an instability in her relationships with others, including her husband.

Borderline personality disorder is characterized by a pattern of unstable and intense interpersonal relationships that is characterized by alternating extremes of idealization and devaluation [6]. Carol exhibited this in her relationships with you and her internal medicine physicians. Carol has made multiple devaluing comments about her husband to staff, but when in his presence, her behavior is ingratiatingly sweet and affectionate (e.g., blowing kisses to him, gazing into his eyes). Borderline personality disorder is also characterized by recurrent suicidal threats and behaviors, which Carol exhibited when she thought she was going to be discharged home.

Moreover, there has been a constellation of several other comorbid personality traits observed in this case. Carol's sudden sobbing followed by euthymia demonstrates an exaggerated expression of emotion, with rapid shifts of emotional display which are consistent with histrionic personality traits. Ben appears to be completely enamored and approval-seeking of Carol, whom he refers to as "My Queen." Ben personally caters to Carol's histrionic needs, apparently dropping everything to bring Carol her favorite products to maintain her grooming and hygiene. Carol also appears to put an inordinate emphasis on her physical appearance, with Ben bringing a suitcase full of clothes to change into and whining when she is not allowed to use a curling iron on the unit.

When arriving in the inpatient unit, she behaves as if the staff members are solely present to meet her needs only, repeatedly requesting special favors, which is consistent with narcissistic personality traits. Carol's obvious self-absorption is evident to the psychiatry staff members, who have already expressed their annoyance to you and one another.

Case continued: You evaluate Carol. You noticed that she is wearing a casual but fashionable and well-coordinated outfit and is wearing bright pink lipstick that matches the pink pattern on her blouse. She immediately profusely apologizes to you for her appearance, saying "I don't usually look this bad. I'm so embarrassed."

Carol then apologizes to you for "those nasty things" she said about you and the hospital yesterday, explaining "I just felt like you were kicking me out of here before I was ready!" You notice that she was more apologetic to you about her appearance than her behavior toward you yesterday.

Choked with sobs, Carol says that she felt like everyone was "abandoning" her and that she needs her doctors to understand that unlike other patients, she needs "A little more TLC" before she is "thrown to the wolves."

When you ask what she meant by wolves, Carol stops sobbing and disdainfully discusses how terrible her life is at home. She reiterates that Ben is a "slob," explaining that he is a "hoarder" who keeps things like old receipts for pet food and other unimportant products for years. Describing herself as "OCD," Carol states that she meticulously cares for all of her belongings, which include antique mahogany furniture. She denied any symptoms of obsessive-compulsive disorder other than preferring that her belongings are "neat and tidy." When asked how she coped with her and her husband's differences for so long, Carol explains that 6 months ago, Ben lost his job, so now, he mopes around all day—watching TV, eating junk food, and constantly asking what she needs.

Carol denies having any suicidal thoughts at the moment, but "You never know."

H. What Do You Do Next?

Carol's admission status is changed to voluntary. Although convinced that she is at very low risk of imminent self-harm, you recommend at least one more day of hospitalization to emotionally prepare her for discharge while communicating that she will not be admitted indefinitely.

Carol described herself as "OCD." She does not meet criteria for obsessive-compulsive disorder; however, as noted in Question 13.3, the prevalence of obsessive-compulsive personality disorder does appear to increase with aging. You highly recommend individual psychotherapy once she is discharged home, and suggest she consider group psychotherapy, specifically dialectical behavioral therapy (DBT) which has been shown to be effective in treating borderline personality disorder and other personality disorders [36]. You also recommend couples counseling.

Divalproex sodium and risperidone are continued, and you confirm that she is still willing and able to continue taking methylprednisolone as prescribed. She is scheduled to see you in clinic in 4 weeks.

Question 13.9

A primary care physician refers a 72-year-old Latina woman ("Bella") to you for "anxiety." A review of her outpatient medical records reveals that Bella has diet-controlled diabetes mellitus and recurrent urinary tract infections, but no other chronic medical illnesses. Her medication list includes a prescription for citalopram written 3 years ago, but it has not been renewed.

You notice dozens of phone calls to her primary care physician's office, averaging 1–2 calls per week in the past year. The calls are related to questions or problems with medications and concerns about having a persistent "low-grade fever," fatigue, and other nonspecific symptoms. She has been seen by multiple specialists in the past several years, including a neurologist after Bella reported feeling numbness in her feet and hands bilaterally, weakness in her upper extremities, and feeling like she is going to faint all of the time.

The neurologist did not find any neurologic deficits on exam, and Bella's nonspecific symptoms did not fit any specific pattern of a known neurologic problem. The neurologist noted that the patient appeared tearful at times and learned that she was still grieving the deaths of all three of her brothers in the past year. Bella was referred to the outpatient psychiatry clinic.

A. Just by Your Review of the Medical Records, What Are Possible Psychiatric Diagnoses on Your List of Differential Diagnoses?

The psychiatric differential diagnoses include major depressive disorder, generalized anxiety disorder, somatic symptom disorder, illness anxiety disorder, conversion disorder, and factitious disorder. You also consider the possibility of personality disorders, which in general are associated with increased utilization of healthcare resources [37, 38].

Case continued: You evaluate Bella, whose husband brought her to the appointment. She says that the only reason she came to the appointment was because her husband, as well as her three children—who happen to be in the healthcare field—have been urging her to see a psychiatrist. Initially tentative and seemingly reserved, Bella readily tells you that the recent deaths of her brothers have devastated her. Bella grew up in Venezuela, the youngest, and only daughter, of a wealthy businessman and his wife.

Bella described her early childhood as idyllic and stable. She said she lived in a "mansion" that her classmates envied, with multiple servants, cooks, and a chauffeur. Admittedly pampered by her family, she had anything and everything

she wanted. However, all that changed after her father was imprisoned for embezzlement. Her family lost all their wealth and lived with relatives in much smaller homes. Describing these family members as "low class," Bella explained that her cousins never learned how to speak proper Spanish and were not raised as she was. Bella eventually married a physician in Venezuela, eventually settling in the United States, where she was a homemaker. Bella said that ever since her brothers died, she has felt "lost" and alone. Bella has made many friends over the years, but has never felt close to anybody other than her brothers.

She described her husband as stoic and reserved, hardworking, and loyal. Bella said that she worries constantly that her husband will die before she does, since he has always taken care of "everything," including all important matters such as health and life insurance, paying bills, and real estate. When discussing her life, she frequently referred to "my husband said…" even when asked specifically about her own opinions. She complained that he and her three children "never listen to me." She gets annoyed when her kids tell her things like, "Mom, I am your daughter, not your doctor," and have recently started asking her to stop calling them all the time about her many physical complaints. Bella got into a big argument recently after one of her daughters, whose personality is similar to that of Bella's husband, told her to "Get a spine, Mom!" Bella discussed in detail how she went out to dinner with her husband. Bella's food was cold, and she wanted to tell the waiter about it, and asked her husband what to do. Her husband told her not to complain, stating, "You complain about everything!" Therefore, Bella begrudgingly ate her cold dinner.

Further evaluation reveals that Bella meets criteria for major depressive disorder, moderate intensity, and generalized anxiety disorder.

B. What Personality Disorder Would You Consider in the Differential Diagnosis Now?

There have been several comorbid personality traits noted in this case. The differential diagnosis of personality disorders includes the following:

1. Narcissistic personality disorder—Bella makes it a point to emphasize that she is from a privileged, upper-class family, and she exhibited a hint of a grandiose sense of self-importance. Spoiled by her brothers while growing up, she has a sense of entitlement to special treatment by others.
2. Dependent personality disorder—thus far, dependent personality disorder seems to most fit Bella's personality. Bella seems to have difficulty making her own decisions about things, even for something as seemingly simple as whether or not to complaint about the food served at the restaurant. During the interview, she frequently refers to her husband, whose opinions are so prominent that it is difficult to decipher what exactly Bella thinks and believes sometimes. Arguments with her adult children seem to be around her dependency on others (including

them). She also needs others to assume responsibility for virtually all aspect of her life and is unrealistically preoccupied with fears of having to take care of herself 1 day.

Question 13.10

You see "Warren," a 71-year-old widowed male who is referred to you by his primary care physician for depression. The primary care physician points out in his referral that after several years of refusing to see a psychiatrist, Warren finally agreed to do so recently. Warren has never been on any psychiatric medications, nor has he ever had a substance use disorder. He has a history of hypertension (treated with a thiazide diuretic), chronic tension headaches, and mild hypercholesterolemia.

Warren arrives 60 min early for his appointment with you. Before starting the appointment, you slowly escort a frail older woman to the front desk, where Warren is standing, impatiently tapping his toes, and looking at his watch.

Upon introducing yourself to him in the lobby, you apologize to him for the delay and explain that you will return to retrieve him for his appointment in a "couple of minutes." Quickly glancing at your name tag, he calls you by your first name and states, "Well, I certainly hope so."

Once in the office, you again apologize for the delay, reassuring him that you will make up the 5 min that you were necessarily delayed. He states tersely, "I will be counting on that because we have a lot to discuss," and takes out a color-coded binder from which he takes out three different sheets of paper, one of which states "Problems to Discuss with the Psychiatrist."

A. What Do You Do Next?

Warren is clearly irritated by the delay in starting the appointment. Warren has obviously prepared for the appointment and seems eager to share his concerns with you. For the sake of developing a good patient-physician rapport for this patient who has avoided seeing a psychiatrist for years, you ask him what his list of problems are.

Case continued: Referring to a numbered list of problems, Warren states, "Number 1—Everyone is against me at the condo association. Number 2—No one listens to me. Number 3—They are discriminating against me." The list includes several other items, but to get to the crux of the matter, you ask him to clarify who is angry with him and proceed from there to clarify what is distressing Warren.

Warren explains that he has been the president of his condominium's Homeowners Association ("Association") for the past 5 years. He said he was doing "great," explaining that as a retired certified public accountant (CPA), he singlehandedly helped the Association get out of debt while reducing Association fees. Warren was incredulous when he was recently asked to step down as president because he is "rigid," "not a team player," and "hard to work with." He states, "I worked for the

same company for 30 years as a CPA, and no one had a problem with my work habits there!"

Warren speculates that some of the homeowners got together to oust him because they are military veterans, and he is not. The Association was recently lambasted by various veterans organizations throughout the country after a homeowner, a Vietnam combat veteran and new homeowner, complained that he had just received a letter from the Association, demanding that an American flag he had displayed on his balcony be flown only during specific holidays, as specified in the Homeowners Association Agreement.

"It is ridiculous!… I mean, rules are rules. If you cannot follow the rules, then move somewhere else!" Warren states and becomes briefly tearful. He explains that he feels "lost" and does not know what to do with himself during the day. Most of his friendships are with those who serve on various Association committees with him. He said he feels "humiliated," has quit all of his Association committees, and stays at home listening to blues music all day. Warren said that he cannot stop thinking about what went wrong, ruminating constantly about the events that led to his ouster.

B. What Is in Your Differential Diagnosis?

The differential diagnosis includes major depressive disorder. The patient does appear anxious, so be sure to rule out generalized anxiety disorder and obsessive-compulsive disorder; obsessive-compulsive personality disorder and narcissistic personality disorder are also considerations. Be sure to confirm that Warren does not have a substance use disorder.

Case continued: Warren endorsed a several-week history of anhedonia, unusual fatigue, difficulty falling asleep, poor appetite, and increased irritability. He denied suicidal or homicidal ideation and all psychotic symptoms.

He admits to "obsessing" about what happened with the Association, but tends not to worry a whole lot about other aspects of his life. He attributes his late wife, whom he described as "happy-go-lucky," disorganized, spontaneous, and fun-loving, as helping him to be less "uptight."

Warren chuckled, saying that 20 years of marriage helped "cure" him somewhat of his "anal retentive" ways, but that since her sudden death from a brain aneurysm 6 years ago, he has reverted to becoming his "old, stubborn self." Warren then weeps silently, saying barely audibly, "I miss her so much. I wish she were still here… Lately, I have been thinking a lot about my wife and how silly she would think all this Association stuff is." He says that he was initially disinterested in taking on the "thankless" task of being president of the Association but agreed to do it to keep himself occupied to distract himself from the grief he felt.

He denies ever having a history of recurrent, distressing thoughts, urges, or images. He said that he "loved" his job as a CPA, especially the 4 months before taxes are due, when he spent all day scrutinizing his firm's tax-related data. He also denied repetitive behaviors such as handwashing or checking or feeling compelled to count or repeat things to himself.

Warren apologizes for being rude to you at the beginning of the visit. He states that he has done a lot of soul-searching in the past few weeks, concluded he needs help, and surprised himself by calling his primary care physician to request a referral to you. He confirms that he has never had a problem with any substance use.

On exam, he is neatly dressed in clean and pressed khaki pants and button-down shirt. His speech is of normal rate and rhythm, with detailed educated vocabulary. His mood is "moderately depressed," and his affect is restricted and mood-congruent. His thought process is logical and linear.

C. What Is Now on Your Differential Diagnosis?

He meets criteria for major depressive disorder, moderate severity, whereas generalized anxiety disorder has been ruled out. You rule out narcissistic personality disorder, as well. His initial presentation hinted at entitlement and grandiosity (e.g., calling you by your first name instead of addressing you as "Dr. __," irritability at your tardiness, and an apparent lack of insight that you were late because you were escorting a frail older woman). However, as the visit progresses, he reports that he had a long, stable marriage until his wife's death and that he had the insight and mental and emotional flexibility to realize that his personality could use some adjustment—all of which argue against narcissistic personality disorder. He also recognizes that his behavior toward you may have been off-putting. You still need to assess for obsessive-compulsive disorder and obsessive-compulsive personality disorder.

D. How Do You Distinguish Between Obsessive-Compulsive Disorder and Obsessive-Compulsive Personality Disorder?

Obsessive-compulsive disorder is characterized by the presence of obsessions, compulsions, or both [6]. According to DSM-5, obsessions refer to "1) recurrent and persistent thoughts, urges, or images that are experienced…as intrusive and unwanted… and causes marked anxiety or distress…and 2) the individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action." The obsessions are not pleasurable or experienced as voluntary.

Compulsions are defined by "1) repetitive behaviors (e.g., handwashing, ordering, checking), or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly…2) the behaviors or mental acts are aimed at preventing or reducing anxiety or distress…or some dreaded event or situation…these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive." The obsessive and/or compulsive behaviors are also time-consuming or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning [6].

Obsessive-compulsive personality disorder is characterized by a pervasive pattern of preoccupation with orderliness, perfectionism, and mental and interpersonal

Table 13.3 Key differences between obsessive-compulsive disorder and obsessive-compulsive personality disorder [6]

Characteristics	Obsessive-compulsive disorder	Obsessive-compulsive personality disorder
Onset	Any time	By early adulthood
Clinical presentation	Thoughts, urges, images, and behaviors typically not relevant to real-life concerns	Thoughts/behaviors typically relevant to real-life concerns and fixated on everyday rules, functions, and order
Functional status	Dysfunction in multiple domains (work, social, and/or family life)	Dysfunction typically in interpersonal relationships (e.g., relationships with coworkers and employers can be strained, but work functioning can be efficient)
Insight	Believe that their thoughts/urges/images/behaviors are irrational (egodystonic) Believe they require treatment	Believe that their thoughts/behaviors are rational (egosyntonic); believe their way is the "right and best way" and feel comfortable with self-imposed systems of rules. Do not believe they require treatment; threat of losing a job or a relationship due to interpersonal conflict may be the motivator for treatment

control, at the expense of flexibility, openness, and efficiency; this pattern begins by early adulthood and is present in a variety of contexts as indicated by four or more of the following (for full diagnostic criteria, the reader is referred to the DSM-5) [6]:

1. Excessive preoccupation with details, rules, lists, order, organization, or schedules
2. Perfectionism interfering with task completion
3. Excessive devotion to work and productivity to the exclusion of leisure activities and friendships
4. Overconscientiousness, scrupulousness, and inflexibility about matters of morality, ethics, or values
5. Inability to get rid of items that no longer have value
6. Difficulty to delegate tasks or to work with others unless they submit to exactly his or her way of doing things
7. Miserly spending style toward both self and others
8. Rigidity and stubbornness

Table 13.3 shows some common differences between obsessive-compulsive disorder and obsessive-compulsive personality disorder [6].

E. Based on Warren's Presentation Above, Do You Suspect Obsessive-Compulsive Disorder and Obsessive-Compulsive Personality Disorder?

You rule out obsessive-compulsive disorder, since Warren denied ever having obsessions and compulsions. However, he meets criteria for obsessive-compulsive personality disorder, many of the symptoms of which served him well as a CPA. Warren

mentioned that he worked for the same firm for 30 years as a CPA and that no one ever complained about being a difficult coworker. It is possible that his colleagues had at least traits of obsessive-compulsive personality disorder, as well, and had similar priorities and attention to detail, which in the CPA world would be rewarded.

Warren's rigidity and lack of empathy for the new homeowner (a combat veteran, no less) who wanted to display an American flag year-around indicate that his priority was for following the "letter of the law" at the expense of the "spirit of the law," which was probably to prevent unsightly décor.

Warren also pointed at being frugal, bragging about decreasing Association fees, and to be reluctant to delegate tasks. Although Warren apparently meets criteria for obsessive-compulsive personality disorder, it is premature to diagnose Warren with this personality disorder now, pending treatment of his depressive disorder.

Case continued: You tell Warren that you suspect that there is a relationship between the loss he is feeling now and the grief at the death of his wife, whose complementary personality kept his obsessive-compulsive tendencies in check throughout their marriage. He acknowledges that if his wife were still alive, she most certainly would have "balanced" him out, preventing Warren from becoming overly rigid in his duties as Association president.

You hypothesize that Warren may have subconsciously reverted to his obsessive-compulsive ways as an emotional defense mechanism to cope with his grief. Warren tells you that this all makes sense to him. He tells you that he feels relief for having talked to you and that, until now, he was confused by his strong reaction to being let go as Association president, especially since the long hours of unpaid work were starting to annoy him, and he had been contemplating quitting the job anyway.

F. What Treatment Do You Recommend?

Warren's response to your psychotherapeutic intervention—associating his recent unexpected ouster as Association president and sudden loss of his wife several years previously—seemed to provide Warren with prompt relief of some of his dysphoria. He demonstrated good insight into his obsessive-compulsive tendencies and had the ability to identify and describe his thoughts and emotions. As such, he is a good candidate for short-term psychotherapy to process some of his unresolved grief issues. Since he has recently lost his social group, which was comprised of Association members, he may benefit from grief-focused group therapy.

Medication treatment with an antidepressant may be indicated if Warren's mood does not improve or worsens after 4–6 weeks of psychotherapy. In the meantime, a short-term, as-needed, medication for insomnia could be of immediate benefit.

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Topic 14: Aging with Neurodevelopmental Disorders: Intellectual Disability and Autism Spectrum Disorder

Question 14.1

Intellectual disability (or intellectual developmental disorder, formerly mental retardation) describes conditions of cognitive and physical disability, with onset in the developmental period (prior to age 18 years) and impairments in adaptive functioning.

Do Older Adults with Intellectual Disability Experience the Same Age-Related Physical Changes as Their Peers in the General Population?

With advancing age, adults with intellectual disability in general can experience the same age-related physiological changes and physical and neurocognitive disorders as the general population. Some continue to live with aging family members who face difficulties with increasing support needs for their dependents [1]. The emergence of major or mild neurocognitive disorder may be masked by an adult's baseline cognitive status and language deficits. Cardiovascular disease is at least as common in the adults with intellectual disability as in the general population [1].

Question 14.2

Ms. A is in her mid-late 50s and has Down syndrome. Two years ago, she transitioned to a retirement home after the loss of her parents. Institutional records noted "grief at the death of her parents," and she was treated for depression with the tricyclic antidepressant amitriptyline 100 mg daily. On admission to the facility, hypothyroidism was discovered and treated. Over the past 12 months, she has displayed

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_14

changes in mental status and functioning. She dropped out of favorite activities. She has had episodes of disorientation. These episodes lasted several weeks and subsided without intervention. There were no apparent precipitating factors for her functional decline. Routine laboratory investigations (complete blood count, electrolytes, glucose, liver/renal/thyroid function tests, and urinalysis) were unremarkable. Her only identified recurrent medical problem was constipation. However, there has continued to be a decline in her overall functioning including getting dressed and showering, along with decreased social engagement. She became disoriented to time, repetitive, and misplaced objects while blaming others for stealing. More recently, she has been agitated and aggressive in the context that she claims that someone was taking her things. She was assessed by her primary care physician and was given haloperidol 5 mg daily. However, parkinsonian extrapyramidal side effects of haloperidol developed, and benztropine 2 mg bid was given. This did not help with her agitation. She again became constipated. An increased thyroid-stimulating hormone was noted on subsequent laboratory investigations, and her thyroid replacement hormone was increased. Due to her increasingly complex presentation, she was referred to a geriatric psychiatric service as well as an intellectual disability specialty service.

A. What Is the Association Between Down Syndrome and Intellectual Disability? What Are the Key Diagnostic Criteria of Intellectual Disability (Intellectual Developmental Disorder)?

The two most common identifiable genetic causes of significant intellectual disability are Down syndrome and fragile X syndrome (which are discussed later at Question 14.13). Down syndrome is also known as trisomy 21. Down syndrome is due to the presence of all or part of a third copy of chromosome 21. In a small number of cases, mosaicism occurs, in which some but not all of the cells are trisomy for chromosome 21. The key diagnostic criteria for intellectual disability (or intellectual developmental disorder) are illustrated in Table 14.1 [2].

Table 14.1 Intellectual disability (intellectual developmental disorder): highlights of the DSM-5 diagnostic criteria [2]

DSM-5 criteria	Comments
Three criteria must be met – Deficits in intellectual functions confirmed by clinical assessment and intelligence testing – Deficits in adaptive functioning that result in failure to meet developmental and sociocultural standards for personal independence and social responsibility – Onset of intellectual and adaptive deficits during the developmental period	The equivalent term for *intellectual disability* in ICD-10 is *intellectual developmental disorders*. Both terms are used in the title to clarify relationships with other classification systems
Specifiers of current severity: Mild/moderate/severe/profound	

B. What Is the Management in This Case?

In this case, constipation is a significant problem and often secondary to inactivity, hypothyroidism, and anticholinergic medications (e.g., amitriptyline, benztropine). Because adults with intellectual disability are often poor historians, bowel impaction should be suspected as it is not only a source of discomfort but also a leading cause of morbidity. Where there is complexity, clinicians should consider interdisciplinary involvement. Services specializing in the interdisciplinary assessment and treatment of those with intellectual disability may be accessible. Geriatric teams are increasingly called upon to assess adults with intellectual disability at earlier ages than the traditional cutoff geriatric age of 65 years. Although there is limited research about aging with intellectual disability, systematic assessment of biopsychosocial variables affecting adults' well-being is foundational and best practice.

Question 14.3

What Are the General Physical Features in Adults with Down Syndrome?

The phenotype in adults with trisomy 21, or Down syndrome, is characterized by a number of distinguishing features as illustrated in Table 14.2 [3]. Studies have shown that adults with Down syndrome may have an abnormally premature aging [4]. This may constitute one of the risk factors predisposing to Alzheimer disease

Table 14.2 General physical features in adults with trisomy 21 (Down syndrome) [3]

Physical features	Craniofacial features	Central nervous system features	Neuropsychiatric features
• Shortened extremities • Short, broad hands, with short fifth finger, hypoplasia of the middle phalanx, and clinodactyly • Single palmar crease • Lax ligaments • Deep groove between the first and second toes • Diastasis recti • Dry skin • Premature aging • Congenital heart defects (septal defects, patent ductus arteriosus, tetralogy of Fallot, mitral valve disease) • Thyroid disease • Diabetes mellitus	• Flat facies • Flat nasal bridge • Hypertelorism • Upward slanting eyes with epicanthal folds at the inner corners, Brushfield spots • Small nose • Small mouth • Protruding tongue • Small and dysplastic ears • Generous nuchal skin • Brachycephalic head	• Moderate to severe intellectual disability (mean IQ 50) • Muscle hypotonia (often improves with age) • Sleep apnea (with hypoxemia/hypercarbia) • Seizure disorders (5–10%); tonic-clonic most common in older adults • Hearing loss	• Psychiatric comorbidity (18–38%) • Depressive disorder • Phobias • Obsessive-compulsive disorder • Psychotic disorder • Neurocognitive disorder, predominantly due to Alzheimer disease

with early deposition of amyloid beta protein and neurofibrillary tangles in the cerebral cortex and oxidative injury causing neurodegeneration in adults with Down syndrome [3]. Notably, trisomy 21 mosaicism can present with minimal or absent manifestations of Down syndrome and may be underdiagnosed as a cause of early-onset Alzheimer disease [5].

Question 14.4

Define the Risk of Neurocognitive Disorder in Adults with Down Syndrome

Down syndrome (or trisomy 21) is the most common single chromosomal cause of intellectual disability. Adults with Down syndrome are at particular increased risk for more rapid decline in cognitive and adaptive functioning than the general population, with resulting major neurocognitive disorder due to Alzheimer disease by middle age [1, 6]. The increased risk of neurocognitive disorder due to Alzheimer disease in those with Down syndrome is in part explained by the trisomy 21 (the extra 21st chromosome) resulting in overexpression of the amyloid precursor protein gene [7]. The rate of cognitive decline in Down syndrome appears to increase with age [8]. Alzheimer-related neuropathological findings (amyloid plaques and neurofibrillary tangles) are evident by the third decade, although expression varies from no clinical manifestation to features of Alzheimer disease appearing in the fourth and fifth decades [6]. It is important to know that the incidence of age-related cognitive impairment is higher in adults with Down syndrome than in the general population [9].

Questions 14.5

What Is the Clinical Presentation of Major Neurocognitive Disorder Due to Alzheimer Disease in Adults with Down Syndrome?

Major neurocognitive disorder in adults with Down syndrome presents a major diagnostic and management challenge because of the combination of learning disabilities, progressive cognitive and functional decline, and associated neuropsychiatric and behavioral symptoms [9]. The median age of onset for major neurocognitive disorder in Down syndrome across all reported studies is below age 60 [9]. It is important to differentiate age-related cognitive decline from early major neurocognitive disorder in adults with Down syndrome. Evidence suggests that the acquisition of cognitive deficits tends to mimic those seen in typical Alzheimer disease. Decline in memory, learning, and orientation and increased dependence on others are among the first signs. Studies suggest that the initial presentation may show more frontal lobe symptoms (i.e., changes in behavior and personality), followed by other global cognitive deficits typical of Alzheimer disease [7]. Alzheimer disease

Table 14.3 Common symptoms of major neurocognitive disorder due to Alzheimer disease in adults with Down syndrome [7]

Neuropsychiatric symptoms	Behavioral symptoms	Neurological symptoms
Cognition Forgetfulness Loss of previously learned skills Confusion *Affect* Depressed mood Anhedonia Disturbed sleep Decreased concentration Anergia Anxiety and fearfulness Irritability *Perception* Hallucinations in any modality	Personality change Increased dependence Social isolation Increased hyperactivity or restlessness Increased uncooperativeness Aggression	Dysphasia/aphasia Agnosia Apraxia Gait disturbance Myoclonus Seizures Urinary incontinence Dystonias Loss of mobility

with premorbid Down syndrome may present with a greater prevalence of low mood, disturbed sleep, hallucinations in any modality, especially auditory, increased motor hyperactivity/restlessness, and increased uncooperativeness [7]. Although this remains unclear, delusions and hallucinations appear to be a less prominent feature in combined intellectual disability and major neurocognitive disorder versus in major neurocognitive disorder alone. Short-term memory, receptive and expressive language, and nonverbal reasoning can be preserved, but there are known to be mild declines in verbal and long-term memory for those older than 50 years, and the ability to form long-term memories and visuospatial construction may become mildly impaired. Table 14.3 summarizes the clinical symptoms of major neurocognitive disorder due to Alzheimer disease in adults with Down syndrome [7].

Question 14.6

What Is the Differential Diagnosis of Major Neurocognitive Disorder in Adults with Down Syndrome?

For the differential diagnosis, it is important to conduct a thorough physical examination, with particular focus on neurological evaluation. In these adults, apraxia may present as an inability to dress or eat without assistance; agnosia may present as an inappropriate use of objects and spatial disorientation that may be evident from difficulty to locate familiar places in their environment. One of the most important diagnoses to rule out is delirium. Other differential diagnoses include psychiatric disorders (e.g., anxiety and depressive disorders), brain infection, thyroid disease, vitamin deficiencies (e.g., B_{12}, D, folate), metabolic disease, brain tumor, cerebrovascular disease, and other non-Alzheimer-related neurocognitive

disorders. Box 14.1 summarizes the differential diagnosis of neurocognitive disorder in adults with Down syndrome [7].

