CHAPTER 1

The Problem of Depression in Late Life

Depressive disorders are emerging as a leading cause of disability for older adults, soon to be second only to heart disease (Chapman & Perry, 2008). Depression is the third leading contributor to the global disease burden, surpassing the psychotic disorders and dementia (Collins et al., 2011). By 2030, major depressive disorder is expected to be second leading cause of disability worldwide after HIV and AIDS and the number one cause of disability in the developed nations (Mathers & Loncar, 2006; Mitchell, Vaze, & Rau, 2009). As a result, the public heath imperative to reduce late-life disability and to compress morbidity into the very end of the lifespan is immense. As mentioned in the introduction, the proportion of older adults who are disabled is declining at the same time that the absolute number of seniors is increasing. Improved treatment of depression will play a major role in furthering this phenomenon. At the same time, depressed older persons are less likely than younger persons to recognize depression symptoms as an illness (Alexopoulos et al., 2004) and less likely to present depression as an initial complaint to their primary care physicians, who treat depressed persons far more often than mental health specialists. Awareness of the situations and conditions associated with the emergence of depression is critical to treatment.

The first part of this chapter examines the epidemiology of depression in late life, offering a picture of who is most likely to be depressed and the extent of the problem. The second discusses diagnosis and presents an overview of the many forms that depression can take in older people.

Epidemiology of Depression

The incidence and prevalence of depression vary widely among older adults based on how the condition is defined, where it is assessed, and the generation under observation. Although the loss of friends and family is an inevitable consequence of aging, it is declining health and the onset of disability that are the twin determinants of the majority of depressive symptoms and disorders in late life. Indeed, as discussed below, depression is rare among healthy older community residents. Yet as the absolute number of older Americans increases, the number of those with poor health and dependency will also increase.

Incidence

Incidence is the number of individuals developing a condition within a specific period of observation. Incidence rate appears with a time frame, the number of new cases divided by the period of observation denoted as person-years. In the community-based Cache County survey using multiple assessment methods, from 1 to 2.5% of adults ages 65–100 developed a first episode of depression over the course of 1 year. Face-to-face interviews demonstrated incidence rates for any type of depressive disorder of 1.3/100 person-years for men and 1.9 for women. When evidence that an antidepressant had been prescribed was included, rates grew to 1.5 for men and 2.3 for women. Adding information from postmortem interviews with collateral informants yielded rates of 2.1 for men and 2.6 for women. Of those with no prior history, the rates for major depression fell to 0.78 for men and 0.87 for women. Rates for minor depression were 1.9 for men and 2.4 for women. Advanced age did not predict incidence (Norton, Skoog, Toone, et al., 2006).

In a systematic review that focused on persons ages 70 and older, Büchtemann et al. (2012) examined 20 studies of depression incidence and associated characteristics. In 14 studies, incidence was defined by

categorical criteria obtained from structured interviews with diagnostic instruments. In the remaining 6, incidence was defined by the more easily obtained dimensional criteria of a clinically significant symptom score. Categorical diagnostic measures identify persons in need of treatment. Dimensional diagnostic measures more accurately identify those at risk and as such denote "probable" depression. However Büchtemann et al. (2012) found the incidence of major depression not to be higher among persons ages 70 and older than among young and middle aged adults. Beyond age 70 neither female gender nor advancing age was consistently or substantially associated with major depression. Rather, physical morbidity, disability, and psychosocial events such as personal losses, change in residence, and diminished autonomy overwhelmed the contribution of age and gender as defining elements of risk. Although the onset of major depression in old age was rare, elevations in depressive symptoms were not. The incidence rate of major depression ranged from 0.2–14.1/100 person-years. The incidence of clinically significant depressive symptoms was 6.8/100 person-years.

Prevalence

Prevalence estimates are snapshots depicting how widespread an illness or condition is at one point in time. As such they are far more common than incidence data, which requires the assembly of a healthy cohort and subsequent observation to determine who remains well and who becomes sick. Prevalence can be used to identify associated characteristics but is less informative about etiology, and risk factors for onset and persistence of illness. Although acknowledging the lack of definitive prevalence estimates, the Committee on the Mental Health Workforce for Geriatric Populations of the Institute of Medicine (Eden et al., 2012) concluded that from 5.6 million to 8 million older Americans have one or more mental health or substance use conditions. Depressive disorders and dementia-related behavioral and psychiatric symptoms were the most prevalent. This means from 14 to 20% of older Americans are affected.