Box 14.1 Differential Diagnosis of Major Neurocognitive Disorder in Adults with Down Syndrome [7]

Depressive disorder
Anxiety disorder
Delirium
Vascular neurocognitive disorder
Neurocognitive disorder with Lewy bodies
Hypothyroidism
Brain tumor
Brain infection
Vitamin deficiencies (e.g., B_{12}, D, folate)
Sleep apnea
Sensory impairment
Medication side effects (e.g., anticholinergics)
Environmental changes
Abuse

Question 14.7

What Are the Clinical Investigations for the Workup of Neurocognitive Disorder in Adults with Down Syndrome?

There are no specific laboratory investigations to diagnose major neurocognitive disorder during life. However, laboratory investigations are helpful to rule out other factors that may be contributing to the cognitive impairment, depending on the individual patient's medical comorbidities (see Box 14.2) [7]. Declines in cognitive and/or adaptive function in adults with Down syndrome may be presumptively attributed to neurocognitive disorder (specifically due to Alzheimer disease) when other disorders contributing to the presentation are excluded (e.g., hypothyroidism, B_{12} deficiency, malnutrition, infections, sensory impairment, depressive disorders, medication side effects, sleep apnea) [10]. Neuroimaging (structural and functional) is used in clinical practice to rule out other causes of cognitive impairment, such as vascular disease or brain tumor, and to identify characteristic changes that suggest Alzheimer disease (e.g., hippocampal atrophy) or another cause of major neurocognitive disorder. Computed tomography (CT) shows cerebral atrophy with reduction in the medial temporal lobe volume in adults with Down syndrome and major neurocognitive disorder [11]. Magnetic resonance imaging (MRI) also shows a pattern of reduced hippocampal volume in those with Alzheimer disease and Down syndrome [9, 12]. Notably, CT scan may be better tolerated than MRI by adults with intellectual disabilities, because of the claustrophobia-provoking nature of MRI procedure. In positron emission tomography (PET) studies of adults with Down syndrome,

changes in glucose metabolism and amyloid burden have been identified across a large age range. Results from Pittsburgh compound B PET imaging show that the earliest site of beta-amyloid accumulation in adults with Down syndrome, as in those with early-onset Alzheimer disease, might be the corpus striatum [13]. Compared with patients with late-onset Alzheimer disease, adults with Down syndrome and major neurocognitive disorder have an initial presentation of frontal predominance of amyloid pathology on PET imaging, which is consistent with clinical predominance of frontal lobe symptoms [14]. As in the general population, a high proportion of adults with Down syndrome are expected to have amyloid deposition at age 50 but without clinically defined major neurocognitive disorder [13]. Blood and cerebrospinal fluid biomarkers have been studied, but blood-based amyloid biomarkers are more difficult to interpret in the context of the disease. Cerebrospinal fluid biomarkers include elevated levels of tau and decreased levels of beta-amyloid. However, lumbar puncture is a challenging procedure in adults with intellectual difficulties. To date, these biomarker tests remain largely experimental, and more work is needed to define how these results can be routinely applied to patients in the clinical setting.

Box 14.2 Clinical Investigations for Neurocognitive Disorder in Down syndrome [7]

Complete blood count
Electrolytes
Urea/creatinine
Liver-associated enzymes
Thyroid function
Blood glucose
Vitamin B_{12}, vitamin D, folate
Erythrocyte sedimentation rate and/or C-reactive protein
Drug serum levels (e.g., digoxin, anticonvulsants)
Urinalysis
Electrocardiogram
Chest X-ray
Electroencephalogram
Vision and hearing tests
Neuroimaging (e.g., CT, MRI, PET)
Cerebrospinal fluid and blood biomarkers

Question 14.8

What Is the Prognosis of Major Neurocognitive Disorder in Adults with Down Syndrome?

Major neurocognitive disorder is usually a progressive illness, and, eventually, in the final stages, the patient may require palliative care. Death may occur from complications of the illness such as respiratory tract infection and thromboembolism [7]. Presently, the aim of treatment involves slowing of and adaptation to decline,

management of distress, and symptomatic treatment rather than attempts to cure or reverse the condition.

Question 14.9

What Are the Management Strategies of Major Neurocognitive Disorder in Adults with Down Syndrome?

Baseline assessment of cognitive and functioning level should be established for future reference. It is essential to take into account management of physical and psychosocial factors. Reversible causes of cognitive impairment must be identified and corrected, including delirium and hypothyroidism. Notably, adults with intellectual disabilities are particularly prone to medication side effects. In adults with intellectual disabilities and major neurocognitive disorder, it is essential to avoid the prescription of anticholinergic medications because of their increased risk of exacerbations in confusional states. Neuropsychiatric symptoms of major neurocognitive disorder, although preferably managed by non-pharmacological strategies, can be treated as recommended for the general adult population [7]. Clinicians should always aim to use drugs with the minimum side effects, as adults with intellectual disabilities may have multiple comorbidities with potential for drug interactions, as well as they already have difficulties to report adverse effects. Antidepressants for treating depression should include a selective serotonin reuptake inhibitor while avoiding tricyclics due to their anticholinergic activity. Carbamazepine and benzodiazepines must be used judiciously in agitation and aggression, due to potential risks of tolerance, oversedation, hyponatremia, cardiac toxicity, and falls. There have been a number of preliminary clinical trials related to cognition in adults with Down syndrome, including lithium carbonate (EudraCT 2008-008342-20), which is an 8-week randomized, single-blind, placebo-controlled phase 2 trial (n = 34, aged 18 years and older) [15]. Antipsychotics given for psychotic symptoms that are distressing to the patient and/or others should include atypical (second and third generation) agents, owing to their better side-effect profile. Evidence shows cholinergic deficits in older adults with Down syndrome. Among cholinesterase inhibitors, donepezil has the strongest evidence base; the results of a systematic review showed that it is reasonably well tolerated but has inconsistent benefits on any measures of cognition or function in adults with Down syndrome [16]. Few studies have been completed with the other cholinesterase inhibitors, galantamine and rivastigmine. The UK National Institute for Health and Care Excellence recommends treatment with cholinesterase inhibitors (donepezil, galantamine, and rivastigmine) and the NMDA receptor antagonist (memantine) for adults with major neurocognitive disorder due to Alzheimer disease, and their use is also approved in the context of this major neurocognitive disorder in adults with learning disabilities [9]. The US guidelines for treatment of adults with intellectual disabilities, however, recommend decisions based on individual patient assessments. The clinical evidence regarding use of memantine is less promising. The MEADOWS study in 173 adults

older than 40 years (mean 51 years) with Down syndrome with or without major neurocognitive disorder confirmed tolerability of memantine but reported no significant advantages over placebo in preventing cognitive impairment [17]. Therefore, effective therapies for patients with Alzheimer disease will not necessarily translate to also being beneficial in older adults with Down syndrome.

Question 14.10

Psychosocial interventions are an essential part of the management of major neurocognitive disorders in general, regardless of etiology.

A. What Are the Psychosocial Interventions in Adults with Major Neurocognitive Disorder and Down Syndrome?

Psychosocial interventions are an important part of the treatment of major neurocognitive disorder in adults with Down syndrome. Patient safety and stability of the environment are crucial elements. stability of the environment helps to reduce confusion, and therefore caregivers and location should not readily be changed. It is recommended that patients be maintained in their habitual living environment for as long as is safely possible. If they have to be relocated, they are more likely to adapt to their new environments if this is implemented earlier, while they retain more cognitive function. Day care facilities can be considered, whereas inpatient admission should be a last resort, because an environmental change may accelerate functional decline.

Reducing sensory impairment in adults with major neurocognitive disorder maximizes their ability to communicate optimally with their caregivers and orient themselves in their environment. Encouraging optimal participation in activities that match their cognitive and functional abilities can be helpful. Minimizing other changes in their lives is essential. Regular medical review can be helpful for monitoring physical and mental state, including thyroid and cardiac status and deteriorating sensory function, so that abnormalities can be addressed in a timely fashion. Support should be offered to caregivers to reduce burnout risk. It is essential to ensure good communication with caregivers at every stage of the illness. Information regarding contact with the Alzheimer's Society or the Down's Syndrome Association in their respective areas is vital for receiving education about the illness progression and available supports. Multidisciplinary team members including nursing staff, physiotherapists, and occupational therapists can assist in rehabilitation and preservation of the patient's skills.

With age, changes in personality and cognition in adults with Down syndrome and intellectual disability require special attention. Clinicians need to be aware that these adults can be misunderstood because they either cannot express themselves or identify their symptoms due to poor expressive skills or a lack of insight [18]. Behavioral disturbances are common in this population across the life span, and thus the tendency to overuse antipsychotics for behavior disturbance in Down

syndrome and intellectual disability has prompted a need for interdisciplinary interventions as well as research on antipsychotic long-term use and adverse events [19].

B. Several Tools Have Been Developed to Assist Clinicians in Adapting Communication Skills and Addressing the Acute or Complex Needs of Adults with Intellectual Disability and Behavioral Disturbance. Examples of These Tools Are "Communicate C.A.R.E." and "H.E.L.P." Frameworks, Which Have Been Devised for Clinicians Seeking to Overcome Communication Barriers and Help Adults with Intellectual Disabilities. Briefly Describe These Tools

"Communicate C.A.R.E." guide encourages the clinician to communicate an attitude of caring when interviewing by allowing sufficient time and providing a comfortable space for the patient. Clinicians are to communicate [20]:

- *C*learly (e.g., on the patient's own terms)
- *A*ttentively (e.g., to verbal and nonverbal cues)
- *R*esponsively (e.g., addressing patient needs empathically)
- *E*ngagingly (e.g., the patient first, with others as appropriate)

H.E.L.P. is a useful framework for considering biopsychosocial variables that could be influencing patient's behavior. H.E.L.P. screens for potential causes of distress or decline [21]. The H.E.L.P. mnemonic stands for:

- *H*ealth (e.g., age-related physiological and medical changes)
- *E*nvironment (e.g., settings and expectations)
- *L*ived experience (e.g., losses, trauma, abuse)
- *P*sychiatric (e.g., neuropsychiatric illness, psychotropic medication side effects)

In addition to utilizing these tools, a careful history with behavior as the presenting problem from knowledgeable informants is helpful in guiding further assessment and specific management.

Question 14.11

What Are the Neurobiological Similarities Between Geriatric Disorders and Neurodevelopmental Disorders?

The neurobiological similarities between geriatric disorders and neurodevelopmental disorders are manifold. Many proteins that are important for the brain development can be dysregulated in geriatric syndromes so that the mechanisms of geriatric syndromes can also cause problems in neurodevelopment. For instance, the amyloid precursor protein is important for formation of amyloid plaques in Alzheimer

disease but also for synapse formation in development. The amyloid precursor protein is located on chromosome 21, being overly produced in trisomy 21, which leads to the early Alzheimer disease in adults with Down syndrome.

Fragile X syndrome, the leading heritable form of intellectual disability, is caused by epigenetic silencing of the fragile X (*FMR1*) gene caused by expansions to greater than 200 CGG repeats. Another protein that is critical for aging and development is the fragile X mental retardation 1 protein (FMRP). As a regulator of translation, FMRP controls approximately 30–50% of the known genes that are mutated in autism spectrum disorder, many of which are important for synaptic plasticity and adult neurogenesis [22, 23]. In the absence of FMRP because of a full mutation, fragile X syndrome (FXS) occurs. FXS is among the most common causes of inherited intellectual disability and the most commonly known genetic cause of autism spectrum disorder. Patients with autism spectrum disorder need a DNA test for fragile X as part of the medical workup. Notably, the fragile X premutation is common in the general population, with a frequency of approximately 1 in 150–200 females and 1 in 400–450 males [24]. Although most patients with the premutation have normal intellectual abilities, premutation repeat expansions (55–200 CGG repeats) can cause many early-onset neurodevelopmental (e.g., autism spectrum disorder, attention deficit disorder, seizure disorder) and late-onset neurodegenerative (e.g., FXTAS) clinical phenotypes through a molecular mechanism involving increased *FMR1* mRNA production and toxicity [25]. With aging, approximately 40% of males and 16% of females with the premutation develop the fragile X-associated tremor/ataxia syndrome (FXTAS), which is a neurodegenerative disorder involving a progressive intention tremor, cerebellar ataxia, neuropathy, mood instability, changes in personality, memory impairment, and other cognitive deficits [26].

Another important protein is DiGeorge syndrome critical region 8 (DGCR8), which is essential for the maturation of microRNAs; DGCR8 is deleted in the 22qdeletion syndrome (22qDS), which is the most common genetic cause of schizophrenia and bipolar disorder in adulthood but also causes neurodevelopmental disorders in childhood including autism spectrum disorder, attention deficit hyperactivity disorder, and anxiety disorder [25].

Mitochondrial dysfunction can lead to the slow movement of mitochondria in neuronal development, resulting in disorders including autism spectrum disorder and fragile X disorders [27, 28]. However, gradual loss of mitochondrial function is also part of the aging process leading to weakness, which is accelerated in many neurodegenerative disorders such as Parkinson disease and Alzheimer disease. In aging patients with many neurodevelopmental disorders (e.g., FXS, 22qDS), Parkinson disease can occur at a higher frequency than the general population [29, 30].

The brain anatomy in brains with autism spectrum disorder has shown a different developmental pattern than typical age-matched peers. In a cross-sectional neuroimaging study of cortical volume, thickness, surface area, and gyrification index in 51 adults (ages 30–75 years) with and 49 without autism spectrum disorder, a premature aging pattern in autism spectrum disorder was not evident [31]. The lack of significant anatomical differences between intellectual able individuals with and without autism spectrum disorder suggests that this neurodevelopmental disorder is not (strongly) related to gray matter morphology in

mid and late adulthood, which seems to counter the previous suggestion of an elevated risk of major neurocognitive disorder in this population [31]. Studies including even older participants are needed to determine whether aging in those with autism spectrum disorder is indeed no risk to major neurocognitive disorder.

Question 14.12

Autism spectrum disorder is a lifelong neurodevelopmental disorder, characterized by social and communication impairments and restricted, stereotypical patterns of behavior.

What Are the Key DSM-5 Diagnostic Criteria for Autism Spectrum Disorder?

Table 14.4 presents the highlights of the DSM-5 diagnostic criteria for autism spectrum disorder [2]. For a full review of these criteria, the reader is referred to the DSM-5 [2].

Table 14.4 Autism spectrum disorder: highlights of the DSM-5 diagnostic criteria [2]

DSM-5 criteria	Specifiers of current severity
A. Persistent deficits in social communication and social interaction across multiple contexts, currently or by history, as manifested by: 1. Deficits in social-emotional reciprocity 2. Deficits in nonverbal communicative behaviors used for social interaction 3. Deficits in developing, maintaining, and understanding relationships	Severity is based on social communication impairments and restricted, repetitive patterns of behavior
B. Restricted, repetitive patterns of behavior, interests, or activities, currently or by history, as manifested by ≥2: 1. Stereotyped or repetitive motor movements, use of objects, or speech 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior 3. Highly restricted, fixated interests that are abnormal in intensity or focus 4. Hyper- or hypo-activity to sensory input or unusual interest in sensory aspects of the environment	Severity is based on social communication impairments and restricted, repetitive patterns of behavior
C. Symptoms must be present in the early developmental period	
D. Symptoms cause clinically significant impairment in current functioning	
Specify: With/without intellectual impairment With/without language impairment Associated with a known medical/genetic condition/environmental factor Associated with another neurodevelopmental/mental/behavioral disorder With catatonia	

Question 14.13

The patient is a 57-year-old male with a history of fragile X premutation. His mother was a fragile X carrier, with a history of fragile X-associated primary ovarian insufficiency with menopause before age 40 and fragile X-associated tremor/ataxia syndrome (FXTAS) with the development of tremor in her 70s followed by ataxia leading to the need for a wheelchair in her 80s. Although he did well in school, he was always socially anxious and had no friends. He was diagnosed with "Asperger syndrome" in childhood because of his social deficits and extreme interest areas in collecting old books that would dominate his conversations. Asperger syndrome is one of several previously separate subtypes of autism that were folded into the single diagnosis of autism spectrum disorder with the publication of the DSM-5. He became an English literature teacher for his career. He married in his early 40s. His daughter is a fragile X carrier but had normal development. By age 50, the patient started to show memory deficits and executive dysfunction. At age 55, on examination, he showed a mild intention tremor, significant ataxia, and could not tandem walk. On cognitive testing, he showed evidence suggestive of major neurocognitive disorder. His brain MRI demonstrated white matter disease in the middle cerebellar peduncle, thin corpus callosum with white matter hyperintensity in the splenium of the corpus callosum, along with generalized cortical atrophy, indicating that he was meeting diagnostic criteria for FXTAS. Recommended treatment is donepezil 5 mg daily for his major neurocognitive disorder and FXTAS.

A. This Case Represents a Fragile X Premutation Involvement in a Patient Diagnosed with Autism Spectrum Disorder and a Family History of Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS). As Previously Stated (see Question 14.11), Premutation Repeat Expansions (55–200 CGG Repeats) Can Cause Many Neurodevelopmental (e.g., Autism Spectrum Disorder) and Neurodegenerative (e.g., FXTAS) Clinical Phenotypes. With Aging, a Significant Proportion of Adults with the Premutation Develop the FXTAS, Which Involves a Progressive Intention Tremor, Cerebellar Ataxia, Neuropathy, Changes in Personality, and Affect Instability, Which Later Go on to Develop Memory Impairment and Other Cognitive Deficits. What Are the Current Diagnostic Criteria of FXTAS? How These Criteria Apply to This Particular Patient?

In order to diagnose FXTAS, an MRI must be ordered. The classic findings in FXTAS are the middle cerebellar peduncle sign along with minor signs identified in Table 14.5 [25, 26, 32]. The patient's brain MRI demonstrated white matter disease in the middle cerebellar peduncle (major FXTAS criteria for diagnosis), thin corpus callosum with white matter hyperintensity in the genu and splenium of the corpus callosum (minor FXTAS criteria), and brain atrophy (minor FXTAS criteria) (see Table 14.5).

The premutation is common in the general population, and it can coexist with many aging disorders including Alzheimer disease, Parkinson disease, multiple sclerosis, fibromyalgia, hypothyroidism, cardiac arrhythmias, congestive heart

Table 14.5 Current diagnostic criteria for FXTAS [25, 26, 32]

Examination and degree	
Molecular	
Major	*FMR1* expansion in gray zone, premutation or unmethylated full mutation range
Radiological	
Major	MRI white matter lesions in the middle cerebellar peduncle
Minor	MRI white matter hyperintensities in the splenium of the corpus callosum
Minor	MRI white matter lesions in cerebral white matter
Minor	Moderate-to-severe generalized atrophy
Clinical	
Major	Intention tremor
Major	Gait ataxia
Minor	Parkinsonism
Minor	Moderate-to-severe short-term memory deficit
Minor	Executive function deficit
Minor	Neuropathy
Neuropathological	
Major	FXTAS inclusions
Diagnostic category	
Presence of expanded CGG repeat (molecular) and:	
Definite	Presence of one major radiological sign plus (1) one major clinical symptom or (2) the presence of FXTAS inclusions
Probable	Presence of one major radiological sign and one minor clinical symptom or two major clinical symptoms
Possible	Presence of one major radiological sign and one major clinical symptom

From: Hagerman R, Ligsay A, Goldberg J. Aging with neurodevelopmental disorders: on-call assessment and future directions. In: Hategan A, Bourgeois JA, Hirsch CH. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer, 2016, page 344; used with permission

failure, and osteoporosis [25]. The patient developed FXTAS, as did his mother, although his FXTAS initially presented with cognitive impairment before motor symptoms, which is unusual. Because of this presentation, the patient may also have had Alzheimer disease in addition to FXTAS. Only the postmortem study of brain pathology would clarify this. Those with FXTAS have eosinophilic intranuclear inclusions that are synuclein and tau negative but positive for ubiquitin and the *FMR1* mRNA [25]. In summary, in order to diagnose FXTAS, an MRI must be ordered, and the classic findings in FXTAS are the middle cerebellar peduncle sign and minor signs identified in Table 14.5. Clinical and neuropathological criteria must be present as well (see Table 14.5).

B. What Are the Medical Comorbidities Associated with the Fragile X Premutation?

A significant number of physical and psychiatric comorbidities have been associated with the fragile X premutation, and some common conditions are listed in Table 14.6 [25].

Table 14.6 Medical and psychiatric features associated with the fragile X premutation [25]

Medical features	Psychiatric features
Fragile X-associated primary ovarian insufficiency	Autism spectrum disorder
Fragile X-associated tremor/ataxia syndrome (FXTAS)	Somatic symptom disorder
Hypothyroidism	Obsessive compulsive disorder
Sleep apnea	Depressive disorders
Hypertension	Social anxiety disorder
Immune-mediated disorders	Neurocognitive disorders
Fibromyalgia	Sleep disorders
Restless legs syndrome	Attention deficit hyperactivity disorder
Seizures	Social deficits
Autonomic dysfunction	

From: Hagerman R, Ligsay A, Goldberg J. Aging with neurodevelopmental disorders: on-call assessment and future directions. In: Hategan A, Bourgeois JA, Hirsch CH. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer, 2016, page 342; used with permission

Question 14.14

Although overt symptoms of autism spectrum disorder become established in the early developmental period, core difficulties tend to persist through life.

Explain Why Recognizing Previously Undiagnosed Autism Spectrum Disorder in Older Adults with or Without Comorbid Neuropsychiatric Syndromes Is Imperative

Clarity of diagnosis in autism spectrum disorder merits special attention. In a case series of older adults (aged 67–84 years) believed to have met the criteria for Asperger syndrome retrospectively, James et al. [33] argued that recognizing and diagnosing autism spectrum disorder in those patients facilitated their treatment; those patients originally were misdiagnosed with "treatment-resistant" depressive and anxiety disorders and may have received unnecessary, lengthy clinical psychiatric care. Notably, the diagnosis of Asperger syndrome was removed in the DSM-5 but included within the autism spectrum disorder along with former terms of autism and pervasive developmental disorder not otherwise specified [2]. James et al. [33] suggested that for older adults with a history of childhood-onset of social skills problems, clinicians should routinely take a lifelong history in understanding patients' interpersonal style, particularly in those patients with a "detached" premorbid personality style, chronic social anxiety, difficulties in coping with change, and unusual behaviors of rigid routines, which may support a new diagnosis of autism spectrum disorder in an older patient.

Question 14.15

Can Clinicians Verify or Diagnose Autism Spectrum Disorder Retrospectively?

Retrospective verification or diagnosis of autism spectrum disorder can be challenging as the diagnosis rests on knowledgeable informants providing history of early developmental period and, where feasible, interdisciplinary assessment of cognitive, behavioral, and adaptive features over time. Clinicians should be aware that childhood-onset psychiatric disorders such as attention deficit hyperactivity disorder, learning disabilities, social communication disorder, or social anxiety disorder can coexist with autism spectrum disorder or present with features of autism spectrum disorder, which further complicates diagnostic identification [34]. As well, schizophrenia may present with similar features or be comorbid with the syndrome of autism spectrum disorder [35]. Even though the diagnostic tools for autism spectrum disorder are generally developed for children, clinicians in specialty services for adults with intellectual and developmental disorders can make the diagnosis of autism spectrum disorder if knowledgeable informants can provide valid early perinatal, developmental, medical, psychological, and social histories.

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Topic 15: Emergencies in Geriatric Psychiatry

Question 15.1

What Common Challenges Can Be Expected in the Emergency Department (ED) Setting Regarding the Care of Geriatric Psychiatric Patients?

The ED environment can induce or exacerbate behaviors that can be mistaken for psychotic, depressive, or major neurocognitive disorders (NCDs), when the problem is, in fact, primarily a systemic medical illness. For example, most cases of hypoactive delirium are not identified by ED physicians, leading to missed diagnoses by hospital physicians at the time of admission [1]. In addition, once medically stabilized and awaiting admission, geriatric patients may not receive adequate monitoring or orienting to prevent or manage delirium [2].

Question 15.2

What Environmental and Other Factors in the ED Increase the Risk of Delirium and Can Induce or Exacerbate Anxiety and Irritability in Older Adults?

The environment and clinical focus of the ED itself may worsen neuropsychiatric symptoms in older patients who present to the ED. These factors include:

- Increased ambient noise (e.g., beeping monitors, emergency medical personnel consulting with physicians via the public announcement system, crying babies, agitated patients).
- Bright lights throughout the day and night.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_15

- The hustle and bustle of busy staff members attending to emergencies.
- Multiple clinical and nonclinical staff speaking with the same patient within an encounter.
- Heightened stress levels among patients and family members.
- The unexpected need for an urgent or emergent evaluation.
- Lack of orienting stimuli such as clocks and windows.
- Older adults with preexisting neurocognitive disorder and other psychiatric disorders are particularly vulnerable to becoming overstimulated in such an environment, overwhelming their already fragile ability to cope.

Question 15.3

How Can Communication Barriers Between Patients with Neurocognitive Disorders (Including Delirium) and ED Staff Lead to Inadequate Evaluation and Treatment of Geriatric Patients?

Patients with neurocognitive disorders often have difficulty effectively communicating their needs. As a result, their hunger, thirst, need to void, pain, and other problems may go unaddressed. Frustrated and suffering, these patients may verbally or physically act out, precluding a thorough assessment and requiring staff to focus on managing the behavior rather on the underlying medical problem.

Question 15.4

What Factors Contribute to "Boarding" of Geriatric Patients in the ED?

Delays in disposition out of the ED—referred to as ED "boarding" or "exit block"—can worsen health outcomes. Unintended prolonged ED stays for psychiatric patients are referred to as "psychiatric boarding" [3]. The duration of boarding varies from 4 h after the decision to admit a psychiatric patient to staying in the ED for more than 24 h [3].

Boarding of patients in the ED is problematic for all patients, but psychiatric patients are disproportionately more greatly affected [4–6]. In a retrospective analysis of all psychiatric and non-psychiatric admissions in a US academic medical center with more than 68,000 ED visits, Nicks and Manthey found that the length of stay (LOS) in the ED was 1089 min for psychiatric patients who were admitted, versus 340 min for non-psychiatric patients, or 3.2 times longer for psychiatric patients [5].

Long-term care facilities are often reticent to accept geriatric patients with preexisting psychiatric illness and/or a history of agitated behaviors, even if the primary need for care is currently due to systemic medical illness. Thus, a geriatric patient with a complex history of systemic medical and psychiatric illnesses may be too "sick" to be dispositioned back home or the community but too "well" to meet criteria for admission to a medical unit. Psychiatric consultants may be asked to evaluate and provide recommendations to treat these patients in the ED for facilitating a transfer to an accepting long-term care facility.

Placement of geriatric patients with comorbid complex systemic medical problems to a psychiatric inpatient facility can be similarly problematic. Unless they are geriatric psychiatric facilities, psychiatric facilities are typically ill equipped to meet the needs of medically ill geriatric patients. For example, they may lack continuous monitoring and treatment devices (e.g., telemetry, vital signs monitoring) and adequate nursing staff to help patients manage urinary or fecal incontinence or to assist patients to complete activities of daily living such as ambulation, grooming and hygiene, and eating. Many psychiatric units do not allow assistive devices such as walkers, canes, or wheelchairs and may not allow treatment devices such as IV poles and continuous positive airway pressure (CPAP) machines.

Question 15.5

Explain the Reciprocal Relationship Between Systemic Medical and Psychiatric Illnesses and Why This Is Particularly Problematic in Geriatric Patients

Psychiatric illness is common in older patients presenting to the ED, and systemic medical illness is common in older psychiatric patients. Data from the Canadian Study of Health and Aging showed a strong correlation between the number of frailty-defining factors and prevalence of psychiatric illness in community-dwelling persons aged 65 or older without major neurocognitive disorders. Over 30% of the most severely frail had psychiatric illness [7].

In patients presenting with confusion, the duration of the cognitive impairment is crucial when developing the differential diagnosis. As with any patient presenting with confusion, having reliable collateral information is critical to identifying the most likely diagnosis as rapidly as possible. (Refer to Table 15.1, which provides a summary of the differential diagnosis of confusion in the geriatric patient presenting to the ED and a comparison of the underlying clinical features [8].)

Table 15.1 Differential diagnosis of confusion in the geriatric emergency department patient and a comparison of clinical features

	Delirium	Major neurocognitive disorder	Major depressive disorder	Psychotic disorder
Onset	Sudden	Gradual	Variable	Variable, from early adulthood to late onset
Duration	Days-months	Lifelong once established	Months	Long term
Course	Fluctuating over hours-days	Months-years	Weeks-months-years	Weeks-months-years
Risk factors	Hospitalization Serious medical illness Preexisting cognitive impairment, especially major neurocognitive disorder Hip fractures Polypharmacy Withdrawal syndromes	Family history Vascular disease Comorbidities	Bereavement Sleep disturbance Disability Female sex	Complex
Attention	Fluctuating	Stable with gradual decline	Preserved	Preserved
Level of consciousness	Varies between somnolent and combative (RASS -3 to +4)	Intact until advanced stages	Intact	Intact
Orientation	Disrupted	Disrupted in advanced stages	Intact	Intact
Psychotic features	Common	Uncommon until advanced stages	Variable	Common
Neuropsychiatric symptoms (NPS) of neurocognitive disorders	Acute delirium may be easily confused with NPS	Common with disease progression	No	No
Treatment	Directed at underlying cause and management of agitation	Few effective treatments	Antidepressants usually effective Psycho-behavioral treatments	Antipsychotics

(continued)

Table 15.1 (continued)

	Delirium	Major neurocognitive disorder	Major depressive disorder	Psychotic disorder
Outcome	Long-term increased mortality risk and increased cognitive impairment. Short-term fall risk as inpatient	Loss of higher cortical functions and progressive dependence	Older patients are high risk of completed suicide if depression is unrecognized or untreated	Longstanding functional decline and social isolation

From: Differential diagnosis of confusion in the geriatric emergency department patient and a comparison of clinical features. Tyler K, Hirsch CH, Scher LM, Stevenson DE. Emergency medicine settings. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 221; used with permission.

Question 15.6

List Patient-Specific Medical Factors That Increase the Risk of Delirium for Geriatric Patients in the ED and Examples of Strategies That Can Be Used to Prevent or Treat Delirium in the ED

Delirium risk is increased with preexisting cognitive impairment, severe pain, severe acute illness, and hip fractures [9, 10]. The literature now includes various strategies to decrease delirium risk for specific conditions. In hip fractures, for example, a multimodal pain strategy is now the standard of care for hip fragility fractures and includes cautiously dosed intravenous opioids, regular acetaminophen, regional anesthesia ideally within the ED, and early operative fixation [11, 12]. Table 15.2 illustrates key components in identification and non-pharmacological management of delirium [13].

Question 15.7

Explain the Rationale for the Use of Pharmacologic Treatments to Treat Delirium in Older Adults in the ED

Employment of non-pharmacological approaches (e.g., minimizing noise levels, turning off lights at night, limiting the number of staff interacting with the patient, and frequent reorienting activities) is ideal. However, the need for urgent stabilization and treatment of acute systemic medical conditions often warrants the use of urgently delivered medications to treat severe agitation in patients with hyperactive delirium. In addition, severe agitation is a serious risk for significant injuries to both patients and staff members [14].

Table 15.2 Identification and non-pharmacological management of delirium

Identification of risk for delirium	
Implement delirium prevention measures for patients • Admitted with altered level of consciousness(LOC)/delirium or • With known risk factors for delirium – Age: ≥70 – History of cognitive impairment, delirium – Functional impairment – Vision impairment – History of alcohol abuse – Comorbidity burden (e.g., stroke, depression)	
Identification of delirium • Use formal instrument, such as the confusion assessment method (CAM), CAM-ICU, months of the year backward, to identify delirium • *Acute* onset (abrupt, within minutes, hours, shifts, days—up to 2 weeks) of *any change* in cognition (inattention, memory loss, disorientation, hallucinations, delusions) – Altered and fluctuating LOC: hyperactive or hypoactive; remember lethargy, falling asleep, staring off into space, and decreased motor activity is *not normal* in older adults with major neurocognitive disorders (dementia) – Disorganized thinking, disorientation – Inattention: assess by asking to say *d*ays of the *w*eek backward or spell *world* backward and by observing for problems focusing, staring off into space, or losing track of questions	
Component	Nursing intervention: identify etiology and provide supportive care
Maintain safety	Maintain airway, prevent aspiration, skin breakdown, falls
Physiologic stability • Infection • Hypoxia • Dehydration • Electrolyte imbalance • Medications • Pain • Urinary retention • Impaction • Immobility • Sleep deprivation • Sensory impairment	• Reduce psychoactive medications and polypharmacy: avoid benzodiazepines, anticholinergic and other deliriogenic medications; monitor for side effects; consult pharmacy as needed • Monitor labs to prevent electrolyte abnormalities and infection • Maintain hydration/nutrition: offer fluids with each encounter, if not on IV fluids • Optimize oxygenation with early mobilization, incentive spirometer and O_2 as indicated • Optimize sleep and sensory input, and progressively mobilize per below • Proactively assess/treat pain with ATC non-opiates and opiates for breakthrough pain • Monitor for impaction or retention: ensure scheduled/prompted voiding and bowel regime • Notify physician of any acute change in behavior or mental status
Sleep promotion	Normalize sleep-wake cycle: goal is to ensure 4–6 h uninterrupted sleep at night • Identify and maintain patient's sleep pattern/routine as much as possible (e.g., identify history sleep disturbance/aides and notify physician) • Optimize sleep-wake cycle with out of bed daytime activity/limited napping and quiet at night • Open blinds during day; close at night; adjust lighting to low level at night • Promote bedtime ritual with warm milk/herbal tea, massage, relaxation music • Cluster care and avoid unnecessary awakening; maintain quiet at night • Avoid caffeine, excessive IV/PO fluids after 6 pm

Table 15.2 (continued)

Identification of risk for delirium	
Activity	• Progressively mobilize to maximal potential and encourage self-care in ADLs, as appropriate – Ensure/assist patient out of bed for all meals unless contraindicated – Discourage napping during day – Ambulate every shift with goal to regain prior level of function as possible • Review for removal of unnecessary lines (catheter, telemetry, IV lines, restraint, etc.) every shift; avoid/minimize restraints • Engage in age-appropriate, meaningful activities; enlist involvement of family/significant other to identify patient-specific routines/interests and incorporate into care plan as possible • Use familiar, calm music, relaxation techniques
Communication enhancement	• Assess for communication deficits and provide assistive devices as needed • Compassionate communication: – Approach in a calm, non-threatening manner. Call person by name, introduce self with each encounter – Set the stage for positive interaction; *smile* – Use active listening, one task/command/step at a time; repeat information using exact words, allow patient time to respond – Search for the meaning/emotion in patient's message and respond to patient feelings – Respond to paranoid or delusional thoughts/expressions by providing comfort to the emotions; (i.e., "you sound angry/scared/sad. I'm here to help; to keep you safe."); avoid arguing and rationalizing and do not take it personally • Redirect agitated patient with validation and distraction (e.g., reminiscence, walk, sweets)
Reality orientation	• Reorient patient frequently within normal conversation; do not quiz patient • Provide simple explanation of nursing care and all activities with each encounter • Foster familiarity: encourage family/friends at bedside, familiar items from home, consistent caregivers and routine as possible, minimize relocations, especially at night • Clock and updated care board with date/orienting information; be sure patient can see it
Sensory stimulation regulation	• Optimize sensory stimulation: ensure patient can see and hear with hearing aid/amplifier, glasses, communication board • Ensure quiet room with good lighting to differentiate day from night (blinds open in day, close at night) • Turn off TV if patient not engaged; use familiar music or relaxation tapes • Limit visitors as needed; minimize noise, interruptions, and distractions • Cluster care to limit unnecessary awakening, especially later in day when patient fatigued

From: Identification and non-pharmacologic management of delirium. Bourgeois JA, Francis DC, Hategan A. Acute Inpatient Medical Settings. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 255–6; used with permission

Even the fastest intravenous medication will still typically take 5–10 min to take full effect. Using the lowest possible dose of psychoactive medication for the shortest possible time should always be a goal, but treating the acute systemic medical condition—especially if life-threatening—must be taken into account. Thus, doses of medications to treat delirium in the ED may be higher than what would be considered acceptable in a clinic or even the acute general medical or psychiatric inpatient setting [14, 15].

Question 15.8

Describe Circumstances in Which Opioids May Be Appropriate for Geriatric Patients in the ED

Untreated acute pain increases the risk of inducing or worsening delirium in geriatric patients. Adequate pain management in the ED setting can prevent unnecessary patient suffering and minimize the onset of clinical complications that this population is already at higher risk for compared to the younger adult population.

All opioids can induce or worsen delirium through their direct effects on cognition, especially in combination with other deliriogenic drugs (e.g., anticholinergics, benzodiazepines). Thus, when opioids are indicated, such as in the case of an acute hip fracture, it is important to provide lowest effective doses of this class of analgesics to have the lowest potential to affect cognition.

Opioid medications with active metabolites and relatively longer half-life (e.g., morphine, meperidine) should be avoided, if possible. Hydromorphone, which has fewer active metabolites, is preferable in geriatric patients, especially those with renal impairment [16, 17].

Evaluate for nonspecific autonomic symptoms of opioid withdrawal in patients who test positive for opioids on urine toxicology tests and/or are known to be taking opioid medications prior to presentation (see Table 15.3) [8]. A low-dose test trial of

Table 15.3 Non-psychiatric symptoms of opioid withdrawal

Early symptoms (first 24 h)	Late symptoms (after 24 h)
Muscle aches	Diarrhea
Lacrimation	Abdominal cramps
Runny nose	Dilated pupils
Frequent yawning	Tachycardia
	Hypertension
	Cutis anserina (“goose bumps”)

From: Non-psychiatric symptoms of opioid withdrawal. Tyler K, Hirsch CH, Scher LM, Stevenson DE. Emergency medicine settings. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 224; used with permission

a short-acting opioid may be of benefit. Opioids can decrease agitation due to its sedating effects, as well as improve blood pressure via its vasodilatory effects, so it is important to assess for the presence of multiple nonspecific signs and symptoms of opioid withdrawal.

Question 15.9

Under certain circumstances, benzodiazepines can be considered in treating geriatric patients with delirium.

A. List Four Clinical Situations in Which Benzodiazepines Should Be Considered in Treating Geriatric Patients with Delirium in the ED

These situations include the following:

1. The patient requires immediate sedation to treat an acute systemic medical condition.
2. To control severe agitation in a patient who is withdrawing from benzodiazepines, alcohol, and/or barbiturates.
3. To control agitation in a substance-induced psychotic episode.
4. When antipsychotic medications are clearly or relatively contraindicated (e.g., neuroleptic malignant syndrome, malignant catatonia, major neurocognitive disorder with Lewy bodies).

B. What Are the Three Most Commonly Used Parenteral Benzodiazepines for Severe Agitation? What Is Their Onset, Half-Life, and Contraindications?

The three most commonly used parenteral benzodiazepines for severe agitation are:

- Lorazepam
- Diazepam
- Midazolam

Their onset, half-life, and contraindications are listed in Table 15.4 [8].

Table 15.4 Comparison of intravenous benzodiazepines for use in severe agitation requiring immediate sedation

	Onset—intravenous	Half-life	Active metabolites	Special considerations	Starting dose in agitated older patient
Lorazepam	15–20 min	14 h	No	Preferred in hepatic dysfunction	0.25 mg IV
Diazepam	5–10 min	Parent drug: 30–60 h Active metabolites: 30–100 h	Yes	Avoid in hepatic dysfunction	1 mg IV
Midazolam	5 min	2.5 h	Yes	Avoid in hepatic dysfunction	0.25 mg IV

From: Tyler K, Hirsch CH, Scher LM, Stevenson DE. Emergency medicine settings. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 225; used with permission

Question 15.10

What Are the Potential Pros and Cons of Using Antipsychotic Medications for the Emergent Treatment of Delirium in Geriatric Patients? What Are the Monitoring Needs with Antipsychotics in the ED?

Potential pros include the following:

- Effective, prompt relief of symptoms
- Not physically addictive
- Tend not to worsen delirium, while benzodiazepines often worsen delirium
- Usually short-term use only
- Relatively low doses required

Potential cons include the following:

- Increased risk of mortality in older adults if used long term, especially in the context of major neurocognitive disorder. The risk of a single or few doses is unknown.
- Prolongation of the QTc interval, attributable to certain antipsychotics (e.g., haloperidol), is associated with a risk of polymorphic ventricular tachycardia, for which geriatric patients have a higher risk for than younger adults.

The monitoring needs with antipsychotics in the ED include:

- Screening ECG prior to administration of antipsychotic.
- In cases of hypokalemia or hypomagnesemia, consider K+ and Mg++ replacement prior to administration.
- Continuous monitoring of ECG if IV haloperidol is to be used.
- Consider use of oral disintegrating tablet formulations of antipsychotic medications (e.g., Zydis (olanzapine) or M-Tabs (risperidone)), which may be better accepted by highly agitated patients. (See Table 15.5 [18].)

Question 15.11

The ED physician requests a psychiatric consultation for an 85-year-old man, Bill, who was dropped off at the ED by family members about 3 h ago, who then left without speaking to anyone. When he arrived, Bill was carrying a grocery bag that included an empty prescription bottle for lorazepam that had the name "William Jones" printed on it with an out-of-state address and prescriber name.

The patient is verbal and says that his name is "Bill," but cannot state his last name, date of birth, or provide any other identifying information. He repeatedly

Table 15.5 Common antipsychotics in emergency geriatric psychiatry

Starting dose/day[a]	Dose adjustments & side effects	
Class-wide side effects: sedation, anticholinergic symptoms, orthostatic hypotension, extrapyramidal symptoms (EPS), akathisia, QTc prolongation, metabolic side effects, acute kidney injury, cognitive decline, cerebrovascular adverse events, and death in patients with neurocognitive disorders. Prominent side effects for specific medications noted below		
Haloperidol (0.25–0.5 mg bid) [IM, LAI, liquid]	–Renal impairment: no adjustment necessary –Hepatic impairment: mild-to-moderate, no adjustment necessary; severe, use is contraindicated –Avoid if QTc >500 ms	–EPS: rigidity/parkinsonism, akathisia, dyskinesia –Increased mortality
Olanzapine (2.5–5 mg) [IM, LAI, ODT]	–No adjustment necessary –Avoid in diabetes	–Anticholinergic, weight gain, hyperglycemia, hypertriglyceridemia
Risperidone (0.25–0.5 mg qd-bid) [IM, LAI, ODT, liquid]	–Renal impairment: reduce dose –Hepatic impairment: reduce dose	–EPS, hyperprolactinemia
Quetiapine (12.5–25 mg)	–Hepatic impairment: reduce dose	–QTc prolongation, orthostatic hypotension, anticholinergic, weight gain, hyperglycemia, hypertriglyceridemia

IM (available as intramuscular formulation for acute treatment; dose often needs reduction as intramuscular is more bioavailable than oral); LAI (available as long-acting injectable formulation; check prescriber guide for dose conversion); ODT (available as oral dissolving/disintegrating tablet)

[a]Use lower dose for patients aged >75 or those >60 with frailty and multiple medication comorbidities

Adapted from: Common on-call medications in geriatric psychiatry. Xiong GL, Javaheri A, Wiechers IR. Psychopharmacology principles. In: Hategan A, Bourgeois JA, Hirsch HC. (Eds). On-Call Geriatric Psychiatry: Handbook of Principles and Practice. Springer International Publishing, Switzerland. 2016; p 39–40; used with permission

says that he wants to go home, while standing up, then walking toward the door. He denied physical complaints other than saying that he is hungry.

Initially passively cooperative and pleasant, Bill has become increasingly verbally abusive toward staff and has been attempting to leave the ED. An hour ago, Bill started screaming "I'm going to kill you all!", pulled out his IV line, and accused staff of false imprisonment. He turned over tables and chairs in the ED, and it required two security guards to subdue him. He finally calmed down after receiving a 2 mg dose of IM lorazepam 20 min ago.

The ED physician requests that Bill be considered for involuntary inpatient psychiatric admission because he is "paranoid, homicidal, and unable to state a reasonable

plan of self-care." In reviewing the medical records, you learn that Bill has been afebrile, and his blood pressure and other vital signs have been normal and stable.

Physical exam findings were unremarkable, and neurologic exam was non-focal. CBC indicates mild normocytic anemia, and comprehensive metabolic panel is normal. A urinalysis has not been obtained because Bill threw the sample cup at the nurse.

A. Based on the Above Data, What Is Your Differential Diagnosis?

The following differential diagnosis is considered:

- Major neurocognitive disorder, formerly dementia. In geriatric presentations to the ED, the most common acute reasons for decompensation are major neurocognitive disorder with behavioral disturbances (e.g., chronic cognitive impairment with recent onset of psychotic symptoms) and delirium. Major neurocognitive disorders are a major chronic risk factor for delirium. The patient's acute behavioral disturbances may have been precipitated by undiagnosed systemic illnesses/conditions; in addition to the unfamiliarity of the ED, physical discomfort (e.g., hunger, thirst) or physical pain/discomfort that he is unable to describe and lack of orienting activities are further factors.
- Delirium due to systemic illnesses/conditions (e.g., urinary tract infection, dehydration, medication use, cardiovascular disease).
- Other psychiatric disorders (e.g., depressive disorder, psychotic disorder, anxiety disorder, substance intoxication, or withdrawal), which can present at any age.

Case continued: You arrive in the ED and find that the patient is asleep. He awakens briefly to multiple loud verbal stimuli but promptly falls back asleep. His vital signs are stable. The patient is casually dressed, but his clothing is disheveled and soiled, some buttons are misaligned to proper buttonholes, and his grooming is marginal (he is unshaven, his hair is matted and dirty, and his fingernails are poorly trimmed).

B. List Common Major or Mild Neurocognitive Disorders That Are Associated with Psychosis

- Alzheimer disease
- Vascular cognitive impairment
- Traumatic brain injury
- Frontotemporal (Pick) disease
- Human immunodeficiency virus (HIV) disease
- Lewy body disease
- Parkinson disease
- Huntington disease

C. What Specific Information Do You Need the ED Social Worker to Obtain? Case Continued

Using information available on the prescription bottle, the social worker was able to obtain Bill's daughter's local contact information. She learned that Bill had been prescribed lorazepam 1 mg tabs, 1 tab 1–3 times a day for anxiety and severe irritability, dispensed as 90 tabs, no refills, which was last filled 5 weeks ago, and donepezil 5 mg PO daily, dispensed as 30 tabs, with 3 refills, which was last filled 3 months ago.

You call the patient's daughter, Dana, who reports that Bill, whom she had been estranged from for several years, moved in with her and her husband from out of state 4 weeks ago. The daughter reluctantly agreed to take in her father, whose 65-year-old wife died suddenly from complications of a stroke 5 years ago. Bill had apparently been physically and emotionally abusive toward his children; she said her father was never a heavy drinker and to her knowledge had never used illicit drugs.

Dana reports that Bill's wife, who was significantly younger than Bill, took care of "everything," including paying bills and household chores, and ensured that Bill kept his doctors' appointments and took his medications as prescribed. Bill was able to manage reasonably well on his own for a few years but then developed an insidious onset of memory problems. This was manifest initially by anomia (inability to name objects) but progressed to worsening word-finding and organizational problems and variably irritable behavior.

As Bill's illness progressed, he was no longer able to manage his own financial and legal matters, and a neighbor stepped in a year ago to help Bill. About 2 months ago, this neighbor called Dana, stating that she was "burned out" and would no longer care for him. Guilt-ridden, Dana agreed to allow her father to move in with her and her husband and their two children. She reported that Bill's presence in her home created a lot of tension in her household and that Bill required near-constant monitoring to ensure his safety. Bill's behaviors were manageable during the day as long as she gave him his lorazepam. She was able to tolerate the stress until 3 days ago, when she ran out of lorazepam. Since then, Bill's behavior became increasingly erratic, and he was verbally and physically abusive toward her and her family.

D. What Other Studies and/or Interventions Do You Need to Clarify the Diagnosis?

The following investigations are recommended:

- Head computerized tomography (CT) scan without contrast to rule out a mass, structural, or vascular lesion such as a subdural hematoma.
- Thyroid-stimulating hormone (TSH), because severe hypo- or hyperthyroidism can present with psychosis.

- Place a Foley catheter, now that the patient is sedated, and obtain a urinalysis to rule out a urinary tract infection; obtain a urine toxicology for substances such as benzodiazepines, opioids, methamphetamines, cannabis, and other illicit substances.
- Blood alcohol level.
- Other routine delirium evaluation laboratory studies (e.g., metabolic panel, liver-associated enzymes, complete blood count (CBC), calcium, vitamin B_{12})

Case continued: The requested evaluations are completed. The only positive result in the workup is a CT of the head with global cortical atrophy and diffuse subcortical white matter disease, though without evidence of a stroke and/or hemorrhage. He is observed in the ED, while disposition is arranged, during which time his psychiatric status and his vital signs remain stable.

Bill is now more alert and able to participate more fully in your evaluation. His affect is perplexed, mildly distressed, but non-tearful, non-labile, and non-melancholic. He denies suicidal/homicidal ideation or psychotic symptoms. He is mildly circumstantial and perseverative with mild not work difficulties, but no cognitive disorganization. He continues to not be able to understand the recent narrative of events, though he does acknowledge that he lives with his daughter and her family "for the time being" locally. His neurological exam is non-focal. His Montreal Cognitive Assessment (MoCA) is 14/30, with notable deficits, among others, in concentration (0/3), recall memory (0/5), and orientation (3/6). His level of consciousness is full, and he remains fully alert (though perplexed) throughout the interview. He is unable to describe how he would care for himself should he leave the ED.

He denies any psychiatric illness until later in life, when he started having "memory problems" in his mid-60s, after which he retired from work. Bill corroborated his daughter's story. He no longer drives. He does not recall the names or doses of any of his medications and stated that lorazepam is the only medicine that helps him feel better. In response to your targeted screening queries regarding depressive, psychotic, and anxiety disorders, he denies symptoms consistent with these illnesses.

E. What Is Your Top Differential Diagnosis Now?

The collateral narrative and exam findings are classic for progressive major neurocognitive disorder. Acute changes in mental status that led to Bill being dropped off in the ED may have been due to acute benzodiazepine withdrawal. There is nothing in the daughter's narrative to strongly suggest any other psychiatric illness.

F. How Should His Case Be Dispositioned?

This is a classic description of "abandoned dementia" which is not uncommon in the ED setting. Depending on local resources, he may need to be briefly admitted to

internal medicine, general psychiatry, or geriatric psychiatry, while alternative placement is obtained. Bill's disposition is likely to be delayed, leading to a prolonged stay in the ED, or "ED boarding" (see Question 15.4 for the factors contributing to ED boarding). Due to the failure of many systems of care to provide appropriately supervised placement for patients with major neurocognitive disorders, plus the obvious caregiver fatigue experienced by family members, acute presentations of patients with major neurocognitive disorders who are themselves clinically stable are not unusual. Clinicians need to appreciate that the context of presentation is an acute "change in social status" that can masquerade as an acute "change in mental status."

Question 15.12

To What Extent Should Geriatric Patients Presenting to the ED Be Evaluated for Substance Use Disorders?

Addiction to prescribed substances such as opioids and benzodiazepines, and to illicit drugs such as marijuana, cocaine, heroin, and methamphetamine, does not stop because the patient has passed age 65. In old age the long-term effects of substance abuse are likely to increase, and clinicians should have a low threshold for examination and detection of substance use in their patients.

Up to 10% of trauma patients over the age of 65 had a detectable blood alcohol level in the ED and at least one positive finding on a urine drug screen nearly 50% of the time [19]. Almost one-third of methamphetamine users in the USA are over the age of 50 [20].

The judicious use of benzodiazepines, opioids, and/or muscle relaxants has been increasingly enforced by government and other agencies in recent years; and federal and state "watch dog" agencies now routinely monitor prescribers, pharmacies, and patients for evidence of misuse and/or diversion. Before the advent of stricter prescription and monitoring guidelines, geriatric patients may have been started on higher and more frequent doses of habit-forming drugs with the expectation that they could continue taking these medications indefinitely.

Question 15.13

The patient is a 65-year-old male with chronic paranoid schizophrenia. He had illness onset in his 20s with an acute presentation of paranoid ideation and intrusive hallucinations of voices mocking his behavior by telling him "you are no good, the Devil will get you." He was treated over the years with multiple trials of antipsychotics, doing the best on clozapine 500 mg at bedtime, which he continues to take.

He has been hospitalized several times, typically for recurrence of psychotic symptoms. He has never received electroconvulsive therapy (ECT). He has been living with his parents (who are both in their 80s) and has additional social supports

provided by the community mental health center. He has never been able to work for pay, but volunteers at various community agencies.

He has been doing relatively well of late, but his father suffered a stroke with aphasia and hemiplegia. In this context, he acutely decompensated, and his case manager brings him to the ED: "He is not dealing with his father's illness, his paranoia is worse, I can't manage him. He is still on his meds but he cannot function like this."

A. What Assessments Need to Be Done in the ED?

While his acute presentation is well, if not fully, explained by distress associated with his father's illness, other evaluations are needed. Since he is on clozapine, he needs to be examined for acute infection or myocarditis, seizure, or delirium. Standard delirium laboratory studies (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis/toxicology, blood alcohol) are needed, as is a 12-lead ECG. Absent a seizure event, EEG is not needed. CT scan is not needed acutely. If locally available, a clozapine level is appropriate.

Case continued: You see him in the presence of his case manager. He is highly regressed, in a defended and near fetal posture, repeatedly saying, "The Devil hurt my Dad, it is all my fault…." He will not answer questions regarding suicidal ideation or homicidal ideation. He turns to an empty corner of the room and yells "You Devil, why did you make my Dad so sick…" repeatedly. He cannot orient to date/time, though he recognizes his case manager as a supportive figure.

B. How Do You Explain His Presentation?

While acute onset of first episode of schizophrenia spectrum illness is extremely rare in older patients, recurrence of psychosis in a patient with an established psychotic illness is common. The context of presentation is often disruption in the "social microenvironment" such as illness in a family member. While delirium and other neurocognitive disorders must of course be considered, as in any patient, this case is well explained by the social disruption (clearly profound) in someone with limited coping skills and poor distress tolerance.

C. How Do You Manage Him?

Assuming the screening laboratory studies and clozapine monitoring laboratory studies do not reveal additional clinical concerns, he needs to be admitted to psychiatry ward for safety and stabilization. Depending on his response to the containment of hospitalization, changes in his treatment (e.g., more robust dosing of clozapine, augmentation with an antidepressant) may be needed. Acutely, he has a significant risk for catatonia given his highly regressed stance at presentation.

D. If He Develops Catatonia, How Would You Manage That?

Clozapine would be continued and a trial of lorazepam 1 mg IV q6 h, escalating daily as needed to a maximum dose of 8 mg IV q6 h with serial Bush-Francis Catatonia Rating Scale assessments to monitor catatonic symptoms. If he fails to respond to the lorazepam trial, ECT would be necessary.

E. How Should New-Onset Psychosis Be Considered in a Geriatric Patient?

New-onset psychosis should be considered a medical emergency in geriatric patients. The term "psychosis" is defined as the loss of reality testing and characterized by the presence of delusions, hallucinations (auditory and/or visual), and/or disorganized thinking, speech, or behavior.

F. What Class of Disorders Is the Most Common Cause of Psychosis in Geriatric Patients?

Neurocognitive disorders such as delirium and major neurocognitive disorders (previously "dementias") are the most common cause of psychosis in geriatric patients. More than half of patients with neurocognitive disorder due to Alzheimer disease will develop delusions or hallucinations during the first few years of clinical onset [21]. Neurocognitive disorder-associated psychosis is associated with more rapid cognitive decline and increased risk of agitation and violence in nursing home settings. Patients with neurocognitive disorders often present to ED for treatment of psychosis, agitation, and disruptive behavior [22].

Question 15.14

You are called to the ED to evaluate a 65-year-old female patient. The ED physician calls to tell you "This woman's family brought her in. For the last month she has been impossible to deal with. They say she is doing all kinds of problematic things. She is sexually inappropriate, seductive, telling off color jokes, irritable and laughing, and rigid in wanting things her way. She used to be agreeable and pleasant."

A. What Diagnostic Considerations Come to Mind Based on This Narrative?

The differential is broad at the moment. Substance abuse must be considered. Irritability is seen in neurocognitive disorders and manic episodes, but manic episodes would have sleep-wake disturbances. Delirium can produce any psychiatric symptoms but would be associated with sleep-wake disturbances and variable symptom presentations.

B. What Evaluations Do You Want the ED Physician to Do Before You See Her?

Standard delirium screening laboratory studies (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis/toxicology, blood alcohol level) are needed. Subacute changes in personality in an older patient mandate neuroimaging. EEG can be considered but in the absence of seizure events is low yield at this time.

Case continued: When you tell the ED physician these recommendations, she says "I can do the labs OK but I don't think she needs a CT. She's just a psych patient."

C. How Do You Respond?

The head CT is needed. Cases presenting as "personality change" have a reasonable possibility of mass/structural lesion or major neurocognitive disorder.