Focused only on noninstitutionalized adults 65 years of age and older, the Health Retirement Study found an age-related increase in depressive symptoms as measured by the Center for Epidemiologic Studies Depression Scale. Ten percent of men ages 65–69 were depressed, compared to 15% of women. But by age 85 the prevalence increased

to 18% among both men and women (Federal Interagency Forum on Aging-Related Statistics, 2012). But methods using more exacting standards yield different results.

As reported in the Weekly Morbidity and Mortality Review (Centers for Disease Control and Prevention, 2010) the Centers for Disease Control and Prevention (CDC) analyzed Behavioral Risk Factor Surveillance System (BRFSS) survey data from 2006 and 2008 to determine the prevalence of current depression among 235,067 adults in 45 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands. Current depression was defined as meeting BRFSS criteria for either "major" or "other" depression. Criteria were based on respondent answers to the eight-item Patient Health Questionnaire (PHQ-8). The questionnaire, usually with nine items, is commonly used in primary care settings to screen and diagnose depressive disorders. The nine-item Patient Health Questionnaire (PHQ-9) is discussed in more detail later in this chapter and can be seen in Figure 1.1. The CDC study omitted question 9 from the PHQ, which queries thoughts of death or self-harm. Interviewers did not have access to clinical risk assessors for suicide and could not ethically inquire about risk without access to a potential intervention. Respondents answering yes to either the depressed mood or anhedonia question plus four others lasting "more than half of the days" during the previous 2 weeks met criteria for major depression. Those responding yes to either depressed mood or anhedonia and at least one other item met criteria for "other depression," which might include dysthymia, minor or subsyndromal depression. Of those ages 65 and older, 1.6% (95% confidence interval [CI] 1.4–1.8) met criteria for major depression, and 5.2% (95% CI 4.9–5.6) for other depression. The combined percentage of 6.8 as well as the figures for major and other depression were lower among those 65 and older than for any other age group. Including all ages, 9.0% met criteria for current depression, including 3.4% for major depression. The prevalence of major depression increased from 2.8% in young adulthood (ages 18–24 years) to 4.6% in middle age (45–64 years), but declined among those ages 65 and older.

Similarly, data from the National Comorbidity Survey Replication (Byers et al., 2010) demonstrated a statistically reliable decline in rates of both depression and anxiety disorders with advancing age. The prevalence of depression was higher among women. However, anxiety disorders were more common than depression across all age groups, for men and women. These two studies are noteworthy for the similarity of

Two-question screening with the PHQ-2:

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
A. Little interest or pleasure in doing things?	**0**	**1**	**2**	**3**
B. Feeling down, depressed, or hopeless?	**0**	**1**	**2**	**3**

If A + B is 3 or greater, ask the following:

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
Feeling tired or having little energy?	**0**	**1**	**2**	**3**
Poor appetite or overeating?	**0**	**1**	**2**	**3**
Trouble falling or staying asleep, or sleeping too much?	**0**	**1**	**2**	**3**
Feeling bad about yourself—or that you are a failure or have let yourself or your family down?	**0**	**1**	**2**	**3**
Trouble concentrating on things, such as reading the newspaper or watching television?	**0**	**1**	**2**	**3**
Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual?	**0**	**1**	**2**	**3**
Thoughts that you would be better off dead, or of hurting yourself?	**0**	**1**	**2**	**3**

FIGURE 1.1. The nine-item Patient Health Questionnaire (PHQ-9): Screening questions and complete assessment. Copyright originally held by Pfizer, Inc. Duplication approved for clinical use. Now designated as in the public domain. Retrieved June 30, 2014, from *www.phqscreeners.com*.