Case continued: You go to see her. Her family members tell you that she has no history of neuropsychiatric illness. They are quite adamant that she has never been a drinker or drug user and they have no suspicions of this now. They reiterate: "her personality is different. She is irritable, impulsive, disinhibited, like a different person." She is sleeping and eating as usual and does not seem to have memory problems, though she is a little forgetful.

On exam, she is fully alert and oriented; MoCA is 29/30. She is irritable and quick to anger, but speech is not loud or pressured. She is a bit perseverative but not disorganized. She dismisses her family's concerns: "they don't know what they are talking about." She denies suicidal and homicidal ideation ("of course not") and psychosis.

D. What Are the Diagnoses at This Time?

Without full spectrum manic symptoms, this is not a manic episode; new onset of bipolar disorder at this age is rare in any case. Her cognitive exam is normal, making major neurocognitive disorder less likely. The absence of hallucinations makes neurocognitive disorder with Lewy bodies unlikely. She is clearly not depressed.

Case continued: The laboratory studies are normal. CT of the head reveals a right frontal lobe mass suspicious for a tumor.

E. What Do You Need to Do Now?

This is classic "frontal lobe syndrome" of subacute behavioral disinhibition experienced as "personality change" without gross cognitive impairment or delirium. She needs acute consultation from neurosurgery. She needs to be considered for a trial of an anticonvulsant to contain behavior while she is worked up for neurosurgery. She cannot be allowed to leave the hospital. She would be declared to have diminished decisional capacity on the basis of the tumor.

Question 15.15

The patient is a 64-year-old white female with no history of psychiatric illness. You receive a panicked call from an oncology colleague: "Sorry to bug you but we have an emergency. Mrs. X has a new diagnosis of colorectal cancer. She actually has a good prognosis if we get her into care right away as I think the disease is localized, but she isn't dealing well. She is telling her family that she is going to die anyway so what is the point of treatment? I am concerned that she will kill herself so I told her family to bring her to the ED right away."

A. Given the Above History, What Is the Working Diagnosis?

Assuming the events are acute (i.e., less than a 2-week time course) and not associated with neurovegetative signs, this is *not* a major depressive disorder associated with cancer, as the time course is inadequate. This is an example of "high-risk" adjustment disorder.

You tell the oncologist that seeking acute care in the ED is highly indicated and that you will go to see her once she arrives. Four hours later, you are called by the ED physician: "Mrs. X is here, suicidal and upset. She says she is not 'mentally ill' but that she can't deal with cancer. She is suicidal and hopeless. You need to admit her to psych till she deals with things better."

B. What Do You Tell the ED Physician?

As with any patient in the ED, delirium must be considered, but early cancer is not particularly associated with high delirium risk. Standard delirium screening laboratory studies (e.g., metabolic panel, liver-associated enzymes, CBC, TSH, calcium, B_{12}, urinalysis/toxicology, blood alcohol level) are reasonable as is a screening physical examination. CNS metastatic disease risk is likely low, so a CT scan is not strongly indicated.

Case continued: You see her in the ED. She is with her spouse and adult son. They both say she is usually a high-functioning, stoic person, but since the cancer diagnosis, she is acutely emotional, tearful, and convinced that her prognosis is poor and has made many catastrophizing statements concerning suicidal intent. She came to the ED only reluctantly, as "what is the point, I am only going to die." Her family members emphasize that these behaviors have only been present since the cancer diagnosis 4 days ago.

You interview her. She is tearful and endorses hopelessness and a great fear of a lingering, painful death and complete dependency on others. She endorses that she "may as well just die and get this over with" but does not have a means for suicide planned, nor does she have any history of same. She has no homicidal ideation ("of course not, why would I?") and no psychosis. She scores a 30/30 on the MoCA. She does endorse that she "hasn't slept at all" since the diagnosis but denies nightmares.

C. What Is the Differential Diagnosis?

Given the acute presentation in the face of normal level of arousal and normal cognitive status, the two diagnostic possibilities are adjustment disorder and acute stress disorder. She does not appear to have the dissociative or PTSD-spectrum symptoms characteristic of acute stress disorder, so adjustment disorder is the diagnosis.

D. How Do You Manage Her?

If she persists in her suicidal ideation, a brief psychiatric admission may be necessary to provide safety and additional treatment. If you can take a supportive and problem-solving approach in the ED, the suicidal ideation could improve to where she is safe to go home. Offering medication for sleep (e.g., mirtazapine or trazodone) may be very helpful. If she can see a more hopeful future once she engages in cancer treatment, she may be safe to go home with close follow-up.

You tell her that you are concerned about her safety and that you and the oncologist are collaborating on her care. You further tell her that an initial catastrophic reaction to serious illness diagnosis is not unusual and that you want to help her through this great challenge. She understands that "I might be overacting a bit but this is very frightening" and she agrees to have you speak to her family. You tell her (in a hopeful stance) that if she can agree to further care and if she can decrease her suicidal thinking, you would be OK letting her go home.

E. What Do You Tell Her Family Members?

Catastrophic reaction to a severe illness diagnosis is not emblematic of premorbid "mental illness" but can be acutely dangerous. If they can remain supportive and she can back off her suicidal thinking, then her psychiatric prognosis is good. You would also tell them that in cancer patients, the same reaction can happen with complications or progression of cancer (e.g., onset of metastatic disease) so that they are forewarned.

Case continued: After talking to her family, you reunite them. She is now less convinced that she has a hopeless prognosis and somewhat sheepishly tells her family members that she is "just scared" and is no longer suicidal.

F. What Do You Do Now?

She is safe to go home. You would treat her insomnia and arrange for follow-up. A preferred treatment model is cancer center-based embedded psychiatric services, depending on local programming. If such is not available, she needs routine psychiatric follow-up.

G. What Do You Tell the Oncologist?

She does not have a history of psychiatric illness to this point. She is cognitively intact and accepting of treatment, with a decrease in suicidal thinking following your ED intervention. The oncologist needs to be vigilant to her mood state and should facilitate her access to cancer center-based psychiatric services as she enrolls in cancer staging and treatment. For any acute suicidality, she should return to the ED.

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Topic 16: Sexuality and Sexual Dysfunctions in Later Life

Question 16.1

Studies suggest that older adults maintain sexual interest well into late life, but many experience sexual dysfunction. To understand the normal sexual response, in 1962, Masters and Johnson described a model of four-phase sexual response.

Briefly Describe the Four Phases of Human Sexual Response Cycle

The human sexual response cycle progresses through four phases [1]. Table 16.1 summarizes these phases and their key characteristics [1, 2].

Question 16.2

Describe the Normative Age-Associated Changes in Sexual Functioning

In men, decreased libido with aging can be due to several etiologies, including decreased testosterone, but only a small fraction of older men with confirmed androgen deficiency are clinically symptomatic [3, 4]. Low testosterone has been associated with the following clinical changes [5–8]:

- Inhibition of morning erections.
- Resultant erections require more physical penile stimulation, longer time to achieve erection, and the duration of orgasm may be shorter and less intense.
- Erectile dysfunction (which is the most common sexual dysfunction in males).
- Potential cognitive changes.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_16

- Decreased bone mineral density.
- Metabolic syndrome (which leads to an increased risk of diabetes mellitus).
- Increased cardiovascular mortality.

In women, postmenopausal hormonal changes, which include lower levels of estrogen, account for the following changes in sexual function [7]:

- Fewer and less intense orgasms
- Decreased vaginal lubrication
- Thinning of the vaginal wall tissue
- Urogenital atrophy
- Painful intercourse (i.e., dyspareunia)
- Increased susceptibility to infections

Table 16.2 highlights the common age-related physiological changes in sexual function [7]. For both sexes, other age-related changes include changes in physical appearance (e.g., decreased skin elasticity and firmness, changes in hair pigmentation).

Table 16.1 Phases of human sexual response cycle [1, 2]

Phase	Characteristics
Excitement	Vascular congestion, generalized muscle tension, increase in cardiorespiratory rate, increased blood flow to the genitals, vaginal lubrication, breast swelling, nipple erection
Plateau	Enlargement of the testes and scrotal contraction, minor increase in penile erection, secretion of semen and seminal fluid into the urethra, continued enlargement of the vaginal wall and labia minora, increase in clitoral sensitivity
Orgasm	Climax of the sexual response cycle, release of sexual tension for both sexes, ejaculation and orgasm occur simultaneously in males, orgasm is achieved via release of general skeletal muscle tone in females
Resolution	Decreased blood flow to the genitals, relaxation of muscles in the perineum, decrease in cardiorespiratory rate, psychological feeling of well-being and intimacy, penis returns to its normal flaccid state, females can return to orgasm phase with minimal refractory time

Table 16.2 Age-associated changes in sexual function [7]

Females	Males
Fewer, less intense orgasms	Shorter, less intense orgasms
Decreased vaginal lubrication	Decreased libido
Vaginal pruritus, soreness, dryness	Increased duration to achieve erection
Vaginal thinning	Increased physical penile stimulation to achieve orgasm
Dyspareunia	Erectile dysfunction
Increased susceptibility to infections	

Question 16.3

Discussing sexual health can be a sensitive topic, irrespective of age.

What Are the Key Elements That Clinicians Should Consider When Taking a Sexual History in an Older Adult?

Sexuality can be an uncomfortable topic for older adults to discuss in clinical practice, and thus, sexual problems in this population often go unrecognized. Psychiatric clinicians should consider assessing the sexual health at a relatively early stage of patient care, with the understanding that a sexual history may not be the focus of a first clinical encounter. The clinician should allow adequate time for the conversation with the patient to foster trust, openness, and respect. For further suggestions regarding strategies for sexual history taking and some examples of more detailed questions to ask once a dialogue has been initiated are presented in Tables 16.3 and 16.4 [9].

Table 16.3 Strategies for sexual history taking in older adults [9]

Steps for clinicians	Comments
Invite the patient to discuss about sexual life	This conveys a sense of respect, control, and empathy; it emphasizes that this type of information sharing is important for an accurate diagnosis and management
Explore the patient's participation in sexual behaviors	Ask about the patient's sexual orientation and interest Ask about sexual intercourse, masturbation, noncoital sex, or visits to sex workers, regardless of marital or health status Consider exploring this during the review of systems or during the review of psychosocial history
Ask the primary care physician to provide recent physical examination and routine laboratory results as part of the intake procedure for psychiatric referrals	This allows for further guided discussion and specialty referrals (e.g., referral to urology or diabetes mellitus care team)
Ask the patient to bring all of the medications taken during the week	This can provide more accurate information than asking for verbal reports; this includes prescription and over-the-counter medications and supplements
Ask about the specific stage of sexual experience in which the reported sexual dysfunction occurs	This can include difficulties with arousal, erection, dyspareunia, ejaculation, or orgasm
Obtain a complete psychiatric, medical, and social history	A history of depressive disorder, anxiety disorder, diabetes mellitus, hypertension, marital strain can reveal potential causes of the sexual dysfunction

Table 16.4 Examples of interviewing questions to assess sexuality in older adults [9]

Interviewing questions	What would you like to tell me about your sexual life?
	Are you currently in an intimate relationship?
	Has there been any relationship strain? If so, why do you think this is?
	If you could, what would you change about your current relationship?
	If you are currently not in an intimate relationship, are you interested in pursuing one? Do you have any concerns about this?
	What is your current experience with intimacy?
	What is your gender identity?
	What is your sexual orientation?
	How is your current level of sexual interest?
	How is your sexual function?
	How is your sexual desire?
	Are you able to experience arousal?
	Do you have any difficulty achieving or maintaining an erection?
	Do you usually achieve ejaculation/orgasm?
	Do you have pain during intercourse?
	How about sexual and physical intimacy? Do you wish this took place more often/less often?
	Do you engage in self-stimulation (e.g., masturbation)?
	What factors do you think are impacting your sexual life?

Other strategies to assess sexual health include the PLISSIT model, developed in 1976 by Annon [10]. PLISSIT is an acronym for Permission (P), Limited Information (LI), Specific Suggestions (SS), and Intensive Therapy (IT) (see Fig. 16.1) [10]. Figure 16.1 summarizes the PLISSIT strategies for assessing and managing sexual health [10, 11].

Question 16.4

There are several tools that can be used to assess sexual behavior, knowledge, and attitudes.

Provide Some Examples of Common Instruments Used for Sexual Behavior Assessment

The Sexual Behavior Questionnaire (SBQ) can give an indication of current and past sexual behavior. The Aging Sexual Knowledge and Attitudes Scale (ASKAS) is conducted in a "true/false/don't know" format combined with items responded to on a 7-point Likert-type scale and has been used in several studies involving nursing home residents [12, 13]. The Staff Attitudes about Intimacy and Dementia (SAID)

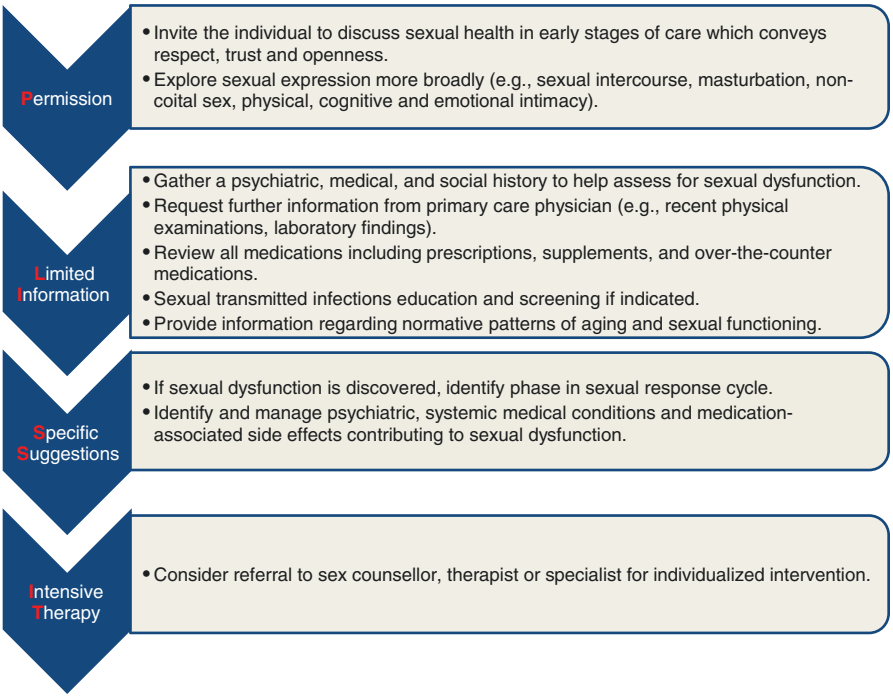


Fig. 16.1 The PLISSIT model for assessing and managing sexual health [10, 11]. From Ambrosini DL, Chackery R, Hategan A. Sexuality and Sexual Dysfunction in Later Life. In: Hategan et al. (Eds.) Geriatric Psychiatry: A Case-Based Textbook; Springer, 2018; used with permission

questionnaire is a public domain instrument and is helpful in stimulating discussion topics for staff education in residential care facilities [14].

Question 16.5

What Are the Common Factors That May Contribute to Sexual Dysfunction?

Common systemic medical conditions that may contribute to sexual dysfunction include hypertension, hyperlipidemia, diabetes mellitus, spinal cord injury, Parkinson disease, prostatectomy, benign prostatic hypertrophy, and prostate cancer. Excessive alcohol intake and smoking are factors that may also cause sexual dysfunction. Additionally, a number of psychiatric disorders and medication classes can lead to sexual dysfunction. Table 16.5 summarizes common factors that may affect sexuality in older adults [15–17].

Table 16.5 Common factors that may affect sexuality in older adults [15–17]

Factors	Characteristics
Psychiatric disorders and other factors	Depressive disorders, anxiety disorders, neurocognitive disorders, substance abuse, history of sexual abuse
Systemic medical conditions	Obesity, diabetes mellitus, hyperthyroidism, other endocrine disorders History of myocardial infarction, hypertension, peripheral vascular disease Dialysis, lower urinary tract symptoms, prostatectomy, benign prostatic hypertrophy, prostate cancer, pelvic surgery, hysterectomy, ovarian cancer Parkinson disease, stroke, epilepsy, multiple sclerosis Respiratory diseases Smoking Lumbar disk disease Spinal cord injury Arthritis
Medications	*Antihypertensives:* Clonidine, beta blockers, angiotensin-converting enzyme inhibitors *Lipid-lowering agents:* Niacin, fibrates *Antiestrogens:* Clomifene, tamoxifen *Antihistamines:* Diphenhydramine, hydroxyzine *Antidepressants:* Related to serotonin and anticholinergic adverse effects, priapism potentially caused by trazodone *Antipsychotics:* Dopamine antagonism with elevated prolactin levels, metabolic effects that affect sexual function *Dopamine agonists and partial dopamine agonists* (through potential increase in sexual interest, arousal, and behavior): Pramipexole, ropinirole, aripiprazole *Mood stabilizers:* Carbamazepine, phenytoin, and phenobarbital can cause possible reduction of free testosterone; valproate can cause polycystic ovarian syndrome, decreased libido, and anorgasmia in women, and reduced testicular volume in men *Benzodiazepines:* Decreased sexual desire, delayed orgasm, and erectile dysfunction; increased sexual desire and sexual disinhibition in some cases *Cognitive enhancers:* Sexually inappropriate behaviors in patients with major neurocognitive disorders in some cases

Question 16.6

What Are the Positive Predictors of Sexual Activity in Late Life? What Are the Barriers to Sexual Expression, Especially in Institutionalized Settings?

Partner availability and good health, including the absence of depressive disorder, greatly predict increased sexual activity in older adults. Those with chronic medical conditions (e.g., hypertension, diabetes mellitus, prostate enlargement, cancer) engage in less sexual activity than their healthier counterparts. Better physical health was also found to be associated with more positive sexual attitudes toward sex. Better cognitive functioning and moderate alcohol consumption are also

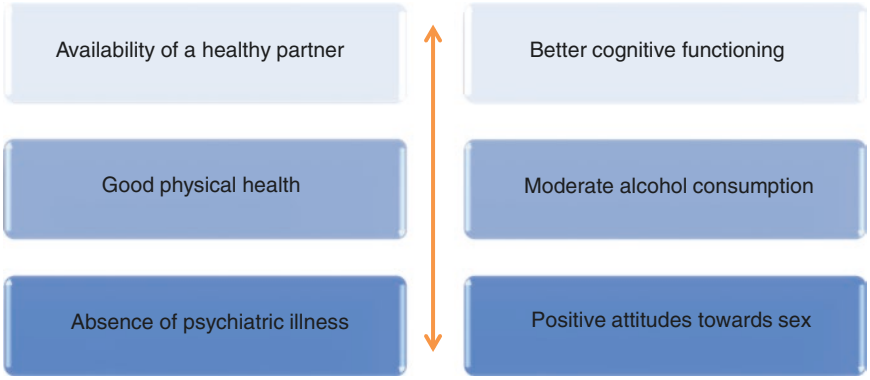


Fig. 16.2 Positive predictors of sexual activity in late life [13]

positive predictors. Figure 16.2 illustrates the positive predictors of sexual activity in late life [13].

The barriers to achieve sexual expression in later life include a number of physiological, ideological, societal, and institutional factors. Most current older adults were raised in the first half of the twentieth century, a time that reflected a western world of conservative norms. The American Associations of Retired Persons (AARP) study provided evidence that women have a less positive attitude toward sexual activity than males of the same age and that women aged 75 or older are less likely to have a partner than older males [18]. Availability of a partner is a strong predictor of sexual activity. In a study of long-term care residents, 30% of men and 40% of women reported that the main reason for sexual inactivity was the lack of a partner [19]. The physical or mental incapacity of a partner could also create lack of opportunity. Poor health in general can be a barrier. Anxiety and depressive disorders have been associated with decreased sexual activity and sexual dysfunction [20, 21]. Adverse side effects of medications could lead to sexual dysfunction and, consequently, decreased sexual activity [21]. In long-term care facilities, there is lack of privacy in one's physical environment, which does not foster privacy for sexual intimacy. Some older adults may choose to live with their families, which may also decrease level of privacy. Another barrier in long-term care facilities is the lack of privacy of information. This could cause limitation for some older adults to seek out information or opportunities for sexual expression. Possible lack of sex education during their youth may be another barrier of sexual activity in older adults. Lack of adequate information regarding normative patterns of aging and sex-related hormonal changes is another factor. Lack of education may also explain the increasing rates of infection with human immunodeficiency virus and acquired immune deficiency syndrome (HIV/AIDS) diagnosed in adults older than age 50 [22]. Societal expectations for sexual fulfillment in older age may lead to misconceptions that play a significant role in assumptions regarding sexual function. Another barrier is the lack of knowledge of lifestyle factors that could contribute to sexual dysfunction. Figure 16.3 summarizes the barriers to sexual expression in late life [13].

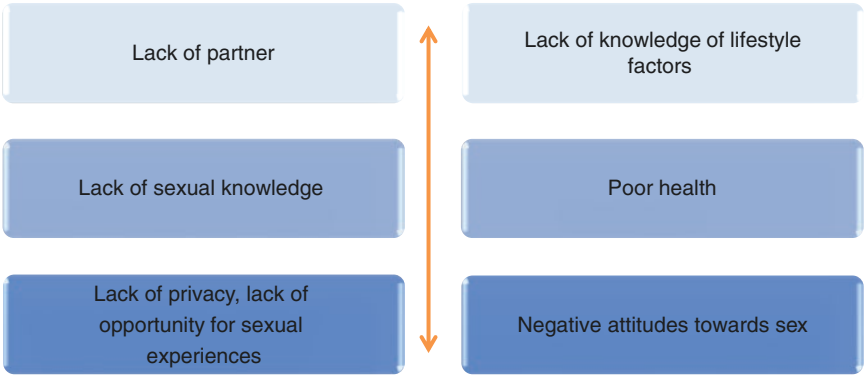


Fig. 16.3 Barriers to sexual expression in institutionalized settings [13]

Question 16.7

What Is the Approach to Diagnosis and Management of Sexual Dysfunction?

The diagnosis of sexual dysfunction requires a minimum duration of 6 months, except for substance- or medication-induced sexual dysfunction and is accompanied by severity specifiers (i.e., mild, moderate, severe). Sexual disorders have specifiers of *lifelong* (i.e., present from first sexual experiences) versus *acquired* (i.e., develop after a period of relatively normal sexual function) and *generalized* (i.e., not limited to context) versus *situational* (i.e., only occur with certain types of stimulation, situations, or partners) [23]. An individual can have multiple sexual dysfunctions at the same time, in which case, all the dysfunctions must be diagnosed. In females, inhibited sexual desire, inability to become aroused, anorgasmia, and dyspareunia are the most common issues. In males, erectile dysfunction, ejaculation disorder, and inhibited sexual desire are the most common sexual dysfunctions.

In both males and females, the first step is to identify the phase in the sexual response cycle at which the dysfunction arises (see Table 16.1). The second step is to identify the etiology (i.e., physical, psychological, medication, or substance effects). Management strategies can include pharmacological, surgical, and psychotherapeutic interventions. Providing education to the patient about normative patterns of physiological aging may help to alleviate any misconceptions. Education on healthy lifestyle factors (e.g., physical exercise, smoking cessation, minimal alcohol use) may also help treat underlying causes. Encouraging various forms of intimacy (e.g., physical, emotional, cognitive) may help foster the sexual experience. Erectile dysfunction in males can be treated with phosphodiesterase enzyme type 5 inhibitors, vacuum pump devices, intraurethral suppositories, penile injections, and penile prostheses [7]. Use of water-based lubricants, low-dose topical estrogen creams, or estrogen-based vaginal suppositories may treat symptoms caused by urogenital atrophy in females [7]. It may be necessary to refer the patient to an appropriate specialist for further management (see Fig. 16.1).

Question 16.8

In long-term care facilities, inappropriate sexual behaviors are more likely to occur in patients with major neurocognitive disorders.

What Is the Treatment of Inappropriate Sexual Behaviors in Patients with Major Neurocognitive Disorders?

Some patients with major neurocognitive disorders may display public behaviors that are typically done privately because they may not be aware of their surroundings. Others may misidentify another person as their loved one and behave in a manner that is inappropriate in the context of that personal relationship. An acute onset of the sexually inappropriate behavior may point to an episode of delirium and the underlying cause should be identified and treated. Table 16.6 enlists some management strategies of sexually disinhibited behaviors in patients with major neurocognitive disorders [24]. In long-term care patients with major neurocognitive disorders, a key point in managing disinhibited behaviors is to recognize the desire for intimacy and determine ways to safely achieve this natural desire for sexual expression. Non-pharmacological interventions are first-line treatment approaches. Additionally, a range of medication classes have been used in these behaviors, but there have been no randomized controlled trials, in part because of the lack of well-defined methodologies and ethical considerations [24].

Table 16.6 Management of sexually disinhibited behaviors in patients with major neurocognitive disorder in long-term care facilities [24]

Non-pharmacological strategies	Pharmacological strategies
Staff knowledgeable of cues indicating need for intimacy Redirect behavior, verbally or physically Indicate to patient that behavior is inappropriate Isolate patient from other residents of the same sex of which the behavior was directed towards Care provided by staff of opposite sex of which the behavior was directed towards Ignore unwanted sexual behaviors and encourage alternate forms of sexual expression Provide clothing that opens from the back Provide live pets and objects to use with their hands	Selective serotonin reuptake inhibitors Trazodone Tricyclic antidepressants Anxiolytic agents (e.g., buspirone) Antipsychotic agents Anticonvulsant agents Cholinesterase inhibitors (i.e., through possible alteration of testosterone levels) Antiandrogens (e.g., medroxyprogesterone acetate, cyproterone acetate through decrease in serum testosterone) Estrogens (i.e., through decrease in LH and FSH but have side effects of fluid retention, nausea, gynecomastia, and erectile dysfunction) Gonadotropin-releasing hormone analogs (i.e., through acting on hypothalamic-pituitary-testicular axis to suppress testosterone production) Beta blockers Combination therapy (but caution with carbamazepine or cimetidine, as these drugs have important effects on hepatic metabolism and pharmacological interactions)

Question 16.9

Is Asexuality in Later Life a Fact or Myth?

Although there does appear to be a decline in sexual activity with aging, asexuality in later life is a myth. Current data on sexual behavior in later life throw light on this myth of asexuality in later life. Research indicates that having a satisfying sexual relationship is important for older adults with a partner [18]. In the National Social Life, Health, and Aging Study, 39% of men and 17% of women between ages 75 and 85 years reported being sexually active [20]. A Swedish postal survey of men aged 50–80 found that there was a decrease in sexual desire with age, but even among the oldest men (aged 70–80), 46% reported orgasm at least monthly [25]. A study in Perth, Australia, found that older men by age group were sexually active in 11% of cases in the group between ages 90 and 95, 19% in the group aged 85–89, 27% in the group aged 80–84, and 40% in the group aged 75–79 [26]. Sexual activity was positively correlated with good health and a prior active sexual history in men and sexual desire and a healthy partner for women [22]. Sexual needs in older adult life appear to be similar to those in younger adult life, with variations in frequency, intensity, and mode of expression.

Question 16.10

The patient is a 75-year-old divorced male with a diagnosis of major neurocognitive disorder, who has been residing in a long-term care facility for the past year. He has become overly familiar with many of the female residents since his arrival at this facility. Allegedly, his behavioral problems have been going on for a while; he made unwanted sexual advances to female residents and touched other co-residents inappropriately, and occasionally, he was spotted viewing pornographic websites in the computer room, which was a publically shared space. Several family members of the other residents have complained to the management about his behavior. He did not have any family. One day, a staff member entered the room of a 79-year-old female resident who also suffered from a major neurocognitive disorder; this male patient was also present in that room. When the staff member found the male patient, he pulled up his pants while the female resident was observed to be trying to yell for assistance. The patient told the staff member not to be concerned and endorsed that it was a consensual sexual activity. The staff member did not report the incident, but a few weeks later, the female resident's daughter was demanding an explanation about the incident, which she heard from her mother, and stated that she would file a lawsuit against the patient and the long-term care facility for failing to protect her mother if an explanation was not forthcoming.

A. What Could Staff Members Have Done at This Time to Promote a Safe Living Environment for All Long-Term Care Facility Residents?

The patient was noted to make unwanted sexual advances, touching other co-residents inappropriately, and viewing pornography in the public computer room, all of which was prior to the observed sexual encounter. Staff members should have documented in writing all the complaints received and incidents observed. If inappropriate sexual behavior continued after an initial warning, the use of time spent on the public computer could have been supervised or limited, and contact with other residents, especially female residents, should have been better monitored or limited. If such behaviors continued, the long-term care facility would have had an obligation to contact the police and possibly may have needed to explore having the patient transferred to another long-term care facility that could have better accommodated and supervised his needs.

B. What Could the Staff Member Have Done Immediately After Observing the Sexual Interaction Between the Patient and the Female Co-resident?

The staff member should have reported the incident to the manager of the long-term care facility, which would likely have triggered an internal investigation and determination of whether this sexual encounter was consensual or not. If it was not, the facility could have taken the appropriate action including contacting the authorities, and if yes, then this could have been explained to the daughter.

C. How Could the Long-Term Care Facility Manager Have Responded to the Daughter in a Manner That Protected Her Mother and Other Residents from Unwanted Sexual Contact in the Future?

The long-term care facility manager should have issued a formal apology for the staff member having not reported the incident. An internal investigation should have been launched to determine the sequence of events and whether the sexual acts were consensual or not. Following the investigation, implementing new practices will be essential. Examples of such practices include:

- Formal process for patients to report unwanted sexual advances
- Staff training to watch for and report inappropriate sexual behavior
- Policies and procedures for breaking rules related to inappropriate sexual practices

- Specialty programs for challenging patients to better manage their sexual behaviors
- Patient education regarding sexuality in older adults

D. In General, a Presumption of Cognitive Capacity Is Independent of Age or Type of Neuropsychiatric Pathology. If Decisional Capacity Is in Question, the Clinician Should Conduct a Formal Decisional Capacity Assessment. Even if Patients May Be Found Incapable for Certain Decisions (e.g., Treatment, Finances), They Could Still Be Capable for Other Decisions (e.g., Sexual Activity). What Elements Should Be Considered When Performing a Sexual Decisional Capacity Assessment? What Role Does the Risk Assessment Play in Patients with Sexual Aggression?

A sexual decisional capacity assessment determines whether a person can understand and appreciate the consequences of sexual activity. In order to consent to sexual relations, a person has to have sufficient knowledge and understanding of the nature of the sexual activity, the reasonably foreseeable consequences, and the capacity to choose whether or not to engage in sexual activity without coercion [27]. The nature of a neuropsychiatric disorder and adherence to medication can impact a person's capacity to consent at various times. Therefore, a person may be capable to consent to sexual relations at one point in time but be incapable at another. Clinicians must also consider an older adult's potentially fluctuating capacity to consent to sexual relationships. The fluctuating decisional capacity poses serious problems for clinicians in assessing decisional capacity of their patients. If the transition from capable to incapable occurs too rapidly, there may not be an opportunity for clinicians, staff members, or other individuals to notice any changes in the decisional capacity of the patient.

As a preemptive action, it may be useful to conduct regular risk assessments with patients in institutional settings known to be of moderate to high risk of sexual aggression, especially in older adults with criminal record for sexual misconduct in the past or aggression associated with major neurocognitive disorders, even where staff members are supervising [28]. It should never be assumed that sexual complaints are illegitimate or delusional in nature. A comprehensive investigation to understand the full context of what events occurred should be accomplished. If that investigation leads to a reasonable belief that sexual misconduct occurred, the police may need to be contacted. If the complainant is diagnosed with a major neurocognitive disorder and if a formal charge occurs, court processes will need to be explained for the complainant to be aware of the subsequent legal steps. For those who have a demonstrated history of sexual harassment, protective practices need to be in place, particularly in institutional settings, to ensure monitoring and seclusion where necessary.

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Topic 17: Elder Abuse and Neglect

Question 17.1

Elder abuse has been recognized as a global problem that has generated significant research, policy, and clinical interest in the past 20 years [1]. The term "elder abuse" proposed by the US National Academy of Sciences in 2003 has become widely accepted and is defined as: "(a) Intentional actions that cause harm or create a serious risk of harm (whether or not harm is intended) to a vulnerable elder by a caregiver or other person who stands in a trust relationship, or (b) failure by a caregiver to satisfy the elder's basic needs or to protect the elder from harm" [2].

List and Describe Five Types of Elder Mistreatment

The 2008 National Elder Mistreatment Study of cognitively intact US adults older than age 60 indicated that 10% experienced various forms of mistreatment in the previous year, the most common being financial abuse (5.2%), followed by neglect (5.1%), psychological abuse (4.6%), and physical abuse, including sexual mistreatment (2.2%) [3]. A systematic review of elder abuse found that nearly 25% of survey respondents reported having experienced neglect, and about 20% responded that they had been psychologically abused [4]. Cognitively impaired older adults are at particular risk for mistreatment. Approximately one-third of US physicians detect elder abuse in a given year, while only half report the abuse to the local health authority [5]. Among 126 geriatric patients assessed for decisional capacity by a hospital geriatric psychiatry service covering both outpatients and inpatients, 16% had suspected or confirmed abuse [6]. Table 17.1 summarizes the types of elder mistreatment and associated characteristics.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_17

Table 17.1 Types of elder abuse and associated examples [1]

Type of mistreatment	Description and examples
Psychological abuse	Acts carried out with the intention of causing emotional pain or injury, e.g., personal insults, threats, or physical and social isolation
Physical abuse	Acts carried out with the intention of causing physical pain or injury, e.g., hitting, slapping, scratching, pinching, biting; unwanted sexual contact; inappropriate restraint by mechanical or chemical means
Neglect	Failure of a designated caregiver to meet the needs of a dependent older person, e.g., assistance with activities of daily living (grooming, hygiene, ambulation); take medications; basic nutrition
Sexual assault	Sexual exploitation of a dependent older person
Material exploitation	Misappropriation of an elder's money or property through theft, fraud, or embezzlement

Elder self-neglect is an often unrecognized problem that is characterized by individuals living in squalor and unsafe living situations [7]. The most common form of mistreatment by Adult Protective Services across the USA [8] is self-neglect due to medical, neurological, or psychiatric disorders that pose barriers to self-care.

Question 17.2

What Are Common Potential Consequences for Mistreatment of the Older Adult Victim?

Common potential consequences for elder mistreatment include the following [9–11]:

- Significant psychiatric illness
- Physical harm
- Exacerbation of chronic illnesses
- Increased risk of hospitalizations and premature mortality

Question 17.3

What Are Risk Factors for Elder Mistreatment?

The following risk factors have been identified as strong predictors for elder mistreatment and neglect in multiple countries around the world [1]:

- *Factors related to victim*: functional dependence/disability, poor physical health, cognitive impairment (such as major neurocognitive disorders, formerly dementia), poor mental health, low income, or socioeconomic status
- *Factors related to Perpetrator*: mental illness, substance abuse, and abuser dependency

Question 17.4

How Can Cognitive Impairment and Caregiver Stress Contribute to Elder Mistreatment?

In a New England (USA) cohort study of older adults, the development of cognitive impairment was associated with a fivefold increased risk of abuse, compared to cognitively intact subjects [12]. Among patients with major neurocognitive disorder (NCD), another study found that one-third of these patients threatened or engaged in assaultive behavior against their caregivers, increasing the risk of reciprocal rage and aggression [13]. In this potentially volatile setting, 12% of these caregivers commit acts of physical violence toward the patient [13].

Question 17.5

What Are Physical and Behavioral Indicators of Elder Mistreatment to Be Aware of?

The following are findings on patient mental status and physical exam, and caregiver behaviors that hint at elder mistreatment [14–16]:

Mental Status Exam of Patient

- *Appearance*: disheveled or unkempt (e.g., uncombed hair, dirt under fingernails), inappropriate attire (e.g., short sleeves, no coat/jacket in cold weather), malodorous (e.g., of urine or feces, obviously unbathed in days or weeks), edentulous but lacking dentures when known to have seen a dentist, lacking glasses or hearing aids
- *Behavior*: reserved, not forthcoming, tentative, deferring to caregiver to answer questions, frequently glancing at caregiver as if seeking approval when answering questions, caregiver speaking on behalf of patient or interrupting patient frequently, avoids eye contact with you or the caregiver when answering specific questions, timid/fearful when interacting directly with the caregiver (e.g., flinching when caregiver comes close to them)

- *Speech*: halting, deflecting or vaguely answering questions regarding suspicious findings/illness. Answers questions as if parroting a rehearsed statement when probed about suspicious injuries or other areas of concern
- *Mood*: fearful, very anxious
- *Affect*: blunted or restricted. Significant variation in patient's affect/interactivity between when interviewing the patient alone (less, more forthcoming) and in the presence of the caregiver
- *Thought process*: disorganized, scattered, perseverative, or other evidence of major neurocognitive disorder
- *Thought content*: inconsistent or implausible explanations for suspicious signs and symptoms

Physical Exam of Patient

- Bruises—multiple bruises at various stages of healing, or in unusual locations (e.g., chest wall, inner thighs), or in suspicious patterns (e.g., circumferential around the arm, as if grabbed)
- Burns—such as from cigarettes
- Lacerations/injuries—as if from bite marks
- Fractures—broken facial bones, evidence of old or misaligned fractures

Caregiver Behaviors

- Appears indifferent, impatient, or hostile toward patient. (Observations of the patient and caregiver before or after the evaluation—when both believe they're not being watched—can be very informative.)
- Evidence of substance abuse, mental illness
- Is defensive, guarded, or hostile toward you and other clinical staff
- Unfamiliar with pertinent details of patient's medical, social, and functional situation. For example, does not recall when the patient last saw a doctor or the name of the patient's pharmacy
- Preoccupied with costs or being inconvenienced with caregiver requirements

Question 17.6

If You Suspect Elder Abuse, What Are Examples of Questions You Could Ask to Elicit More Information About Suspected Physical or Psychological Abuse and/or Neglect?

A number of screening tools have been developed to assist in identifying patients at risk for elder abuse and mistreatment [17–20]. Yaffe et al. developed and validated the Elder Abuse Suspicion Index (EASI) to assist family physicians screen for patients at risk for elder abuse [19]. The EASI is designed to be used for patients 65 years and

older with a Mini-Mental State Examination of at least 24 and may be a useful screening tool. The purpose of EASI is to help physicians identify patients who require additional inquiry to rule out mistreatment. Comprised of six questions, EASI can be rapidly administered as part of a routine clinic visit. All six questions are in a closed-ended YES/NO format that should be answered in succession.

The first five questions are asked by the physician to the patient. For example, one question is "Has anyone prevented you from getting food, clothes, medication, glasses, hearing aids, or medical care or from being with people you wanted to be with?" The sixth, and final, question is for the physician to ask himself or herself with information on findings on exam that warrant further exploration and the prompt, "Did you notice any of these today or in the past 12 months?"

If you suspect sexual abuse, you can ask questions such as: "Has anyone made lewd or sexually offensive comments to you?" "Has anyone touched you sexually without your consent or touched you inappropriately in a way that made you feel uncomfortable?"

Question 17.7

Is Anyone on the Healthcare Team Legally Obligated to Report Suspected Elder Mistreatment?

Most US states have mandatory reporting requirements for suspected abuse of dependent older adults to agencies such as Adult Protective Services (APS), which then initiates an investigation. Reporting laws vary by province or territory in Canada, with most provinces limiting reporting to health professionals.

Question 17.8

Ms. M, an 85-year-old white female, was brought to the emergency department (ED) by family members after she became acutely psychotic and behaviorally disruptive at home. The ED physician calls you, explaining, "This lady's acutely psychotic. We scanned her head, nothing was found. Her vitals, renal panel, and CBC were normal. She is medically cleared for an admission to psychiatry."

A. Based on This Narrative, What Are the Likely Diagnoses to Consider?

Always consider delirium with subacute to acute mental status changes. She could have developed major neurocognitive disorder with agitation, not necessarily

delirium. Drug or alcohol abuse needs to be considered. Thyroid disease, especially with noncompliance, can lead to psychotic and/or cognitive decompensation. Other psychiatric disorders (e.g., chronic schizophrenia; major depressive disorder, severe, with psychotic features; bipolar disorder) also need to be considered.

B. What Assessments Do You Request Before You See Her in the ED?

A partial delirium work has been done. But she also needs liver-associated enzymes, full thyroid panel, calcium, B_{12}, urinalysis/toxicology, and blood alcohol level. An ECG is needed.

Case continued: When you get to the ED, Ms. M's son (Ron) pulls you aside and asks why it took you so long to see his mother. He describes himself as his mother's primary caregiver and states that he needs to leave the ED because he cannot afford to lose another job by being late again. Ron stated that Ms. M had been doing "fine" until a week ago, when she started getting out of bed at night and wandered around the house, singing or yelling loudly. Ron and his girlfriend have been awakened at all hours of the night as a result. Tonight, Ms. M barged into his bedroom and started screaming "President Kennedy is calling me to The White House!" Ron denied that his mother has ever had a psychiatric disorder and chuckled when asked if Ms. M has ever had a substance abuse problem. He rolled his eyes and said "Are you kidding me? That woman's a teetotaling goody two shoes. She gets all freaked out if I have a few beers." He said "I have no idea" when asked about Ms. M's medical and surgical history, but recalled that she had "some kind of surgery in her neck" at about the time she sold her real estate company 15 years ago. Ron did not know if Ms. M is on any medications, the name of her physician, or what pharmacy she goes to, if any. Ron reveals that Ms. M's husband (his stepfather) was a "fancy lawyer" and died from "heart trouble … 5 or 10 years ago." Ron asks if you think Ms. M has schizophrenia.

C. What Do You Tell Ron?

Schizophrenia with onset over age of 60 is rare [21]. Most likely causes of a psychotic presentation in older patients are delirium and/or major neurocognitive disorder [22].

Case continued: Ron insisted that he be present as Ms. M was interviewed, explaining that he needed to make sure Ms. M provided accurate information. On exam, Ms. M is disheveled and anxiously dysphoric, fully alert, but psychotic, repeating her delusions about the President. She denies auditory or visual hallucinations and suicidal or homicidal ideation. She is mildly tangential and perseverative. She is guarded, anxiously glancing at Ron, then blurting out: "They're after me," and "I don't like that woman." She refused to elaborate, at which point Ron states,

"As you can see, she's crazy! She's making absolutely no sense." A Montreal Cognitive Assessment (MoCA) is 16/30 with deficits in multiple domains. Additional laboratory studies reveal TSH of 85 mIU/L (elevated value), with full thyroid panel pending.

D. What Is the Diagnosis?

The diagnosis is a neurocognitive disorder due to another medical condition (hypothyroidism in this case) [23, 24]. Whether this is delirium per se or major neurocognitive disorder with behavioral disturbances/psychotic features due to hypothyroidism is somewhat of an academic point.

E. She Obviously Needs Thyroid Replacement. How Do You Approach Her Psychiatric Management?

She is admitted to internal medicine to manage her profound hypothyroidism. While classically associated with melancholic depression, profound hypothyroidism can be associated with a primary psychotic presentation, delirium, or major neurocognitive disorder [25]. She should receive standard delirium precautions. She is started on an antipsychotic (e.g., risperidone 0.5 mg or 1 mg PO bid) with close monitoring of her psychiatric status, including serial MoCA, as her psychotic symptoms are likely affecting her MoCA score.

Case continued: She is started on thyroid replacement and risperidone. Within 1 week she is no longer as delusional and her MoCA is 20/30. She still cannot take care of herself safely due to residual symptoms. The internal medicine resident says that her levothyroxine has been restarted and she is "medically cleared" now "since her hypothyroidism is now an outpatient problem; she just needs a repeat thyroid panel in 6–8 weeks."

The internal medicine team later learns that the patient had a thyroidectomy about 20 years ago, and had been on levothyroxine 125 mcg daily since that time. It turns out that Ms. M's iatrogenic hypothyroidism had been well controlled since then and was previously compliant in taking her medications.

F. What Recommendations Do You Have Regarding Future Psychiatric Treatment?

She needs to stay on antipsychotics until her delusional symptoms are in complete remission and her thyroid status has (with treatment) renormalized. Once she is taking oral thyroid medication, she could be transferred to an inpatient psychiatric unit if her lingering psychiatric symptoms justify this treatment model.

G. What Parts of Ms. M's Presentation Are Concerning for Elder Mistreatment?

1. Her son's behavior was notably self-absorbed. Rather than concern for his mother's welfare, he was worried about his and his girlfriend's lack of sleep and potential loss of a new job.
2. Her son gave hints of financial instability in his own life, which apparently contrasts with that of his mother and stepfather (he just got a relatively unskilled, low-paying job, has a history of job loss and tardiness to work).
3. Her son made statements suggesting that his mother's values/lifestyle differ from his own; e.g., his snide remark regarding Ms. M being a "teetotaler," and possible minimization of his own drinking behaviors.
4. Ron insists on being present for the interview, possibly in an attempt to intimidate his mother into keeping silent. On exam, Ms. M appears anxious and guarded in Ron's presence and made vague statements about someone being "after" her and about her dislike for "that woman." Ron dismisses these statements. Rather than assuming that these statements were part of her paranoia, it is important to investigate whether the patient was referring to Ron and his girlfriend.
5. Although describing himself as Ms. M's caregiver, Ron had poor knowledge of the patient's medical problems and medication history. Attentive caregivers typically know the names and contact information of their charges' physicians and pharmacy.

Case continued: Further investigation by the medical social worker reveals that Ron and his unemployed girlfriend moved into Ms. M's home about 6 months ago, presumably to assist Ms. M with transportation to medical appointments, grocery shopping, and to help with chores around the house. Ron did have a part time job as a cashier but spent his money on nonessentials such as video games, beer, and cigarettes. An APS investigation reveals that the patient lives in a large home that she owns in an upper middle-class neighborhood. The home, which was previously meticulously kept, is in disarray, with empty food containers and other trash strewn about the house.

Ms. M has uncharacteristically missed two scheduled appointments with her primary care physician and had failed to obtain requisite laboratory monitoring studies in the past several months. A call to her pharmacy reveals that she had not picked up her prescriptions for levothyroxine for the past 2 months. Concerned, the pharmacist called Ms. M at home, but her telephone line had been disconnected due to failure to pay the phone bill.

H. What Is Your Diagnostic Impression?

The medical social workers' findings strongly suggest elder neglect and are very suspicious for psychological abuse and financial exploitation.

Question 17.9

A 67-year-old white male with no previous psychiatric history presents to your clinic with a complaint of "losing my memory. I think I am getting Alzheimer's like my father did. It's hopeless. I cannot remember things and I can't function." He denied having any memory problems until 6 months ago. After his wife was diagnosed with cancer 2 years ago, he retired earlier than he had previously planned from his job as a district manager of a four-star hotel chain. He said he "loved" his job, which allowed him to travel all over the world and to meet many different people. His wife died about a year ago, and he said that his mood has been "down in the dumps" since then.

He began to have some struggles with sleep and sometimes would drink wine "to chill me out and help me to sleep" but "I don't do it every day, I don't drink and drive, so it really isn't a problem." He spends a lot of time at home, much of it sitting on the couch, watching television. He said he has lost about 50 pounds in the past year because he does not feel like eating. Describing himself as a "former gym rat" who worked out 5 days a week, he now leads a sedentary lifestyle. Previously an enthusiastic cook who tried new recipes all the time, he now has to force himself to eat even once a day ("Usually ramen noodles.")

Previously a "clean-cut suit and tie type of guy" who sometimes took two showers a day, he now forces himself to take a shower once a week. Increasingly, his major concern is memory and concentration. He has difficulty sustaining attention in conversation and forgets things he has just learned, and it takes much longer for him to recall names of people, names of places he has been, and news items. He denies unsafe behavior, problems with driving, and wandering.

His medical history includes chronic hypertension and mild hyperlipidemia, both of which are treated with medications. He is a former smoker ("used to be one pack/day due to the stress"), but he stopped at age 55 due to health concerns. He has no history of cerebrovascular accidents, cardiac events, or diabetes mellitus. He has no psychiatric history, and family psychiatric history is positive for vascular neurocognitive disorder in his late father. His social environment is stable; he owns his home and his two adult sons live in the area. He is well insured and has no financial problems.

On exam, he is very slender and is wearing baggy slacks and a rumpled button-down shirt that is stained with coffee. His hair is greasy and uncombed; he has several-day growth of facial hair. He is interpersonally reserved, avoids eye contact, and apologizes several times for his appearance. He is mildly anxious and dysphoric, non-tearful, non-labile, and non-melancholic. He denies suicidal ideation or psychotic symptoms. He has clear psychomotor retardation without a movement disorder. He is organized and mildly perseverative and tends to repeat himself.

On formal cognitive testing with the MoCA, he scores 21/30, with 0/5 on recall memory, 1/3 on concentration, 0/1 on attention, and 0/1 on list generation. Notably, he quickly gives up if he struggles with an individual item and reacts with a catastrophic statement; e.g., "see, I told you I am losing it." Hamilton Depression Rating Scale (Ham-D) is 24 (consistent with moderate/severe depression). He initially

balks at the recommendation for neuroimaging but then says "it will prove that I have Alzheimer's so we had better do it."

A. What Are the Main Diagnostic Probabilities at This Time?

His differential diagnosis includes the following: major depressive disorder, major neurocognitive disorder due to Alzheimer disease and/or vascular disease, or some combination of these [26].

B. What Workup Would You Propose at This Time?

Due to the first lifetime episode of depressive disorder with cognitive impairment on formal testing, he needs neuroimaging for evidence of vascular disease and/or Alzheimer disease. He also needs TSH; other screening laboratory studies include renal panel, liver-associated enzymes, CBC, B_{12}, and urinalysis/toxicology. His alcohol use is not helping, but there is not persuasive evidence of alcohol use disorder per se.

C. How Would You Approach Treating His Obvious Self-Neglect?

Previously a healthy, fit, and socially engaged man who took care of himself, the patient's mental and physical states are far from his baseline. His mood is currently too depressed for him to exert more than a minimal effort to maintain his health and hygiene. However, his repeated apologies to you about his appearance, as well as his help-seeking behaviors (keeping his appointment and willingness to complete laboratory assessment and other studies), suggest that pointing out his previous high-functional status, and inquiring more about his previous social life could boost his ego functioning.

Case continued: The patient admits, after much probing, that he has a wide circle of friends and a solid relationship with his sons but has been avoiding them because he is so embarrassed by his worsening memory and inability to care for himself. He admitted that many of his former gym and work buddies have attempted to reach out to him, even offering to bring him food, but he has refused.

He initially resists your suggestion to start getting in contact with his family and friends again, saying: "I'm used to taking care of everybody else. I don't feel comfortable asking for help." He eventually agrees to consider it after you point out that going to the gym 5 days a week probably was not always "comfortable" either but that he was able to discipline himself to do it anyways. He spontaneously mentions that his "pride" has kept him from accepting help from his many friends and family members and agrees to call his sons to help him set up a plan to ensure that he starts eating regular meals and develop a schedule to get him out of the house regularly.

The magnetic resonance imaging (MRI) shows diffuse white matter disease, no focal areas of atrophy, and questionably slight diffuse cortical atrophy. Other laboratory studies are normal.

D. How Do the Results of Neuroimaging Refine Your Diagnosis?

The positive neuroimaging, vascular disease risk factors, and cognitive impairment mean that this is not "typical" major depression. Alzheimer disease would likely show more notable atrophy than vascular findings but is still possible. Normal range TSH rules out hypothyroidism.

E. What Would Be Your Clinical Approach Now?

With this constellation of findings, empirical treatment of his depressive disorder is imperative. Venlafaxine is avoided in hypertensive patients. A selective reuptake inhibitor (SSRI) (e.g., sertraline, citalopram) or serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g., duloxetine) can be considered. However, given the significant insomnia and appetite loss, the first approach should be mirtazapine (a noradrenergic and specific serotonergic antidepressant (NaSSA), which will address these neurovegetative signs promptly. At follow-up, reassessment of cognitive status is needed.

Case continued: He reluctantly accepts that depression is present and hopes "that you are right about this, otherwise I have Alzheimer's and it's hopeless." You prescribe mirtazapine 15 mg at bedtime, with an increase to 30 mg at bedtime after 2 weeks. He returns in 4 weeks, stating that his sleep and appetite seem better, and though he is not sure if his memory is much better, "at least it isn't worse, and maybe the sleep is helping me to think better and be less stressed." On exam he is a bit brighter in his affect, scores a 24/30 on the MoCA, and his Ham-D has improved to 14 (mostly attributable to improved sleep and appetite symptoms).

F. Now What Do You Do?

He should be maintained on mirtazapine indefinitely with serial MoCA and Ham-Ds. You should communicate with his internist and suggest maximally aggressive control of blood pressure and lipid status to mitigate the risk of vascular neurocognitive disorder. You also advise him to cease alcohol intake altogether, since it may be contributing to his dysphoria. You schedule a face-to-face follow-up visit with you in 4 weeks and inform him that a clinic nurse will call him in 1–2 weeks to see how he is doing.

Question 17.10

Harry, an 84-year-old widowed Asian male, is admitted to the general medical floor for "failure to thrive." The internal medicine resident requests a psychiatric consult for "Depression. Transfer to inpatient psychiatry after medically cleared." A review of the medical records indicates that Harry has a history of diabetes mellitus type 2, gout, and gastroesophageal reflux disease, but has never been hospitalized before. His home medication regimen includes metformin, lisinopril, colchicine, and pantoprazole. He has no psychiatric or substance abuse history.

Family members have noticed a gradually deteriorating cognitive and social functioning in the past 6 months. Family members are having to do more and more to help him and report that he seems "depressed, withdrawn" and sometimes "we think he is seeing things" as he reaches out to grasp things that are not there. He is also not walking well, stumbling and needing assistance, and says that "the feeling in my legs isn't right." Family members are not sure what to make of that "as he always has a lot of physical complaints that the doctor can never find a cause for." They report that Harry is originally from China and immigrated to the USA when he was 20 years old. His wife of 55 years died 3 years ago; his four children have offered to take them into their homes, but Harry has refused, explaining that he did not want to be a "burden" on them.

A. What Diagnostic Possibilities Do You Entertain Based on the Narrative?

An episode of depressive disorder can present primarily as cognitive and social impairment being more dramatic than tearfulness/hopelessness/mood symptoms. However, dementia (major neurocognitive disorder) syndromes could present in a much similar way, so rule out of neurocognitive disorders needs to be done concurrently. He has some psychotic symptoms (apparent visual hallucinations); new-onset psychosis in older patients is most commonly associated with neurocognitive disorder, less commonly with depressive disorder, and only rarely with a *forme fruste* of new-onset schizophrenia-spectrum disorder.

B. What Diagnostic Workup Do You Request?

Computerized tomography (CT) of head, metabolic panel, liver-associated enzymes, CBC, TSH, B_{12}, and calcium will need to be ordered, as these are standard workup laboratory studies in major neurocognitive disorder.

Case continued: On exam, Harry is alert, with good eye contact, no restlessness, with Richmond Agitation and Sedation Scale (RASS) score of 0. He is ill appearing, cachectic, and marginally groomed and speaks in hushed tones only; his affect is bluntly perplexed and is non-tearful. He cannot tell you much about recent events,

only that he is "not doing good," and relies on his family for mostly everything. He reports "seeing birds and butterflies in here" (he reaches out as if to catch one which he then "shows" you). Thought process is concrete but organized. Ham-D is 20, and MoCA performed in Mandarin language with a translator is 15/30.

C. What Are the Diagnostic Possibilities?

He currently looks like a "3 Ds" patient, with possible delirium, depression, and/or dementia (major neurocognitive disorder), with likely some elements of all three. The acute presentation mandates a full delirium workup, whereas the cognitive impairment directs a workup for a major neurocognitive disorder, including neuroimaging.

D. How Do You Intervene Now?

It is prudent to offer a PRN (on-demand) antipsychotic for his hallucinatory symptoms, though you do not observe agitated behavior or obvious distress associated with them. A low dose of risperidone (e.g., 0.25 mg q6h PRN) would be typical.

Case continued: CT scan reveals cortical atrophy and white matter disease. There is evidence of mild dehydration and macrocytic anemia. Liver-associated enzymes are normal. TSH is within normal range. B_{12} is 189 pg/mL; the medicine resident tells you "that's good, that is the normal range."

E. How Do You Interpret These Findings?

The CT findings are more consistent with major neurocognitive disorder than major depressive disorder, though such findings are often incidental in many patients. The B_{12} level, though within reference range (but values may vary among laboratories), is *not* "normal" in a patient with depressive and cognitive symptoms. In patients who are symptomatic, B_{12} supplementation is needed to bring the level to >350 pg/mL (> 250 pmol/L) and then reassess the depressed patient [27, 28].

Case continued: You call Harry's son with the results and inquire more about Harry's eating habits. You learn that until a year ago, one of Harry's daughters used to stop by Harry's house 5 days a week during her lunch hour, dropping off food that she bought from various takeout and deli restaurants; he typically had enough food for lunch and dinner. This daughter moved out of the area about a year ago. Before doing so, she arranged for a local Meals-on-Wheels program to deliver meals to her father every weekday. When visiting Harry on weekends, this son found piles of unopened boxes of food that had been delivered by the Meals-on-Wheels program. Harry reports to you that he did not like most of the food that was delivered to him and made himself instant ramen noodles to eat when he was hungry.