findings despite the use of different sampling procedures and diagnostic methodologies. But both offer a conservative, perhaps overly conservative, view of depression among older adults for a number of reasons (Byers et al., 2010). Lowered prevalence may reflect selective mortality in which vulnerable depressed individuals die before reaching older age. Other conditions associated with depression may result in change from community to institutional residence, making the older adult inaccessible for survey studies. Indeed, the prevalence of clinically relevant depressive symptoms increases to one senior in four in primary care, assisted living, and acute-care settings (Alexopoulos et al., 2005b). Frailty, cognitive impairment, and sensory deficits may make participation difficult or unreliable. Older adults may be less comfortable expressing depressive symptoms or experience their distress more in terms of anxiety than mood disturbance. Apathy, irritability, and social withdrawal may be more characteristic of late-life depression. Depressive symptoms associated with a physical condition or ascribed to bereavement may not be attributed to mental illness, yet amplify disability and distress in a clinically significant fashion (Pickett et al., 2014a). Efforts to distinguish primary from secondary depression among older adults do not effectively direct interventions.

Among community-residing older adults, declining health and increasing disability are the major predictors of both the emergence and persistence of clinically significant depressive symptoms (Kennedy et al., 1990, 1991). As a result, the prevalence of all forms of depression would be expected to be higher in primary care settings given the association of physical illness and disability with depressive symptoms. At least 6% of older primary care patients meet criteria for major depression (O'Connor et al., 2009), with another 6% meeting criteria for minor depression or dysthymia. An additional 10% meet criteria for subsyndromal depression, meaning they score above the recovery threshold of the Hamilton Depression Rating Scale (HAM-D) and may be at risk for a major depressive episode (Lyness et al., 1999).

In sum, the incidence of major depression is low among community-dwelling older adults. However, the prevalence of clinically significant depressive symptoms and disorders among primary care patients is substantial. An examination of age per se suggests an optimistic view toward depression in late life. Rather than age, it is the age-related experience of illness, disability, and loss that determine much of the risk of old-age affective disorders. And because each of these is a relatively discrete event, detection and interventions are feasible. The rest of this chapter

focuses on detection and examines the varying ways that depression can present.

Diagnosing Depression in Late Life

Diagnosing depression as an illness is a challenge in older adults. Criteria for a major depressive disorder include five symptoms, one of which must be either depressed mood or loss of interest in pleasurable activities nearly every day for the previous 2 weeks (DSM-5; American Psychiatric Association, 2013). However, the emotional disturbance of major depressive disorder may not be the most disabling aspect of the illness. If there is loss of interest compounded by disturbances in physical and cognitive function an episode of major depression may be present. As a result one need not have depressed mood to have a major depressive disorder. Supporting symptoms include change in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness or excess guilt, difficulty concentrating, and recurrent thoughts of death, dying, or suicide. All must directly cause significant distress or social impairment. The disability the patient experiences must not be due to drugs, medications, or medical conditions, and symptoms must not simply be the effects of bereavement. A major depressive disorder may be diagnosed during a period of bereavement if the distress exceeds expectations based on the individual's history, cultural norms, and clinical judgment. These criteria encompass many different forms of depression, including recurrent or treatment-resistant depression, depression with psychosis, and depression with anxiety, each of which may require differing forms of medication and psychotherapy. Among younger persons depressive disorders most commonly occur exclusive of concurrent physical illness. However, concurrent physical illness is the norm rather than the exception among older patients. The question the practitioner must ask is "Is there some form of a depressive disorder that might be adding excess, potentially reversible disability to the patient's condition?"

The PHQ-9 is commonly used in primary care settings to assist in the screening and diagnosis of major depressive disorders. (The first two questions alone, the PHQ-2, can also be used as a screening instrument.) At a score of 10 or greater, the nine depression items achieve a sensitivity of 88% and specificity of 88% for major depressive disorder among primary care patients, as compared to a structured diagnostic interview from a mental health professional (Kroenke & Spitzer, 2002). As shown

in Figure 1.1, the PHQ-9 questions closely resemble the DSM-5 array of depressive symptoms and similarly require either depressed mood or loss of interest and pleasure to be present most days in the previous 2 weeks. The PHQ-9 score can be used as a severity indicator for the initiation or modification of treatment, as well as for justifying the request for psychiatric consultation (see Table 1.1). As shown in Table 1.2, the serial administration of the PHQ-9 can be used to assess treatment response and the adequacy of antidepressant treatment (Oxman, 2003). As discussed in Chapter 2, executive dysfunction is a predictor of poor response to treatment for depression. Brief assessments of executive dysfunction can be found in Chapter 2 and in Table 2.2.