Table 17.2 Medications that lower vitamin B_{12} concentration

Interacting medication	Proposed mechanism
Metformin	Multifactorial: effect on intestinal motility, bacterial overgrowth, altered calcium-dependent uptake of vitamin B_{12}/intrinsic factor complex in the terminal ileum
Proton pump inhibitors (PPIs)	Increased gastric pH (i.e., more alkaline), which can impair the activation of pepsin (pepsinogen is not as effectively converted to pepsin); pepsin is necessary to free B_{12} bound to protein in the ingested food in order to bind to an R-binder
Histamine 2 receptor antagonists	Increased gastric pH (i.e., more alkaline), which can impair the activation of pepsin, similar to PPIs
Chloramphenicol	Possibly through bone marrow suppression, depriving red blood cells from utilizing available B_{12}
Colchicine	Impairs/inhibits the receptors in the terminal ileum for which B_{12}/intrinsic factor complexes bid to for absorption
Alcohol	Impaired intestinal absorption and ability of pancreas to secrete proteases necessary to release B_{12} from R-binders within the duodenum

From: Busti AJ. "Medications known to decrease Vitamin B12 levels" in Evidence-Based Medicine. https://www.ebmconsult.com/articles/vitamin-b12-medication-interactions-lower-levels?action=search&search_box=b12&search_within=&type_of_search=&onetimeadvanced=auto. October 2015

F. What Factors May Have Contributed to Harry's Vitamin B_{12} Deficiency?

Since he stopped receiving daily meals from his daughter, Harry's diet has probably been low in sources of vitamin B_{12}, which tend to also be high in protein and iron, which explains his mild macrocytic anemia. Dietary sources high in vitamin B_{12} include shellfish (clams, mussels, oysters), fatty fish (mackerel, salmon, sardines), beef, and fortified hot and cold cereals. In addition, Harry is currently taking three different medications—metformin, colchicine, and proton pump inhibitors—that may be lowering Harry's B_{12} levels. Refer to Table 17.2 for medications that lower vitamin B_{12} concentration [29].

G. What Treatment Do You Recommend Next?

Have the internal medicine resident order oral B_{12}, where a typical dose is 1000 mcg/day. If oral B_{12} cannot reliably be delivered, intramuscular alternatives can be considered. You also order a dietary/nutrition consult to further assess Harry's diet and to make recommendations to Harry and his family for how to meet his nutritional need.

H. What Recommendations Do You Make to Treat His Psychiatric Symptoms?

It would be prudent to empirically treat Harry's depressive and psychotic symptoms while monitoring his cognitive symptoms. If the bulk of his presentation is actually

due to B_{12} deficiency, he may respond symptomatically to B_{12} supplementation and not necessarily need indefinite treatment with antidepressant or antipsychotic. With close clinical follow-up and monitoring, starting doses of mirtazapine 7.5 mg at bedtime and risperidone 0.5 mg at bedtime could be initiated, and titrated as needed to optimize response.

I. What Kind of Follow-Up Do You Recommend for Harry After He Is Discharged from the Hospital?

Regular clinic follow-up includes serial Ham-Ds and MoCAs, at least. Once the Ham-D score is no longer in the depressive disorder range (typically <16 and a 50% improvement from initial value), he is no longer psychotic, and his B_{12} level is now safely above 350 pg/mL, you need to decide whether continued mirtazapine and risperidone are still indicated.

Harry's presentation includes self-neglect, even with the presence of engaged, concerned family members in his life. Home health visits, and engagement with an outpatient social service program may be of benefit for Harry. It is possible that Harry will be more amenable to having non-family members help him and will feel like he is less of a "burden" if he is getting assistance from "professionals."

Despite his family's efforts to meet his nutritional needs, Harry did not eat the food that was delivered to him. It is possible that Harry's diet would improve if he participated in a nutrition program that targeted older Asian people in his community. Harry might also benefit from more social interactions, especially now that his daughter is no longer visiting him every weekday. Rather than a meal delivery program, a nutrition program that is based at a culturally specific community center—common in larger cities—may be available.

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Topic 18: End-of-Life Care

Question 18.1

A. What Is End-of-Life (EOL) Care?

People are living longer, and at increasingly older ages, often with multiple medical problems that complicate end-of-life (EOL) care [1, 2]. The definition of EOL care varies, with the National Institutes of Health making a consensus statement in 2004 that "evidence does not support a precise definition of the interval referred to as end of life or its transitions" [3] and that EOL should not be defined by a specific time frame unless evidence can support reliable prognostication. Nevertheless, various agencies, independent organizations, researchers, and clinicians generally regard EOL as the time when individuals are likely to die within 12 months. This includes patients whose death is imminent (hours to days) and those with advanced, progressive, or incurable conditions whose general frailty and/or coexisting conditions indicate that they are expected to die within 12 months [4].

B. How Does EOL Care Affect Older Patients and Their Families?

Since the 1990s, the inadequacy of EOL care among the older adult population has received increasing attention in the medical literature [5, 6], with studies indicating that patients were not receiving the type of care they wanted at the end of the lives [7]. In the past decade, improving palliative care and the completion of advance care planning (ACP) have been the focus of efforts to meet the needs of patients at the end of their lives [8].

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_18

C. According to EOL Studies, What Factors Are Important to Patients for a "Good Death"?

These factors include the following: input into the dying process, symptom management (especially pain-free status), emotional well-being, avoiding prolonged dying, achieving a sense of control, relieving family burden, and strengthening family relationships [8–11]. Meier et al. analyzed the results of 36 studies published between 1996 and 2015 conducted in the USA (n = 13), the UK (n = 7), Japan (n = 3), the Netherlands (n = 3), Thailand (n = 2), Canada including Nova Scotia (n = 2), and Iran, Israel, Saudi Arabia, South Korea, Sweden, and Turkey (all n = 1). In their analysis of the literature, Meier et al. identified 11 core themes. The core themes for a "good death" included preferences for the dying process (e.g., during sleep, death scene), pain-free status, emotional well-being, family (e.g., support, acceptance of death), dignity, life completion (e.g., saying goodbye, life well lived), religiosity/spirituality, treatment preferences (e.g., not prolonging life, control over treatment), quality of life, relationship with clinician (e.g., trust/support/comfort), and other (e.g., physical touch, presence of pets).

Having EOL discussions before death is associated with lower rates of aggressive care (such as mechanical ventilation, resuscitation), earlier enrollment in hospice care, and lower rates of depressive disorders among surviving caregivers after the death of loved ones [9, 12].

D. When Should EOL Discussions with Patients Occur?

Ideally, EOL discussions will occur prior to emergent or urgent situations. Normalizing EOL discussions allows patients to learn about their prerogative for high-quality symptom management and educates clinicians about patients' values and goals. Incorporation of EOL topics can become part of discussions physicians already have regarding diagnoses, prognoses, and treatment options.

Suggested indications for EOL discussions include poor prognosis, when treatment options have a low probability of success, if patients raise concerns about their mortality, and if physicians would not be surprised if the patient died in 6–12 months [13]. Indications for urgent discussions about end-of-life care include (1) patients facing imminent death, (2) patients talking about wanting to die, (3) patients or families inquiring about hospice, (4) recent hospitalization for severe progressive illness, and (5) suffering out of proportion to prognosis.

Question 18.2

Clara is a 65-year-old married Caucasian woman with a history of chronic obstructive pulmonary disease (COPD) who was admitted to the ICU 3 days ago due to acute respiratory failure from pneumonia. Clara was intubated and started on IV antibiotics and corticosteroids. She was transferred to the general medical unit this

afternoon, after she was successfully extubated 24 h ago. The internal medicine service has consulted psychiatry for "severe depression."

This is Clara's first-ever hospitalization but that she has been to the emergency department five times in the past 2 years for COPD exacerbation. She is typically discharged home after treatment with a nebulizer; and she is advised to quit smoking, given prescriptions for corticosteroids and a rescue inhaler, and instructed to follow up with her primary care physician.

You note that Clara is sitting up in bed, breathing comfortably on room air, and finishing her lunch as you enter her room. Upon greeting, Clara starts sobbing, saying that she had been waiting all day to speak with you because she was "devastated" to learn that she was "terminal" and that her doctor told her that the focus would be on palliative care.

Clara reports that ever since she was told that her COPD was "incurable," she has been crying because her doctor told her "there's nothing more" they could do for her. She denies having a history of inpatient or outpatient psychiatric treatment and lacks a history of alcohol or illicit substance abuse. Clara endorses depressed mood and anhedonia since learning from her physician about her poor prognosis. She also denied having thoughts of suicide, homicide, or symptoms of psychosis.

She says that she dreads having to tell her young grandchildren that "Grandma's going to die soon" and laments that she'll never get to see them reach milestones such as graduating from high school and getting married. Clara says that her husband of 40 years took the news of her impending death stoically, and she is hurt because he is still planning to go out of state for the next 3 weeks for his temporary oil field job.

Clara started smoking cigarettes at 14 years old and has been smoking 1–2 packs per day for 40 years. She says that now that she will die soon anyways, there is no point in stopping smoking. She denies having other chronic medical conditions.

Clara asks you to be present as she and her husband inform their adult children of her terminal illness before she is discharged home "to die." She also requests referrals for grief counseling for her and her family.

What Do You Do Next?

Despite evidence to the contrary, Clara is convinced that her death is imminent. Before agreeing to meet with Clara and her family, you need more information. The internal medicine physician informs you that he never told Clara that she was about to die, but informed her that her COPD appears to be worsening, that COPD is generally not considered "reversible," and that she would be referred to a pulmonologist to clarify the extent of her disease. He confirmed that he had used the words "palliative care," by which he meant that the focus on her treatment will be on symptom control and quality of life and not necessarily a "cure."

At your recommendation, this physician agrees to speak with Clara again and to clarify that Clara is currently *not* at risk of imminent death and that although COPD is currently not "curable," she may have several more years of living a relatively

healthy life, provided that she stops smoking and follows the other recommendations of her pulmonologist.

You meet with Clara again and notice that her mood is much brighter than it was when you first met her. She explains that the physician clarified what he meant by palliative care, that she is not expected to die soon. She said her husband had *not* assumed that she was about to die soon, which is why he had planned on working out of state for the next 3 weeks.

Question 18.3

Case continued: Clara sees her primary care physician, Dr. Abernethy, whom she has been seeing for the 10 years, in a post-hospitalization visit. Clara has cut down her cigarette smoking from 2 to 1 pack per day but continues to crave cigarettes. Clara saw her new pulmonologist last week and was informed that based on her FEV1 of 45%, she has severe COPD. Dr. Abernethy explains that COPD is a chronic condition that currently does not have a "cure" but that the severity of Clara's symptoms can be managed with various scheduled and as-needed inhalers and other medications.

She also explains that quitting smoking can help slow down the progression of COPD and will decrease her risk of acute exacerbations and recommends bupropion to help with her quit smoking. Clara agrees to start bupropion and schedules an extended follow-up visit with Dr. Abernethy, who would like to discuss ACP with Clara. Dr. Abernethy gives Clara a booklet about ACP and asks that she review the material before their next appointment. The booklet includes questions and fill-in-the-blank lines for Clara to complete, preferably with her husband and/or another loved one.

What Is Advance Care Planning (ACP)?

ACP is a process in which patients, together with their healthcare providers, family members, and other pertinent individuals, make decisions about their future healthcare, should the patients become incapable of participating in medical treatment decisions [8]. ACP and the importance of EOL care have been supported by legislation and professional medical associations in Australia, the UK, and the USA [14–17]. The provision of ACP appears to increase the frequency of care outside of the acute inpatient setting and compliance with the EOL wishes of patients [13].

Contrary to the assumption that discussion of EOL causes unnecessary distress among dying patients and their family members, intervention study results suggest that it may do the opposite—improve patient and family satisfaction and reduce stress, anxiety, and depressive symptoms among surviving family members and caregivers after the death of the patient [9, 18]. Mignani et al. completed a review of qualitative studies between 2000 and 2015 that explored the perspectives of older adults living in long-term care facilities regarding ACP [19]. They found that the majority of residents in long-term care facilities had already formally made their wishes known about nonmedical matters upon their death such as finances and property, but had not yet addressed the actual process of their deaths via ACPs.

Furthermore, their review indicated that patients and their family members "rely on healthcare professionals' expertise and judgment" on EOL and expect and want healthcare providers who know the older adult well to initiate ACP discussions.

Question 18.4

Case continued: Clara reviews the ACP booklet. Fearing that her husband will get upset by discussing her wishes regarding her future healthcare, Clara avoided reviewing the material with her husband prior to the visit. Clara was pleasantly surprised that the three of them had a calm discussion about her wishes and agreed to participate in a palliative care program for people with severe COPD.

The program includes classes for smoking cessation, anxiety, depression, energy conservation, and exercise, caregiver support groups, individual visits with counselors and chaplains for crises, and an internist who is board certified in hospice and palliative care medicine who is available by referral for patients with end-stage COPD.

Recalling her own reaction to hearing the word "palliative care" before, Clara now realized that the program could encourage her to stop smoking, help manage her COPD symptoms, and give her the support she needed so that she would not be a "burden" on her family.

What Is Palliative Care?

Palliative care is specialized, interdisciplinary medical care for patients with serious illness that focuses on symptom management and explores with patients and families how to improve quality of life, despite the presence of progressive and life-limiting illnesses. In the above example, Clara wrongly assumed that "palliative care" only refers to EOL care. Although palliative care is an important part of EOL care, it is *not* limited to that part of a patient's life.

In fact, the palliative care approach would ideally be incorporated into a patient's care from the time of diagnosis—rather than toward the end of life—since it promotes optimal quality of life throughout the course of illness. As the example of Clara illustrates, however, clinical staff must be careful in how they communicate prognosis and treatment recommendations to their patients. Terms such as "palliative," "chronic," "end of life," and "incurable" need to be explained carefully to ensure that patients understand what is actually meant by these terms.

Question 18.5

Case continued: It has been 5 years since Clara was admitted to the ICU (See case described at Question 18.2). She completely quit smoking for about 2 months but gradually started smoking again thereafter. She attended the palliative care program's COPD support group once a week for about a year and at least once a month since then.

Three years ago, she was diagnosed with bronchogenic carcinoma and treated with surgery and chemotherapy. Despite the rigors of treatment, she continued attending her COPD support group once a month as she underwent cancer treatment.

Several weeks ago, Clara stopped attending groups due to fatigue and weakness. Her support group leader kept in touch with Clara via phone calls and urged her to schedule an appointment with her primary care physician Dr. Abernethy as soon as possible, which she did. Dr. Abernethy found that Clara has unintentionally lost 10 pounds in the past 3 months. Concerned, Dr. Abernethy communicated with her oncologist, who initiated a repeated workup.

The workup revealed recurrence of her lung cancer with brain metastatic disease. She was also found to have systemic hyperparathyroidism and hypercalcemia. The oncologist requested a psychiatric consultation while the patient was admitted for the cancer recurrence workup. The oncologist says "She's upset and depressed about the recurrence of cancer, but is more depressed than most patients in this situation. I don't think she understands everything I am telling her. The depression must be affecting her judgment."

A. What Psychiatric Diagnoses Are to Be Considered?

While depressive disorder is common in cancer, especially with a worsening of prognosis, depressive disorder will not typically dramatically affect cognitive function. You suspect major neurocognitive disorder (NCD) due to the destruction of cortical tissue from metastatic disease and/or delirium from the cancer, hypercalcemia, perilesion edema, and perhaps hypoxia from compromised pulmonary status. Distinguishing delirium and major neurocognitive disorder from direct central nervous system (CNS) disease burden is not always possible with complete confidence.

Case continued: On examination, you find that Clara is debilitated, wasted, and somnolent. When you speak to her, she is able to arouse and maintain eye contact (Richmond Agitation and Sedation Scale (RASS) -1). Though easily fatigued, with effort she can complete the interview. Her affect is blunted and dysphoric. She denies suicidal ideation. However, she says "there are mice all over the place here" (she gestures to the corner of the room) and is perseverative in her thought process. She is aware that she has cancer ("I have had it for years it's mostly my fault, all that stupid smoking") but is not able to describe the recent recurrence or the CNS findings. Her Montreal Cognitive Assessment (MoCA) score is 12/30, with notable deficits in recall, orientation, concentration, and attention.

B. What Is the Diagnosis Based on the Interview?

While she manifests dysphoric affect, her level of consciousness and cognitive status are markedly impaired. A depressive disorder cannot account for all of these

findings. While it can be argued that she has depressed *mood*, it is not persuasive that she has a primary *depressive disorder*. Delirium is a "whole-brain" disease and can present with any psychiatric symptom, including depressed mood.

C. What Workup Would You Recommend?

The following workup is recommended: the usual delirium laboratories (most of which have probably been done by oncology), including renal panel, liver-associated enzymes, and complete blood count (CBC), TSH, calcium, and B_{12}.

D. How Would You Manage Her? What Do You Tell the Oncologist?

This is *not* a depressive disorder, as delirium is the most important psychiatric illness at present. Initiate standard delirium precautions (avoid benzodiazepines, opioids, and anticholinergics), conduct serial cognitive assessments, and use a low dose of a sedating antipsychotic at night (e.g., olanzapine 2.5 or 5 mg) plus PRNs for breakthrough agitation.

E. How Long Should You Continue Olanzapine, Assuming a Positive Response to Treatment?

With stage IV cancer, especially if paraneoplastic syndromes are present, the risk of recurrence of delirium is very high [20]. Therefore, it is preferred that delirium pharmacology be continued indefinitely with serial cognitive assessments.

Question 18.6

Case continued: Clara's mental status improves. She is less perseverative, is alert during the day, and has not had any visual hallucinations since starting olanzapine. She is discharged home with a prescription for olanzapine 2.5 mg PO qhs and with plans for home healthcare services. She is also referred for hospice care.

A. What Is Hospice Care?

Hospice care is multidisciplinary care for patients who have a serious illness in which further curative treatment is not available and for whom life expectancy is no more than 6 months. Hospice care includes *aggressive* comfort ("palliative") care for patients from the medical, emotional, and spiritual perspectives and ideally includes bereavement services for family members and caregivers.

B. What Are the Differences Between Palliative Care and Hospice Care?

Palliative care is specialized, interdisciplinary medical care for patients with serious illness such as COPD that focuses on symptom management and improved quality of life despite the presence of progressive and life-limiting illnesses. Clara's treatment in the past 5 years has had a palliative care approach from the time she was diagnosed with severe COPD. Since then, her palliative care team has helped Clara optimize her quality of life via education, support groups, and individual counseling as she coped with worsening COPD, as well as her diagnosis of bronchogenic carcinoma.

Now diagnosed with stage IV cancer, Clara's life expectancy is anticipated to be no more than 6 months, and her care is transitioning to hospice. Refer to Table 18.1 to see the differences between palliative and hospice care [21–23].

Table 18.1 Differences between palliative and hospice care [21–23]

	Palliative care	Hospice care
Who can be treated?	Anyone with a serious illness for which cure is not anticipated	Anyone with a serious illness in which care is not anticipated *and* whom physicians have certified have <6 months to live
Definition	Comfort care with or without curative intent	Comfort care *without* curative intent. It does not hasten death and is focused on prolonging a life of quality
Will curative treatments be available?	Yes, at the discretion of the patient	No, only symptom relief will be provided
When does it begin?	At the discretion of the physician at any time, at any stage of illness, (serious to end stage)	physicians certify that patient has <6 months to live if disease follows usual course
Duration of care	It depends on the care the patient needs	As long as patient meets criteria of an illness with a life expectancy of months, not years
Where care occurs?	Typically in the hospital but may occur in the home, assisted living facility, and nursing home	Wherever the patient considers "home": usual home or homelike hospice residences, nursing homes, assisted living, veterans' facilities, and hospitals
Who pays for it?	Some private insurers, the patient, and charity	In the USA, >90% paid for by the Medicare hospice benefit
What provides the care?	Interdisciplinary teams address physical, emotional, and spiritual	Interdisciplinary teams address physical, emotional, and spiritual

C. When Did Palliative and Hospice Care Become Recognized as a Medical Specialty?

The concepts of hospice and palliative care have only recently become recognized as a medical specialty in the USA. Between 1996 and 2008, more than 2100 physicians obtained board certification via the American Board of Hospice and Palliative Medicine (ABHPM). The American Board of Medical Specialties (ABMS) approved the creation of the hospice and palliative medicine (HPM) as a subspecialty of ten participating boards—including the American Board of Psychiatry and Neurology—in 2006 [24]. Since 2013, eligibility for HPM certification is only available to physicians who have completed fellowship programs that have been approved by the Accreditation Council for Graduate Medical Education (ACGME). In Canada, palliative care had its start as a specific clinical discipline in 1975. It was not until 1999 that the Royal College of Physicians and Surgeons of Canada (RCPSC) and the College of Family Physicians of Canada (CFPC) sponsored a jointly accredited 1-year training program in palliative medicine, referred to as a year of added competence (YAC). Subsequently, there was significant push to recognize palliative care as a RCPSC-recognized subspecialty. In 2013, palliative medicine became a 2-year subspecialty program recognized by the RCPSC. Subspecialty training can be entered by graduates of internal medicine, anesthesia, neurology, or pediatrics residencies. Family medicine residents who are interested in palliative medicine can still do a 1-year enhanced skills training program in palliative care to obtain a certificate of added competence awarded by the CFPC.

Question 18.7

Case continued: Clara was approved for hospice services by Medicare and has been home from the hospital for 4 weeks. Her medical team predicts that she has 4–6 months to live. Arrangements are made for Clara to receive up to 4 h of nursing care per day in her home. Durable medical equipment such as a hospital bed, bedside commode, and monitoring devices are now available in her home.

An internist who is board certified in HPM oversees a home healthcare team comprised of registered nurses, a pharmacist (PharmD), social workers, certified nursing assistants (CNA), occupational and physical therapists (OT and PT), chaplain, and a registered dietitian (RD). This interdisciplinary team works together to ensure that Clara's medical, emotional, social, and spiritual needs are met.

The internist keeps Clara's longtime primary care physician up to date on Clara's progress. Physicians specializing in psychiatry, anesthesiology, physical medicine, and rehabilitation who are board certified in HPM are available as consultants, as needed.

Clara spends much of the day sleeping but is able to get out of bed with assistance. She typically has 1–2 hospice care team members visiting her daily to take care of her nursing and rehabilitation needs. During their weekly meeting, hospice

team members have noticed that Clara has appeared more "depressed" lately and request that she be seen by a psychiatrist.

A. Clara Has Been Scheduled to See You in Your Office. What Questions Do You Have for the Hospice Team Prior to Seeing Her?

Knowledge of the patient's prognosis and her current level of functioning and engagement with her various therapies is crucial. Obtain a list of current scheduled and as-needed medications, impressions by OT and PT regarding her level of motivation and participation in treatment, information on whether or not she and/or family members are meeting with the team's chaplain and Clara's comments to them about her mood and social interactivity, and her current nutritional status (including her appetite and any recent weight changes).

Case continued: The hospice team sends you a summary of her current diagnoses, treatment plan, and medication list. She is currently on a beta-agonist bronchodilator, phosphodiesterase-4 inhibitor, calcitonin, bisphosphonate, a nonsteroidal anti-inflammatory agent, an opioid, and olanzapine 2.5 mg PO qhs. The OT and PT report that Clara reluctantly and passively engages in treatment with them. Clara has stopped attending support group meetings and avoids accepting calls from concerned members, many of whom she has gotten to know well in the past 5 years. She has lost 5 pounds from her already-slight frame due to poor appetite.

Clara arrives to her appointment with her husband, John. Clara appears frail and gaunt and much older than her stated age. She reports that her mood had been "blah" for several months but has worsened in the past few weeks. She endorsed feeling tired all the time and has difficulty staying asleep. She missed watching several episodes of her favorite soap opera recently, explaining, "Who cares what these crazy people do? It's just a stupid soap opera." This past week, she "got all weepy" after seeing a commercial for a greeting card. ("I couldn't believe it … I started bawling for no reason.").

A few days ago, Clara started thinking about overdosing on her pain medications because she feels so hopeless and worthless. Even when she is feeling physically good, her mood is so "blue" all the time that she would rather die than be so miserable. She is ashamed for having these thoughts because her family would be devastated if she killed herself. Her husband states that Clara has not really had any episodes of confusion since she was discharged from the hospital.

She mentioned being aggrieved about her poor prognosis, but that due to the excellent care received through the palliative care program, she had actually come to terms with her failing health a few years ago. Last week, she started hearing her deceased mother's voice calling to her in the middle of the night, which terrifies her. A few days ago, she started hearing children's voices berating her for being "lazy" and "stupid." She denied having any visual hallucinations. Clara said that she deserves to suffer because she was "too lazy and selfish" to quit smoking. She constantly feels guilty for all the trouble she is causing her family and does not think she deserve all the help she is getting from the hospice team, who have been working so hard to help her. Her MoCA score is 18/30.

Clara wears a breathing mask and gets continuous oxygen at bedtime. At least four times a week, she awakens gasping for air after her oxygen mask slips off her face. She feels "panicky" because she cannot breathe and gets nauseated, and her body feels "tingly" all over. These symptoms subside within a few minutes after putting her oxygen mask on, but it takes more than an hour to fall back asleep. Clara denied feeling particularly anxious during the day because she has her oxygen tank by her side.

B. What Are Clara's Psychiatric Diagnoses?

When you saw her in the hospital a month ago, Clara endorsed depressed mood, but her presentation was more consistent with delirium. On exam today, symptoms of depression predominate. You diagnose her with major depressive disorder (MDD), severe with psychotic features, and anxiety disorder due to COPD.

C. What Is Preparatory Grief, and How Does It Differ from Depression?

Concepts regarding grief reactions to the death of loved ones may be applied to patients who are dying. In palliative care, the term "preparatory grief" is described as a normative process that is experienced by seriously ill patients as they approach death [25]. Preparatory grief can cause significant distress but is considered to be distinct from a depressive disorder.

Preparatory grief and depression can include symptoms such as crying, depressed mood, social withdrawal, and thoughts of suicide. Before diagnosing either, however, it is important to rule out unresolved physical symptoms that could be causing the distress. With preparatory grief, mood symptoms wax and wane over time, self-esteem is preserved, and patients may worry about separation from loved ones as the illness progresses or at death. Preparatory grief may include thoughts of suicide, but it tends to be fleeting.

Preparatory grief tends to respond well to psychosocial and grief counseling. Depressive disorders, however, include a persistent and pervasively depressed mood and/or anhedonia, poor self-worth, hopelessness, ruminations about death and suicide, and an active desire for an expedited death [25].

D. What Are the Differences Between Demoralization, Normative Grief, Complicated Grief, and a Depressive Disorder?

In the palliative care setting, researchers have identified different types of emotional distress in response to losses such as the death of a loved one or being diagnosed with severe life-limiting illnesses, grief, demoralization, and depressive disorders, as noted in Table 18.2 [26–28]. Distinguishing between these types of distress has implications for treatment.

E. What Are Some Challenges in Diagnosing Depression in Palliative Care?

Fatigue, poor appetite, loss of energy, and poor concentration are generalized symptoms associated with advanced medical illnesses such as end-stage COPD and cancer. Medication and other treatments can also cause these symptoms. Since these generalized symptoms are also symptoms of depressive disorders, psychological symptoms need to be given more weight when assessing for depression in the palliative care population [29]. Clara endorsed multiple psychological symptoms of a major depressive episode, including severely depressed mood, tearfulness with minimal provocation, recent onset of suicidal ideation, anhedonia, guilt, and hopelessness.

The concept of "demoralization" was introduced about 50 years ago and has many common features of a depressive disorder, e.g., feelings of hopelessness and helplessness. Palliative care researchers have recently proposed the demoralization syndrome as a diagnostic category separate from depression and as recognizable in the palliative care and hospice settings. Untreated demoralization increases psychic distress, depressive disorders, social withdrawal, impulsive suicidal behaviors, and requests for physician-assisted suicide [28].

Clara's passive involvement in her therapies indicate that she is struggling with demoralization, but the severity and persistence of anhedonia and dysphoria indicate the need for more than psychosocial support and psychotherapy. As noted in Table 18.2, grief can cause significant distress but can be distinguished from a major depressive episode by the preservation of self-worth and episodic feelings of happiness and pleasure. With grief, feelings of sadness tend to occur when an individual is reminded of their impending death and their multiple losses such as their health and well-being, independence, and future opportunities.

Clara, however, reports feeling "constantly" guilty and has feelings of hopelessness and despair even when she feels physically good. Her avoidance of social interactions with those whom she had previously sought out for support and recent onset of suicidal ideation indicate that she is severely depressed.

F. What Is the Rationale in Starting an Antidepressant in a Patient Such as Clara?

Patients such as Clara who are expected to live for several months or longer may benefit from antidepressants. Treatment with standard antidepressants has been shown to be well tolerated in the palliative care population and to be superior to placebo [30]. See Table 18.3 for a list of antidepressant medications [31, 32].

G. What Antidepressant Medication Do You Recommend for Clara?

Patients with lung cancer and CNS metastasis are at particularly high risk for the syndrome of inappropriate antidiuretic hormone secretion (SIADH), so SSRIs, SNRIs,

Table 18.2 Demoralization, grief, and depression in the palliative care setting [26–28]

Diagnosis	Clinical features	Recommended treatment
Demoralization [28]	Perceived incompetence, inability to cope, hopelessness, existential despair, meaninglessness frequently prompting individuals to seek mental health treatment A sense of "giving up" because the individual feels hopeless and that the amount of energy utilized to accomplish a goal does not translate into a tangible result Core features: meaninglessness, helplessness Periods of positive mood and feelings of pleasure when engaging in enjoyable activities	Psychosocial support Psychotherapy
Normative grief	Assuming that grief reactions to a death are similar to grief after learning of one's impending death: predominant affect is feelings of emptiness or loss: Can cause significant suffering, but is considered non-pathologic Dysphoria is experienced as "pangs" or "waves" and tends to decrease in intensity over days to weeks There may be periods of positive emotions or humor Preoccupation with process of dying Self-esteem is generally preserved Initial phase characterized by period of shock, disbelief, or denial, followed by period of distressing emotional and physical symptoms Able to eventually emotionally and mentally process and integrate the loss Activities of daily living preserved Duration varies	Psychosocial support Psychotherapy
Complicated grief	About 15–25% of bereaved individuals Reactive distress to the death, social/identity disruption Disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning Note: has been proposed as a "further area of study" in the DSM-5 as "persistent complex bereavement disorder"	Psychosocial support Psychotherapy May require medication treatment
Depressive disorder	In contrast to grief reaction in general, symptoms of major depressive episode (MDE) include: Persistent depressed mood and the inability to anticipate happiness or pleasure Not associated with specific thoughts or preoccupations to the object of loss Pervasive unhappiness and misery Feelings of worthlessness, self-loathing If preoccupied with death and dying, the thoughts are focused on ending one's own life due to feelings of worthlessness, undeserving of life, or inability to cope with the pain of depression	Psychosocial support Psychotherapy May require medication treatment

Table 18.3 Medication management for depression in palliative care [31, 32]

Medication	Administration availability	Initial starting dose (maximum daily dosage)	Notes
SSRI			– Well tolerated with fewer drug interactions and side effects than TCAs – May take 6–8 weeks for full effect
Fluoxetine	PO (tab, liquid)	20 mg/day (40 mg)	– Numerous drug-drug interactions (e.g., methadone)
Paroxetine	PO (tab, liquid)	20 mg/day (40 mg)	– Numerous drug-drug interactions – Has significant anticholinergic side effects – Short half-life so risk for discontinuation syndrome if stopped abruptly
Sertraline	PO (tab, liquid)	50 mg/day (200 mg)	– Few drug-drug interactions – Well tolerated
Citalopram	PO (tab, liquid)	20 mg/day (maximum 20 mg in patients older than age 60, 40 mg for others)	– Few drug-drug interactions – Increased QTc – Well tolerated
Escitalopram	PO (tab, liquid)	10 mg/day (maximum 10 mg in patients older than age 65, 20 mg for others)	– Few drug-drug interactions – Increased QTc – Well tolerated
SNRI			– Often used concurrently to treat neuropathic pain – May take 6–8 weeks for full effect
Venlafaxine	PO (tab, capsule)	Extended release: 75 mg/day (225 mg)	– May have stimulating effect, increased blood pressure – Monitor for discontinuation syndrome
Desvenlafaxine	PO (tab)	50 mg/day (100 mg)	– Limited data in palliative care setting
Duloxetine	PO (capsule)	30 mg/day (120 mg)	– Frequently used in fibromyalgia and neuropathic pain – Monitor for discontinuation syndrome – Avoid in renal/hepatic disease
Miscellaneous antidepressants			– Used to augment SSRI or SNRI

Table 18.3 (continued)

Bupropion	PO (tab, capsule)	Slow release: 150 mg/day (400 mg) Extended release: 150 mg/day (450 mg)	– Avoid in seizures and eating disorders
Mirtazapine	PO (tab, ODT)	15 mg qhs (60 mg)	– Useful in insomnia and anorexia in lower doses – Decreases nausea, stimulates appetite
TCA			– Cautiously used in patients with cardiac history – Has significant anticholinergic effects – May be useful in neuropathic pain at doses lower than those used to treat depression – May need 4–8 weeks for full effect – Dose at night because of sedating effects
Desipramine	PO (tab)	25 mg qhs (15 0 mg)	– Less anticholinergic than amitriptyline or imipramine, so preferred agent
Imipramine	PO (tab, capsule)	25 mg qhs (100 mg)	
Amitriptyline	PO (tab)	25 mg qhs (150 mg)	
Nortriptyline	PO (capsule, solution)	25 mg qhs (150 mg)	– Less anticholinergic than amitriptyline or imipramine, so preferred agent
Doxepin	PO (capsule, liquid)	25 mg qhs (300 mg)	– Useful for pruritus – Extremely sedating
Psychostimulant			– Effective within a few days – Used in patients with prognosis of days to weeks
Methylphenidate	PO (tab, capsule, liquid)	2.5 mg BID (second dose no later than 1–2 pm) (20 mg)	– Monitor for use in patients with cardiac history – May cause anorexia and insomnia
Wakefulness promoter			
Modafinil	PO (tab)	100 mg/day (400 mg)	– Used often limited by cost – Used primarily for cancer-related fatigue

Note: BID, twice a day; ODT, oral disintegrating tablet; PO, oral; qhs, bedtime. From Leung MW, Kaplan L, Bourgeois JA. Palliative Care for Geriatric Psychiatric Patients with Life-limiting Illness. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018.

and TCAs should be avoided by Clara. The severity of Clara's depressive disorder suggests that the risks of starting an antidepressant are outweighed by its potential benefit. The antidepressant of choice in solid tumor cancers is mirtazapine, which has the added benefit of potentially promoting sleep and improved appetite for Clara.

Case continued: You start Clara on mirtazapine 7.5 mg PO qhs, with instructions to increase it to 15 mg after 1 week.

H. Should Clara Continue Taking Olanzapine?

Yes, a higher dose of olanzapine is indicated to better target the psychotic symptoms and may further help with her sleep and appetite. Clara reported new onset of mood-congruent auditory hallucinations, the presentation of which seems more consistent with depressive disorder-associated psychotic features versus a recurrence of delirium. Clara, who continues to be at risk for delirium, responded well to olanzapine and tolerated it well. Olanzapine may have prevented the recurrence of delirium thus far.

I. What Do You Do About Clara's Dyspnea-Induced Panic Symptoms?

Clara mentioned that she awakens at night when her mask falls off. She has lost a significant amount OF weight, so her current mask is probably too large for her. Since Clara is only awakening and getting panic symptoms when her mask falls off, a top priority is to ensure the adequate delivery of oxygen to Clara as she sleeps.

Recommend that she speak with the RN on her hospice team to be refitted for a new mask as soon as possible. In the meantime, the hospice team OT may be able to offer suggestions on how to retrofit her current mask, so it does not keep falling off of her face (e.g., surgical tape for sensitive skin, use of foam, and other materials to secure the mask on her face).

Benzodiazepines should generally be avoided in patients like Clara, who are at high risk for delirium. In addition, she reported prompt amelioration of her panic symptoms once she got the mask back on her face. If she is given a prescription for benzodiazepines, Clara might be tempted to forgo fixing the mask problem. She risks getting hypoxic if her mask falls off, since her respiratory rate might not compensate fast enough if she is on a benzodiazepine, especially since she is also taking an opioid.

Furthermore, Clara reported having suicidal thoughts of overdosing on her pain medications. The availability of benzodiazepines would provide her with another medication that could be potentially lethal. Clara agrees with your recommendation to have her husband lock up all her medications until she sees you in a few weeks.

Question 18.8

Some palliative care patients develop debilitating anxiety symptoms or have preexisting anxiety disorders that worsen after they are diagnosed with life-limiting illnesses.

What Are the Medication Options for Palliative Care Patients with Anxiety?

See Table 18.4 for a list of medication treatment options for anxiety [31, 32].

Table 18.4 Medication management for anxiety in palliative care [31, 32]

Medication	Administration availability	Initial starting dose (maximum daily dosage)	Notes
SSRI			Refer to Table 18.3
SNRI			Refer to Table 18.3
Benzodiazepines			– Avoid alprazolam because of short half-life – Cautious use because of risk for sedation and falls
Lorazepam	PO (tab, liquid, IM, IV, SC)	0.25–1 mg q60 min PRN anxiety Titrate to effect	– Preferred use in liver disease – Useful in status epilepticus – Can be scheduled or given PRN
Diazepam	PO (tab, liquid, rectal gel, injection, IM)		– Minimize use given active metabolite can extend half-life
Clonazepam	PO (tab)	0.25–2 mg/day Titrate to effect	– Consider scheduling given slow onset
Other medications with anxiolytic properties			
Propranolol	PO (tab, liquid, capsule, IV)	10 mg BID or TID	– Often used in palliative care to help with tremors – Monitor vital signs
Gabapentin	PO (tab, capsule, liquid)	100 mg BID or TID (3600 mg)	– Often used to treat neuropathic pain – Decrease dose in renal failure
Trazodone	PO (tab)	25 mg (500 mg)	– Risk for sedation, priapism, orthostasis

Note: BID, twice daily; PO, oral; PRN, *pro re nata* (as needed); TID, thrice daily. From Leung MW, Kaplan L, Bourgeois JA. Palliative Care for Geriatric Psychiatric Patients with Life-limiting Illness. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018.

Question 18.9

Case continued: You see Clara in clinic a few weeks later. She reports that her mood is still depressed, but she feels better because she is now sleeping through the night after also getting a smaller oxygen mask. The auditory hallucinations stopped as soon as she started taking a higher dose of olanzapine, and she said she "sleeps like a rock" with her new medication regimen.

Clara jokes that her appetite is "Maybe a little too good … I gained 2 pounds in 2 weeks!" and that she is less fatigued. She stopped having thoughts of suicide about a week ago. She denied having any problems with her medications. You recommend that she increase mirtazapine to 30 mg PO qhs and continue olanzapine 5 mg PO qhs. You also recommend that she consider psychotherapy.

What Psychotherapeutic Modalities Have Been Demonstrated to Be Effective for Patients in Hospice Care?

Even patients with a prognosis of days to weeks may benefit from supportive psychotherapy that validates worries and feelings, reflects, explores fears, and shares in the experience of being ill [31].

By design and necessity, psychotherapy for patients in hospice care is time limited and determined by the patient's ability to physically participate in psychotherapy. A number of evidence-based, brief, semi-structured psychotherapies in the palliative care population have demonstrated improvement in overall well-being [32]. Psychotherapies include cognitive behavior therapy, dignity therapy, meaning-centered psychotherapy, and managing cancer and living meaningfully (CALM).

Question 18.10

Case continued: You see Clara in clinic several weeks later. She reports that her mood is no longer depressed. Although she is feeling physically tired, she is more motivated to participate in her various therapies. Her fatigue keeps her in bed most of the time, but she is now able to sit up for 1–2 h at a time to watch some of her favorite TV shows.

Her sleep is still good, and she continues to deny having any auditory or visual hallucinations or suicidal thoughts. She is looking forward to attending her granddaughter's graduation from high school next month. Clara has met with a therapist four times already and said that she has found it extremely helpful for her. She started attending the COPD support group again last week and is looking forward to continuing attending groups. Clara said that her therapist plans to help her mentally and emotionally process what she will experience as she approaches the end of her life. The therapist recommended that she get more information from her physicians about what symptoms to expect in the next several months of her life.

How Do You Manage Her at This Point?

You recommend that she continue taking mirtazapine 30 mg PO qhs and olanzapine 5 mg PO qhs, continue weekly psychotherapy visits with her therapist, attend as many group sessions as she physically can, and speak with her oncologist and/or hospice physicians about what symptoms to anticipate in the next several months. You schedule a follow-up visit in 4 weeks.

Question 18.11

A. What Are Common Medical and Neurological Symptoms During the Final Months, Weeks, and Days of Life?

Common symptoms are fatigue, which may be associated with drowsiness, weakness, and sleep disturbance [33]. Methylphenidate may be useful in some patients. Dyspnea is a particularly distressing symptom, often increasing in the last weeks and days of life. Depending on the etiology of dyspnea, opioids, bronchodilators, and/or supplemental oxygen may be of benefit.

An estimated 30–75% of patients experience pain during the final few days of their lives [34, 35]. In hospice settings very high doses of opiates appear to be rarely indicated [36], and contrary to the expressed fears of family members, opiate use is not associated with hastened death [36–38]. See Table 18.5 for a list of psychotropic medications that can be used "off-label" to treat various symptoms in the palliative care setting.

Delirium is a common neuropsychiatric complication in geriatric patients and is referred to as "terminal delirium," "terminal restlessness," or "terminal agitation" when it occurs at the end of life. Delirium may be reversible but is less so during the final hours to days of life [39–41]. Delirium is characterized by an abrupt onset of disturbances in awareness, attention, cognition, and perceptions that fluctuate over the course of the day.

Table 18.5 Off-label psychotropic medications used in the palliative setting [31, 32]

Symptom	Palliative medications
Nausea and vomiting	Haloperidol, olanzapine, mirtazapine
Fatigue	Methylphenidate
Hiccups	Chlorpromazine, gabapentin
Neuropathic pain	Methadone, amitriptyline, nortriptyline, venlafaxine, mirtazapine, gabapentin
Refractory pain	Ketamine
Pruritus	Paroxetine, sertraline, fluvoxamine, mirtazapine

From: Leung MW, Kaplan L, Bourgeois JA. Palliative Care for Geriatric Psychiatric Patients with Life-limiting Illness. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018.

Terminal delirium occurs before death in 50–90% of terminally ill patients [42], most commonly hypoactive delirium. Treatment includes minimizing deliriogenic medications (e.g., corticosteroids, chemotherapeutics, benzodiazepines, anticholinergics) and consideration of antipsychotic agents such as haloperidol, olanzapine, and risperidone (refer to Table 18.6).

Table 18.6 Medication management for terminal delirium [31, 32]

Medication	Administration availability	Initial starting dose (maximum daily dosage)	Notes
Haloperidol	PO (tab, liquid), PR, SC, IM, IV	1 mg PO or 0.5 mg IV or SC q1 h PRN, then every 6–12 h in divided doses (20 mg)	– In emergent cases, give IV every 15 min until symptoms resolved. Once symptoms resolved, take total amount used in 24 h and divide over 24-h period – Parenteral doses twice as potent as oral doses – Useful in treating nausea
Chlorpromazine	PO, PR, SC, IM, IV	25–50 mg PO or IV or PR q1 h (1000 mg)	– Consider if more sedation needed – Monitor for anticholinergic effects and hypotension
Olanzapine	PO (ODT), IM	2.5 mg daily (40 mg)	– Useful in treating nausea
Quetiapine	PO	25 mg PO q12 h (800 mg)	– Monitor for anticholinergic effects and hypotension
Lorazepam	PO (tab, liquid), PR, SC, IM, IV	0.5–1 mg any route (40 mg)	
Midazolam	PO (liquid), SC, IM, IV	0.1–0.2 mg/kg IV/SC loading dose, then repeat every 30 min PRN agitation Maintenance dose: 0.02–0.2 mg/kg/h (240 mg)	– Give 25% of total dose needed to control symptoms as continuous infusion – Medication most frequently used for palliative sedation
Phenobarbital	PO (tab, liquid), PR, SC, IV	50–100 mg IV loading dose every 10–15 min until comfortable Maintenance: 60–800 mg divided over 24 h (800 mg)	– Used primarily for palliative sedation

Note: IM, intramuscular; *IV*, intravenous; *ODT*, oral disintegrating tablet; *PO*, per oral; *PR,* per rectum; *PRN*, pro re nata (as needed); *SC*, subcutaneous. From: Leung MW, Kaplan L, Bourgeois JA. Palliative Care for Geriatric Psychiatric Patients with Life-limiting Illness. In: Hategan A, Bourgeois JA, Hirsch CH, Giroux C, Eds: Geriatric Psychiatry: A Case-Based Textbook. Springer International Publishing, 2018.

In an estimated 15–52% of dying patients, delirium does not respond to standard pharmacological treatments, and palliative sedation may be the best treatment option [43, 44]. With the goal of relieving suffering during the final hours and days of life, palliative sedation may be induced with medications such as midazolam and/or phenobarbital [45, 46]. The goal of palliative sedation is to provide the lowest level of sedation to relieve symptoms and has not been shown to hasten death [47, 48]. Palliative sedation should also be considered for refractory dyspnea.

Other common neurological syndromes at the end of life include major neurocognitive disorder/dementia, seizures, headaches (e.g., from brain tumors, metastatic brain lesions, meningeal carcinomatosis), and neuropathic pain syndromes (e.g., mononeuropathies; plexopathies such as cervical, brachial, lumbosacral; radiculopathies; and epidural spinal cord compressions) [49].

B. What Are Common Symptom Clusters for Patients with Advanced Cancer?

A systematic review of observational studies concluded that patients with advanced cancer have four common clusters of symptoms: anxiety-depression, nausea-vomiting, nausea-appetite loss, and fatigue-dyspnea-drowsiness-pain [50].

Question 18.12

Case continued: It has been more than 5 months since Clara was diagnosed with metastatic lung cancer. Clara's husband (John) called to cancel Clara's last appointment with you because she was too weak to sit up in a wheelchair for more than a few minutes. At that time, John reported that despite her declining health, Clara's mood seemed "pretty good." Although she slept most of the day, she welcomed visits from members of her support group, family, and friends.

In the past several weeks, the hospice team's social worker has met with Clara and John to update and confirm Clara's advance care plan that had been arranged 5 years ago and to help them plan ahead. John recently met with the social worker alone. A major topic of discussion was what he and the family should expect during the final days and hours of Clara's life.

A. What Is Impending Death? What Are Some of the Most Common Signs of Impending Death?

Impending death refers to an irreversible physiologic process that includes a characteristic constellation of symptoms and typically occurs during the final 3 days of life [33]. During this time, patients usually experience a progressive decline in their neurocognitive, cardiovascular, respiratory, gastrointestinal, genitourinary, and/or muscular function.

Accurately diagnosing impending death is crucial because it informs healthcare decisions such as hospital discharge, initiation or discontinuation of medications, artificial nutrition, use of life support measures, and communication with family members. The patient and family may wish to notify specific individuals to be present at the time of death.

Clinicians may hesitate to diagnose impending death and often overestimate survival [51, 52]. Hui et al. identified eight physical signs that were highly specific in diagnosing death within 3 days in a prospective longitudinal cohort study of 357 patients with advanced cancer who were admitted to acute palliative care units at two tertiary cancer care centers [53].

Of the 52 physical signs that were systematically documented every 12 h, the following eight signs were found to be highly diagnostic of impending death: nonreactive pupils, decreased response to verbal stimuli, decreased response to visual stimuli, inability to close eyelids, drooping of the nasolabial fold, hyperextension of the neck, grunting of vocal cords, and upper gastrointestinal bleeding.

B. What Can Clinicians Do to Help Prepare Patients and Families for a Loved One's Impending Death [33]?

1. Provide education about what symptoms are likely to occur during the final weeks and days of life.
2. Articulate a plan to respond to each specific symptom. Inform them that not all symptoms can be completely ameliorated with treatment, and help them set up reasonable expectations regarding their love ones' response to treatment.
3. Address fears or concern that family members may have.
4. Provide reassurance to them that allowing life to end is appropriate at this time.
5. Family members often find it helpful to participate in the care of their dying loved one by doing something—no matter how small—during the period of impending death. For example, they can do things like moisten the patient's mouth with swabs.
6. Inform the family that during the final days of life, patients often have limited, transitory moments of lucidity. Let them know that this is a common phenomenon during the dying process and does not necessarily signal that the patient is doing better than predicted. Patients may be aware of the presence of others; loved ones can be encouraged to speak to the patient as if he or she can hear them.
7. Patients may experience a decreased desire to eat or drink, as evidenced by clenched teeth or turning from offered food and fluids. Reframing will include teaching the family to provide ice chips or a moistened oral applicator to keep a patient's mouth and lips moist.
8. If available, offer to have a chaplain to be consulted as early as possible if the family accepts this assistance.

Question 18.13

Case continued: You are on call at the hospital and receive a consult to see Clara, who was admitted to the acute palliative care unit a few hours ago after she became acutely agitated and attempted to hurl herself out of bed at home. The oncologist informs you that for the previous 2 days, Clara has been sleeping most of the time, with 5–10-min periods of lucidity a few times a day. She is on continuous oxygen. She has not eaten anything for the past 3 days.

On exam, Clara is asleep, but her eyelids are only partially closed. She requires multiple loud verbal prompts to awaken. She opens her eyes, stares at you blankly, and then falls asleep again. John reports: "She's been like this for the past few days. Sometimes, though, she'll start kicking off her blankets, and moving around a lot. She's really restless. This morning, she suddenly opened her eyes, and tried to jump out of the hospital bed."

A. What Do You Do Next?

You speak to Clara's husband, John, who has power of attorney for her personal care. You explain that Clara's exam is consistent with delirium, which is usually a reversible condition that can be at least partially resolved by identifying and addressing precipitating and inducing factors by obtaining blood work and completing other studies.

John decides that Clara would not have wanted to have more testing done on her. He also signs paperwork so that Clara has a do-not-resuscitate/do-not-intubate order in her medical records.

B. What Can You Do to Help Clara Be as Comfortable as Possible?

Aggressive management of delirium is appropriate in virtually all cases of delirium during the period of impending death, which Clara appears to be in based on your exam (decreased response to verbal and visual stimuli, inability to close eyelids). Non-pharmacological interventions are usually not effective for controlling the symptoms of delirium during the period of impending death.

In general, haloperidol is the first-line treatment for treatment of delirium in geriatric patients [54]. Chlorpromazine is also an option to promote sedation. If pain is contributing significantly to delirium, consider opioids.

Clara has had a complete and adequate response to low doses of olanzapine for the past 5+ months. Since Clara likely has fewer than 3 days left to live, you prefer to continue a medication that has worked in the past versus starting a new medication that may not work and/or may cause an adverse reaction. You recommend increasing scheduled olanzapine to 7.5 mg PO qhs, and add 2.5 mg PO q4 h PRN for irritability/delirium.

C. Clara's Delirium Does Not Improve Even After She Received a Total of 15 mg Olanzapine over a 16-h Period. In Addition, Clara's Breathing Becomes Increasingly Labored. What Do You Recommend?

You recommend palliative sedation due to strong evidence of impending death and worsening dyspnea. Furthermore, her failure to respond to a previously effective medication suggests that her delirium is irreversible. Introducing another medication such as haloperidol to treat delirium that is likely to be intractable may lead to more suffering without improving her quality of life or her life expectancy. John agrees to palliative sedation.

At your recommendation, John notifies loved ones who may want to say their final "goodbyes" to Clara. Less than 24 h after starting palliative sedation, Clara dies peacefully, surrounded by her husband, children, and her grandchildren.

Question 18.14

A. Explain How Advanced Major Neurocognitive Disorder Can Be Considered a Terminal Diagnosis

Memory loss, personality changes, and difficulties with activities of daily living characterize major neurocognitive disorder. When advanced, major neurocognitive disorder can be conceptualized as a terminal diagnosis due to its irreversible and increasingly debilitating nature.

B. What Potential Complications Do Patients with Advanced Major Neurocognitive Disorder Often Develop?

Patients with advanced major neurocognitive disorder are at increased risk for infections, accidental injuries due to falls (with risk of hip fracture) and other preventable conditions such as pressure wounds due to an inability to ambulate, and malnutrition due to eating problems such as "forgetting" how to use a fork or how to chew. Pneumonia, fevers, and eating problems are frequent complications and have been found to be associated with a 6-month mortality rate of 38–47% [55]. Clinicians who are working with patients with advanced major neurocognitive disorder must carefully consider the potential risks and benefits of treating conditions such as urinary tract infections and pneumonia, treatment of which may not necessarily lead to improved quality of life or life expectancy [56, 57].

C. Why Is Advance Care Planning (ACP) Imperative for Patients with Advanced Major Neurocognitive Disorder?

ACP needs to be initiated early in the course of the disease while patients are capable of communicating their treatment goals and have decision-making capacity. To

avoid repeat hospitalizations that could lead to workups and treatments with minimal benefit, some patients may include "do-not-hospitalize" requests in their ACPs. In anticipation of future feeding problems in advanced major neurocognitive disorder, patients will ideally also address their wishes for "artificial nutrition" via tube feedings, which has been found to be of equivocal benefit for those with advanced major neurocognitive disorder [58].

The patient is a 66-year-old male with amyotrophic lateral sclerosis (ALS), with a rapidly progressive course with quadriplegia, respiratory failure (requiring mechanical ventilation through a tracheostomy), inability to speak, and increasing problems with memory. Fortunately, while he was functioning better cognitively, he agreed to be in DNR status. His family members, aware of his disease state, fully supported this decision. As a contingency, his wife agreed to serve as surrogate decision maker if he were to become incapacitated.

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Topic 19: Caregiver Burnout

Question 19.1

Caregiver burnout is a state of where a caregiver's physical health or emotional well-being is negatively impacted as a result of the stress associated with caring for someone with significant care needs. Burnout typically occurs where the caregiver does not receive enough supports or if the caregiver overextends himself/herself with too many tasks and responsibilities. Caregivers of patients with major neurocognitive disorders are usually females and are more likely to be spouses (61%) than children (29%) or other relatives (11%) [1].

What Is the Prevalence of Caregiving?

According to 2015 US data from a survey by the National Alliance for Caregiving and American Association of Retired Persons, there were approximately 43.5 million caregivers providing unpaid care to an adult or child in the 12-month period prior to survey, and about 34.2 million residents of the USA were providing unpaid care to an adult aged 50 or older—this translated to a prevalence of 18.2% for adult and child care recipients and 14.3% for the aged 50+ care recipients [2]. The survey also revealed the following:

- Nearly 7% of the caregivers were aged 75 years or older.
- The top three reasons that caregivers were providing care were "old age" (14%), Alzheimer disease or dementia (major neurocognitive disorder) (8%), and surgery/wounds (8%).
- Many of the caregivers had no other unpaid caregiver help (47%), and only 37% had paid help from aides.
- Two in five caregivers consider their caregiving situation to be emotionally stressful (see Fig. 19.1).
- Half the caregivers reported that they had no choice in taking on the caregiving responsibilities.

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_19

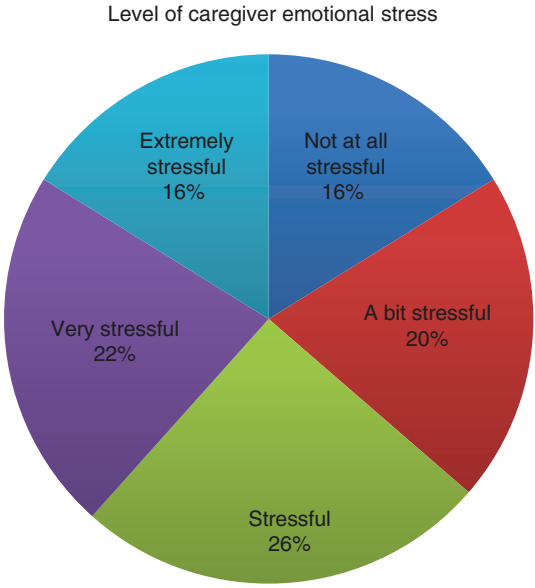


Fig. 19.1 Rating of caregiver emotional stress from Caregiving in the U.S. 2015 report [2]

- 56% of caregivers still worked full time (an average 34.7 h/week) in addition to their caregiving responsibilities.
- Only one-third of caregivers were asked by a healthcare provider (such as a physician, nurse, or social worker) about what was needed to care for their recipient.
- Only 16% of caregivers were asked by a healthcare provider what they needed to take care of themselves.

Given that caregivers are needed to support a significant proportion of our population, it is essential that clinicians identify those caregivers who are at risk of burnout and to direct them to available resources in the community to help them cope.

Question 19.2

Caregiving is often referred to as a chronic stress experience. Caregiving can cause physical and psychological strain; it is a task that is often unpredictable; it may cause secondary problems in other life domains such as work and relationships; and it often requires a high level of vigilance.

What Are Some Symptoms of Caregiver Burnout?

These symptoms include:

- Withdrawal from friends, family, and other loved ones
- Loss of interest in activities previously enjoyed

- Feeling blue, hopeless, and helpless
- Changes in appetite/weight
- Lack of energy
- Changes in sleep patterns
- Frequent illnesses
- Headaches, stomachaches, and other physical problems
- Emotional and physical exhaustion
- Neglecting own physical and emotional needs
- Increase in irritability and less patience with the care recipient

Question 19.3

Mr. G is a 65-year-old gentleman you have been following for many years for chronic schizophrenia. Over the years, his cognition has also started to decline. His children have been getting increasingly concerned that Mr. G was not managing well independently at home, and perhaps he needs to move to a more supportive environment. Mr. G adamantly refuses to consider moving to a retirement home or a nursing home, stating that he is too young to move into an "old age home." Mr. G is willing to consider moving in with one of his children. The family comes to you today to discuss this issue. They wondered what your opinion is of Mr. G moving in with his daughter Laura. Laura is single and lives in a one-story home. She is currently off work on long-term disability due to her own psychiatric illness. The rest of the family thought this would be a good idea as Laura would be home full time to take care of Mr. G (the rest of his children all work full time).

What Are Some Risk Factors for Caregiver Burnout Identified in This Case?

Generally, patients who require higher level of care and assistance with their activities of daily living and instrumental activities are associated with a greater burnout risk [3, 4]. A poor premorbid relationship between the caregiver and care recipient also increases the risk of excess caregiver burden [5]. Other risk factors may be divided into care recipient characteristics and caregiver characteristics. Table 19.1 outlines some of these characteristics.

As Laura presumably suffers from a psychiatric illness (as she is off work on disability), she may not have the necessary coping skills or stamina to deal with the challenges she may face as a caregiver. The family should discuss any foreseeable problems that may arise should Mr. G move in with Laura and come up with potential solutions to these problems. Other things to consider would be assessing the potential of other assistance if needed. While Laura may be the main caregiver, would the other siblings be able to assist on a regular basis (e.g., help out on the weekends), or only in emergencies? If Laura feels that she is not managing well, what is the backup plan? These are all things that the family should consider prior to making the decision, to ensure that proper supports are in place.

Table 19.1 Characteristics of care recipients and caregivers that are associated with a higher risk of caregiver burnout [6]

Care recipient characteristics	Caregiver characteristics
Lower education level	Lower education level
Lower cognitive functioning	Caucasian ethnicity
Agitation	Female sex
Hoarding	Comorbid physical illness
Verbal or physical aggression	Comorbid depressive and anxiety symptoms
Incontinence	Poor coping skills
Apathy	Poor social support
Sleep disturbances	Lower monthly income
Gait/balance problems	
Visual/hearing impairments	

Question 19.4

What Are Some Protective Factors That Lower Caregiver Burnout?

A bigger social support network and better caregiver resources are associated with less caregiver burden, greater life satisfaction, and fewer physical health concerns compared to caregivers with fewer social connections [6]. Some positive psychological factors have also been suggested to decrease risk of caregiver burnout. These factors include [6]:

- Caregiver confidence is associated with lower levels of depression.
- Feelings of "uplift" associated with the act of caregiving leads to less caregiver distress.
- The satisfaction derived from caregiving contributes to a more positive caregiving outcome.
- Caregivers who are better able to find "higher meaning" through caregiving is associated with lower levels of depression.
- A caregiver's ability to conceptualize caregiving as enhancing or enriching his/her life can moderate caregiving stress.

Question 19.5

Mrs. C is an 85-year-old widowed female who had suffered a stroke some years ago. Since that time, she has declined both physically and cognitively, and she was no longer able to manage living independently. Her daughter moved in with her a year ago to provide care for Mrs. C. The last two times that Mrs. C came to your office for assessment, you noticed that she appeared more unkempt, that her clothes smelled slightly of urine. Today, when speaking with Mrs. C alone, she tells you that she is not sleeping well, that she has been spending most days at home as she just does not feel like socializing anymore. She has even stopped going to church, which is something she has always enjoyed. When her daughter comes back to the room,

Mrs. C seems even more withdrawn, not really wanting to say anything. She appeared scared of her daughter. When you ask Mrs. C's daughter about the patient's decline in appearance, she tells you that Mrs. C has declined cognitively in the past 2–3 months and she is finding it harder to care for her mother. She admits that she often yells at her mother out of frustration. You have some concerns that Mrs. C's daughter may not be treating Mrs. C well at home.

What Are Some Signs of Elder Abuse/Maltreatment?

The World Health Organization defines elder abuse as "a single, or repeated act, or lack of appropriate action, occurring within any relationship where there is an expectation of trust which causes harm or distress to an older person." The abuse can be financial, physical, psychological, and/or sexual. It can also be the result of intentional or unintentional neglect. Studies suggest that one in four vulnerable older adults are at risk of abuse and that only a small proportion of this is detected [7]. Caregivers who are burned out are at risk of perpetrating elder abuse [6]. Physical abuse is generally easier to detect as there are likely signs of physical injuries, whereas it may be harder to detect financial or psychological abuse. Table 19.2 lists some of the signs that may suggest elder abuse. Being vigilant for signs of maltreatment may potentially protect a vulnerable patient from further harm and

Table 19.2 Signs suggesting possibility of elder abuse

Type of abuse	Suggestive signs
Physical	Bruises Pressure marks Broken bones Burns Unexplained bleeding
Psychological	Strained or tense relationship between caregiver and patient Frequent arguments between caregiver and patient Unexplained withdrawal from activities Sudden change in behaviors Depression, loss of interest Insomnia
Financial	Sudden change in financial situation Legal documents that have been changed or disappeared Unpaid bills Large, unexplained withdrawals from bank accounts
Sexual	Bruises around the breasts or genital area Sexually transmitted infections Vaginal/anal bleeding Torn or bloody clothes, especially underwear
Neglect	Poor hygiene Unusual weight loss Unattended medical needs Missing/broken dentures, eyeglasses, hearing aids

risk. Depending on the jurisdiction, reporting of elder abuse may or may not be mandatory. Mandatory reporting may also be related to the patient's place of dwelling (e.g., living at home in the community versus living in a long-term care facility).

In Mrs. C's case, although you may suspect elder abuse, it is also possible that her decline in hygiene is simply due to a further decline in her cognition; e.g., Mrs. C becomes agitated when her daughter tries to change her clothes; rather than fight and get Mrs. C upset, her daughter leaves her be. Mrs. C may also be experiencing some depressive symptoms that would explain her withdrawal from social activities. In interviewing Mrs. C's daughter, a delicate approach should be adopted so as to minimize risk of her becoming defensive. Questions should be non-threatening and voiced in a sympathetic or neutral tone (rather than accusatory). If Mrs. C's daughter confides in you and admits she has not been caring for her mother as well because she is overwhelmed, crisis support should be offered to alleviate the care stress at home that is fueling the maltreatment. If you determine that Mrs. C's life may actually be in danger or at risk (e.g., you find signs of significant physical abuse), then Mrs. C should be removed from the home until further investigations can be done to ensure her safety at home.

Question 19.6

You are seeing Mr. T, a 90-year-old gentleman for a consultation at the request of his primary care physician to assess his worsening cognition. Mr. T came to today's appointment with his wife, who you guess is in her late 80s. As soon as you sit down with them in the interview room, Mrs. T bursts out in tears as she tells you she just does not know what to do anymore, that she just cannot manage at home. She then collects herself and tells you that she is just having a bad day, that you should go ahead with the assessment as they are here today for her husband, not to "hear an old lady complain."

What Should Be Your Next Steps in Assessment?

When providing clinical care for a dependent older adult, especially one with cognitive concerns, care should be centered on the physician-patient-caregiver triad, as lack of information and support for the caregiver is associated with a higher risk of caregiver burnout. In Mr. T's case, you should:

- Assure that Mrs. T is no longer upset before you continue on with assessment. Communicate to her that you will also have time to address any of her concerns and challenges, as it is important for you to know what her concerns are to optimize Mr. T's care.
- Complete your assessment of Mr. T. Interview Mrs. T separately if possible for collateral information, as she may be uncomfortable talking about Mr. T and his issues with him in the room. Make sure that you spend some time discussing about her earlier comments of not managing at home.

- Explore and assess whether Mrs. T has any signs or symptoms of caregiver burnout (see Question 19.2).
- If there are indications that she is not managing well, discuss the possibility of additional in-home supports (either other family members or paid care).
- Provide both Mr. T and Mrs. T with as much information as possible regarding diagnosis and recommendations. Key information should be written down, as they may be too overwhelmed by the information and not be able to recall what was discussed once they get home.
- Refer Mr. and Mrs. T to appropriate community resources for additional help/information.

Question 19.7

There have been a number of interventions that have been developed to help support caregivers.

Name Some Interventions That Help Decrease Caregiver Burden

Individual counseling for caregivers and family counseling sessions may have a positive effect on the physical health of vulnerable caregivers [8]. Counseling aimed at improving caregiver self-esteem, uplifts and satisfaction of caregiving, and finding meaning and gains in the caregiving experience have been shown to have positive effects [6]. Psychoeducation interventions may also reduce caregiver stress [9]. A systematic review looking at meditative intervention suggests that meditation can help improve a caregiver's mood and anxiety and decrease caregiver burden [10].

The Alzheimer's Society also has programs aimed at providing caregivers with support, helping caregivers learn coping skills, and helping them to optimize caregiver health. Adult day programs, in-home assistance, visiting nurses, and meal delivery are also some community services that may help caregivers manage their daily tasks, thus, lowering their overall stress.

Question 19.8

Name Some Tools Used to Measure Caregiver Stress

The Zarit Burden Interview (ZBI) is a structured self-report scale developed in 1980 as a way to measure levels of stress in family members or caregivers of patients with Alzheimer disease. Studies have shown that the ZBI is a valid and reliable tool in assessing caregiver burden [11, 12]. The original version is a 29-item questionnaire, with each item being ranked on a 5-point scale (scale ranges from 0 to 4). Since then, shorter versions of 22, 18, and 12 items have been released. The questions focus on whether the caregiver/family member feels stressed or embarrassed by the

care recipient and whether there has been any negative effects on relationships, work, and health as a result of the caregiving.

The Caregiver Burden Scale (CBS), developed in 1996, is 22-item self-report questionnaire that measures the subjective burden of caregivers. The CBS is centered on five domains: general strain, isolation, disappointment, emotional involvement, and environment.

Another validated scale is the Perceived Caregiver Burden Scale (PCBS). The original 31-item scale was developed in 1990. Since then, a shorter 13-item version was released in 1999. The shorter revised version focuses on three dimensions of burden: impact on finances, impact on health of caregiver, and sense of entrapment.

Question 19.9

When considering caregiver burnout, while we typically think of the burnout experienced by family caregivers, burnout can also occur in health professionals. Several types of occupational stress have been identified, including burnout, compassion fatigue, and vicarious traumatization [13].

Define Compassion Fatigue and How Is This Different from Burnout

Compassion fatigue has been defined as the "natural consequent behaviors and emotions resulting from knowing about a traumatizing event experienced by a significant other—the stress resulting from helping, or wanting to help, a suffering person" [14]. It is a condition characterized by a gradual lessening of compassion over time, occurring commonly in therapists, nurses, teachers, physicians, police officers, paramedics, and informal caregivers.

While compassion fatigue involves exposure to traumatic stress, burnout itself is not directly related to trauma and suffering. Anyone in any job can experience burnout. For example, a waiter in a restaurant can experience burnout, but this is unrelated to trauma exposure. The onset of burnout is usually gradual, whereas compassion fatigue usually has more rapid onset as a result of exposure to a single traumatic event [13]. Job burnout can result as a consequence of compassion fatigue.

Question 19.10

What Is the Prevalence of Burnout in Physicians?

About 25–65% of physicians across all specialties report burnout [15]. In a recent survey of more than 14,000 physicians from over 30 specialties, although 42% of psychiatrists report feeling burned-out—defined as loss of enthusiasm for work,

Table 19.3 Top ten causes of burnout identified by psychiatrists [16]

Reasons for burnout in psychiatrist	1. Too many bureaucratic tasks
	2. Feeling like just a "cog in the wheel"
	3. Spending too many hours at work
	4. Increasing computerization of practice
	5. Compassion fatigue
	6. Inability to provide patients with the quality care they need
	7. Too many patient appointments in a day
	8. Lack of professional fulfillment
	9. Insurance issues
	10. Income not high enough

feelings of cynicism, and a low sense of personal accomplishment—psychiatry was still one of the more "satisfied" specialties. The highest rate of burnout was among emergency medicine physicians, with a prevalence of 59% [16]. The top two reasons for burnout identified by psychiatrists were too many bureaucratic tasks and feeling like just a "cog in the wheel" (see Table 19.3). Burnout appears to have a marked effect on psychiatrists' non-work lives as only 41% report feeling very to extremely happy outside the workplace, compared with 70% of those who do not report burnout [16].

As clinicians, not only do we need to ensure that our patients are healthy, we also need to make sure attention is paid to our own health and to how work stress may impact on our well-being. As in the case of an airplane emergency, where you have to put on your own oxygen mask first before helping anyone else, you must help yourself first if you are starting to show signs of burnout, before you can help your patients.

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Topic 20: Physicians as Leaders in Improving Healthcare

Question 20.1

What Is Leadership?

While there are many definitions of leadership, one of the defining characteristics of leadership is a social influence process in which a person steers or enlists members of a group to pursue the accomplishment of a common goal [1].

Question 20.2

List Some Key Features of Effective Physician Leadership

Some characteristics of effective leadership are listed in Box 20.1 [2].

Box 20.1 Characteristic of Effective Leadership [2]

Leaders change things
Leadership is an action, not a position
Leadership is not victimhood
Leaders define reality with data
Leaders develop and test changes
Leadership takes courage
Leaders persuade
Leaders are not daunted by the loudest negative voice
Leaders do much of their work outside of their immediate area of responsibility

© Springer International Publishing AG, part of Springer Nature 2018
A. Hategan et al., *Geriatric Psychiatry Study Guide*,
https://doi.org/10.1007/978-3-319-77128-1_20

Question 20.3

What Could Be a Critical First Step to Leadership Enhancement?

In contrast to self-perception, the empirical evidence favors rated leadership by others. A critical first step to leadership enhancement is that physician leaders should actively seek feedback on their leadership styles [1].

Question 20.4

A. According to Bass and Avolio's Model, What Are the Three Major Constructs in Leadership Behaviors?

The three major constructs in leadership are [1]:

- Transformational—it targets the motivations of followers to act toward exceptional performance and ethically inspired goals.
- Transactional—it refers to a social exchange process of providing valued rewards in exchange for performance.
- Laissez-faire—it refers to indifferent or no leadership.

B. Briefly Describe These Three Leadership Behaviors

Transformational leadership has four components [1]:

- Idealized influence
- Inspirational motivation
- Intellectual stimulation
- Individualized consideration

Transformational leadership focuses on stimulating the needs for intellectual and motivational growth of the followers toward achieving higher goals, followed by facilitation of such growth through individualized, mentoring, or coaching relationships. In clinical practice, exceptional performance implies efforts to improve healthcare quality.

Transactional leadership has two subconstructs [1]:

- Contingent reward
- Management by exception

Contingent reward is a process of exchanging valued rewards for good performance. Management by exception proactively seeks to identify potential problems and provide feedback to correct deviations from the norm.

Laissez-faire leadership is nonleadership [1]. In this case, the leader is perceived as indifferent to follower's actions and performance, and organizational outcomes, and as evading responsibility to address important issues [1].

Question 20.5

There is no right or wrong type of leadership style.

What Are Some Common Examples of Different Leadership Styles?

Some common leadership styles are [1]:

- Directive—also known as autocratic
- Participative—sometimes referred to as inclusive
- Delegative—also known as laissez-faire

Many leaders employ combinations of leadership styles to fit given situations and particular staff members.

Question 20.6

The Terms "Leader" and "Manager" Are Not Used Interchangeably. How Are These Terms Different?

Leadership and management do share many similar duties, which consist of working with people and influencing others to achieve goals. However, leadership skills are used to focus on the ability to affect change in a positive manner by establishing direction, and motivating and inspiring, whereas management skills are used to oversee the day-to-day operations of an organization, as well as plan, build, and direct organizational systems to accomplish missions and goals [3].

Question 20.7

Case 1. Small Organization
Dr. A. is a newly hired geriatric psychiatrist at a small, rural, government-operated geriatric medicine clinic. She recently finished her residency and fellowship training before taking the current position. Her colleagues are three nurse practitioners, two physician assistants, one clinical psychologist, one social worker, two registered nurses, and five administrative/business personnel. The clinic is in a community of 5000 and is the only geriatric medicine clinic within 50 miles.

There is a small community hospital 10 miles away. The nearest comprehensive university medical center is 75 miles away. The clinic is on solid ground financially; it is not in deficit and has adequate cash on hand for predicted needs. Due to her being the only physician assigned to the clinic, the clinic board of directors has put her in charge, even though some of the other clinicians have more years in clinical practice in their respective disciplines and more experience in this particular clinic.

Dr. A. accepts this clinical leadership role as part of her recruitment. She has agreed to a maximum of 50% time in direct patient care (focusing primarily on geriatric psychiatry cases as there are other primary care physicians in town, while she is the only psychiatrist). The balance of her time will be devoted to supervision and clinic management (e.g., she will provide clinical oversight to the nurse practitioners and physician assistants as well as administrative and business leadership to the administrative personnel).

Dr. A. meets with her staff early in her first week. She establishes a plan for weekly "all ranks" meetings with the whole clinic team (administrators and clinicians alike) to discuss overall clinical operations. She decides to have a separate meeting weekly with all clinicians to discuss specific clinical and health system problem-solving. She has an additional clinical supervision meeting with the nurse practitioners and physician assistants, for whom she provides direct case-based supervision and oversight. She also has a weekly 1-h meeting with the lead administrator to discuss business and financial matters exclusively.

Case 2. Middle-Sized Organization

Dr. J. is a middle-aged geriatric psychiatrist who has been with the same large clinic group for 20 years. He was one of the original members, when a group of six physicians (previously having trained at the same university) started a multispecialty group practice. Over the years, with steady growth in demand for services and targeted, focused recruitment, the group has expanded to now include 20 physicians, including primary care internal medicine, general, consultation-liaison and geriatric psychiatry, general surgery, and endocrinology. Dr. J. has been an active member of the group as it decided to engage in strategic growth. Dr. X., the previous practice group leader, has "had enough of administration" and stepped down. The informal leadership structure of the practice agreed that Dr. J. was the logical successor, and he agreed to take on this leadership "for 5 years" without a commitment to serve beyond then. This was acceptable to the practice group.

Dr. J., recognizing that the group had grown substantially beyond its original concept, quickly realizes that a maturing and growing organization needs more of a formal administrative arm to grow and function efficiently. In discussions with the practice group, he has advocated for a more centralized structure, with the group's first full-time, professional group practice manager (previously, family members of the clinicians served in this station, supervising billing and administration personnel on a rotating and informal basis). Dr. J. also recognizes the need for other physician leaders, and he asks Dr. R. to serve as assistant practice group leader and for a group of five of the senior clinicians to serve as an advisory group. He also proposes that

the group codify its operating routines as a set of clear bylaws to organize administrative activities.

Regarding personnel, Dr. J. recognizes that the practice group needs to move beyond its historical model of "physicians only" providing direct clinical services. He seeks to diversify the clinical services model by development of physician assistant and nurse practitioner positions to increase operating efficiency by having these professionals (with oversight and supervision in a structured way) added to the group practice. He leads the effort to integrate this more diverse group of independently licensed professionals into the group as well, by hiring clinical psychologists, pharmacists, optometrists, and podiatrists. He then publicizes how the group has expanded its role and mission by providing a broader range of clinical services by inclusion of this broader group of health professionals.

Case 3. Large Organization

Dr. W. is a middle-aged female geriatric psychiatrist. Long having had an additional interest in medical leadership, she completed an executive M.B.A. degree 5 years ago. At her 200-bed community hospital in a city of 15,000, she has previously held a series of leadership roles. She has served as the chair of the small psychiatry department (which has three other physicians plus clinical psychologists and nurse practitioners), during which time she led steady growth of her department with recruitment of an additional physician, two psychologists, and the department's first two nurse practitioners. She initiated the use of telemedicine to better serve rural primary care clinics that are reliant on the hospital department of psychiatry to support the primary care management of psychiatric illness. She also was in charge of the department when the hospital adopted a comprehensive electronic medical record, which also required her directing the department administrator to assure that the somewhat esoteric psychiatric billing codes were properly loaded into the EMR system at the time of rollout.

After successful management of the psychiatry department, she was tapped to serve as the chief of the medical staff for the hospital. This role required oversight of privileging functions and assurance of physician mastery of government and regulatory agency requirement, standards, and compliance. She reinvigorated the previously moribund and vestigial physician health committee, providing confidential professional services to physicians and other professionals struggling with addictive illness; this role involved direct interface with state licensing boards to adjudicate the cases of the affected physicians. After successful navigation of this role for 5 years, the role of hospital director (never previously held by a physician) opened up with the retirement of the senior RN who previously held this post. After a series of interviews and position papers, she was the choice of the board to become hospital director. To avoid problematic conflict of interest challenges, she resigned from the medical staff leadership role.

Upon assuming the hospital directorship role, Dr. W. began her tenure with a series of position statements regarding her goals for both "inside" operations (e.g., optimizing efficiency of operations, supply chain management, personnel management, safety and compliance) and a renewed focus on the hospital's relationships

with "outside" stakeholders (e.g., insurance payors/contractors; government agencies at the local, state, and federal levels; other large institutions within the community). Taking advantage of the experience and credibility she had gained from her previous administrative positions, she advocated for greater physician involvement and responsibility for roles previously solely held by administrators. She was able to persuade several more junior physicians to also seek M.B.A.s and assume medical center leadership roles. She was able to parlay the more active involvement of the physician group to favorable actions by insurance payors regarding bundled payment contracts, clinical initiatives in models of care delivery, and seeking new markets for clinical services. Her hospital became regionally known for being more "physician led" than competitors, which offered stakeholders a sense that the medical staff was more intimately locally involved in important contemporary endeavors such as population health management, quality improvement, and experimentation with systems of care delivery initiatives.

Case 4. Government Agency

Dr. G. is a senior academic geriatric psychiatrist with long experience at the "triple threat" career classically associated with a successful academic career (excellence at patient care, directing meaningful research, and being a well-regarded instructor). After a successful career in academia, wherein he briefly served as vice chair of his department, he was sought out to be an administrator of a government agency involved in regulatory activities and healthcare resource planning. Though not heretofore involved in government activities directly per se, his experience with interfacing with granting agencies and regulatory bodies provided him with a sense of government operations that provided some advantage.

Early on in this position, he took stock of the clinical backgrounds and acumen of his administrative team. Concerning to him was that he, as agency leader, was unfortunately the only physician in the organization. There were two RNs and a pharmacist on his staff, however. He learned that the balance of his team were career administrators and bureaucrats, who know their own regulations rather well, but did not have the clinical savvy sense needed to best appreciate the operations of hospitals.

Dr. G. sought to diversify his administrative team by seeking out physician executives (the typical background being medical specialty experience plus M.B.A. and administration positions) and was able to recruit three such people for his team. He provided much face time between his administrative professionals with all of his clinician colleagues, to impart more of a clinician perspective to his whole team. While appreciating that not all the hospitals in his purview had the same academic perspective that he had, he endeavored to appreciate the role of community hospitals, with a sole focus on direct patient care, not the tripartite goals model of an academic medical center.

Dr. G. endeavored to define the different direction he wanted the agency to take; in the past, their sole focus was on detailed regulatory compliance, while he wanted the organization to focus more on quality improvement and process analysis than checklist compliance with discrete items as a main focus. He was able to capitalize

on his academic experience to impart a sense of "what really matters" in government oversight of healthcare groups, rather than the previous sense that "it must be important since it has a number attached to it." By bringing his own clinical focus and those of his newly hired colleagues, he was able to transform his organization from one where stakeholders primarily tried to "pass inspections" to one wherein his group provided evidence based and validated advice regarding process improvement and goal setting that stakeholders came to regard as genuinely pragmatic, specific, and measurably beneficial interventions as part of their regulatory activity.

Based on the Case Scenarios Provided, Briefly Describe the Key Important Qualities for a Good Physician Leader

Physician leadership is becoming more common and relevant. Approximately 5% of hospital leaders are physicians, but this number will increase exponentially as the health system moves from a volume-based toward a value-based care [4, 5]. Given the aging of our population, the increasing rates of chronic diseases, and the growing shortages of physicians and nurses, the current medical environment offers significant opportunities for physicians to provide leadership and develop lasting improvements in healthcare delivery [5]. Many factors position physicians at the center of this stage including the public health-oriented focus toward wellness on the management of populations, the redesign of clinical care models in certain settings, and the financial payment models that reward healthcare organizations for clinical excellence and coordinated care at reduced cost [5]. The intrinsic and necessary qualities of a good physician leader are further described [4, 5].

Listening and Communication Skills

Studies have shown that participative leadership is most productive on its own, allowing leaders to seek out the opinions of the followers while still retaining the ultimate decision-making role. The followers feel appreciated and engaged and are learning to respect the leader who shows them respect in return. Listening is not a skill that comes naturally to many physicians. Communication has often less to do with talking and more to do with listening. But good communication skills are essential for good medical leaders.

Vision

It is very important to have vision when working in the healthcare system. Good physician leaders can juggle the "here and now" and create a mission and goals for overall improvement.

Integrity

A physician leader sets a moral tone for the rest of the staff. A good physician leader ponders why they are there and holds tightly to the moral compass that initially called them to become clinicians.

Empathy

Empathy is considered a basic human quality. In a healthcare setting, we empathize greatly with patients, but sometimes we neglect to extend the same consideration to our coworkers. Good leaders listen and put themselves in their colleagues' place. They create strong relationships and keep valuable connections to their followers.

Optimism and Enthusiasm

As physician leaders, we need to direct that optimism toward other clinicians. Physicians can face multiple changes in the healthcare system, which can be often disconcerting. The leaders that can stand and face them with cheer and excitement and view these changes as opportunities to improve will inspire those around them. Creating enthusiasm can be accomplished in many ways including creating a safe environment that allows people to enjoy themselves while still working hard.

Question 20.8

What Is the Least and the Most Successful Leadership Style?

Of the leadership styles mentioned at Question 20.5, the directive or autocratic style has been shown to be the least successful. Autocrats are not necessarily authoritarian people; sometimes they are new and eager to impart change and set the tone of change. Others think they will be able to quickly demand respect, but respect usually needs to be earned. Physician leaders who listen and communicate, maintain integrity, express clear vision, express empathy and instill optimism are set to be successful [4, 5]. (Also see Question 20.7.)

Question 20.9

What Are the Key Components of Effective Interprofessional Collaboration?

The core competencies of effective interprofessional collaboration for a patient-centered collaborative practice are the following [6]:

- Understanding and appreciating professional roles and responsibilities
- Communicating effectively

Interprofessional collaboration involves developing and maintaining effective interprofessional working relationships with trainees, clinicians, patients, and their families to facilitate optimal health outcomes through shared decision making, partnerships, mutual respect, and trust. Effective interprofessional collaboration requires

integration of role clarification, collaborative leadership, and a patient-centered focus to care supported through interprofessional communication. Effective interprofessional communication is contingent on the ability manage conflicting viewpoints and reach reasonable agreements.

Question 20.10

Physician development for leadership roles in residency redesign helps better prepare graduates for medical practice. Therefore, residency programs must prepare their graduates for a changing medical delivery system.

Name Five Leadership Actions That Have Been Associated with Successful Implementation of Innovations and Residency Transformation

Increasing the understanding of leadership skills and planning to undertake meaningful change are important steps in residency programs. According to Kozakowski et al. [7], five leadership actions have been associated with successful implementation of innovations and residency transformation (see Table 20.1).

Table 20.1 Leadership actions and skills necessary for successful residency transformation [7]

Leadership actions	Successful leadership skills
Manage change	Effectively communicate the vision of a better future for the program; articulate the value innovations added to the program; build effective relationships; measure, evaluate, and communicate progress; be flexible when undertaking course readjustments
Develop financial acumen	Determine the financial worth of the program; generate new financial resources to cover added expenses; recognize that innovations require time for planning, implementation, and administrative coordination while building these financial and time considerations into the budgets
Adapt best evidence educational strategies to the local environment	Focus on how innovative programmatic changes made sense from an educational perspective; residents and faculty may need to become co-learners to produce a learning community with multidirectional learning and enhanced education, without reducing patient services
Create and sustain a vision that engages stakeholders	Manage complex set of relationships with local stakeholders, with ability to articulate and sustain a compelling vision
Demonstrate courage and resilience	Show courage and resilience to faculty, residents, and staff while managing many risks; redesign residency programs and simultaneously meet patient care, educational, and local institutional demands

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A. Hategan et al., *Geriatric Psychiatry Study Guide*,
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