Assessing Suicide Risk

As discussed in more detail in Chapter 9, older adults represented 13% of the U.S. population in 2010 but accounted for 15% of suicides (Murphy, Xu, & Kochanek, 2013). As noted above, the ninth item of the PHQ-9 is an initial screen for suicidal ideation and should not be omitted. When patients express thoughts of death or suicide or have several risk factors (even if denying thoughts of death), the level of suicide risk should be assessed. Table 1.3 outlines procedural guidelines for the practitioner. When risk is not high, consider referral for cognitive-behavioral therapy (CBT) for suicidality, described in Chapter 4.

TABLE 1.1. Indications for the Initiation of Antidepressant Treatment Based on the PHQ-9

PHQ-9 score	Depression severity	Clinician response
1–4	None	None
5–9	Mild to moderate	If not currently treated, rescreen in 2 weeks. If currently treated, optimize antidepressant and rescreen in 2 weeks.
10–15	Major depressive disorder	Initiate antidepressant.
15 and above	Major depressive disorder	Initiate antidepressant, obtain psychiatric consultation if suicidality or psychosis suspected.

TABLE 1.2. Prescriber Response Guidelines at 4 Weeks Based on the PHQ-9 and the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Studies

PHQ-9 score or change	Outcome	Clinician response
No decrease or increase	Nonresponse	Switch medication.
Decrease of 2–4 points	Partial response	Add medication.
Decrease 5 or more points	Response	Maintain medication.
PHQ-9 < 5	Remission	Maintain medication.

TABLE 1.3. Practitioner-Based Interventions to Reduce the Risk of Late-Life Suicide

If few risk factors are present:
- Screen annually for depression.
- Advanced directives (Patient Self-Determination Act).
- Encourage abstinence or moderation in alcohol intake.
- Encourage smoking cessation.
- Encourage social engagement.

If several risks factors are present but suicidal ideas are denied:
- As above if indicated, and . . .
  - Optimize treatment of depression, anxiety, insomnia, pain, alcohol abuse.

If thoughts of suicide are present but without intent or a plan:
- As above if indicated, and . . .
  - Make family aware of elevated risk and ensure practitioner availability.
  - Instruct family or third party to remove lethal means and alcohol.
  - Identify reasons to live (concern for family, religion, life event goals).
  - Fix an appointment (not as needed); ask that family attend.

If lethal means are available, a plan is expressed, or intent is evident:
- Refer for emergency psychiatric evaluation (involuntary, if needed).
- Consider hospitalization, electroconvulsive therapy.

If suicide has been attempted, or countervailing forces are not available to prevent recurrent attempts:
- Refer for emergency psychiatric evaluation (involuntary, if needed).
- Hospitalize if intent not convincingly recanted or attempt is a recurrence.

Note. Adapted from Kennedy (2000, p. 237). Copyright 2000 by The Guilford Press. Adapted by permission.

Response, Remission, Relapse, and Recurrence

In studies of antidepressants or psychotherapy, the terms "response" and "remission" describe, respectively, patients who are made better and those who are made well by the intervention. "Partial response" describes patients who have improved but not to the extent of meeting criteria for a genuine response. The distinctions are important because of empirical findings regarding their association with prognosis both in the near and far term, and thereby the adequacy of therapy. The longer it takes a person to respond, the less likely he or she is to achieve remission and to subsequently recover. Chances of success are even lower if the response is only partial, which will predispose the person to relapse. Relapse is defined as an exacerbation of symptoms despite transient improvement. Similarly, meeting the more stringent criteria for remission means reducing the likelihood of recurrence. For clinical investigation the standard baseline measure of symptom severity is the Ham-D, with a score of 18–20, in addition to meeting DSM-5 criteria for major depression. Response is defined as a 50% reduction from the baseline in the total HAM-D score. Partial responses are defined as a reduction of 30% or more but less than 50%. For remission either a score of 10, or more stringently 7, must be reached. Stated differently, persons virtually free of depressive symptoms are least likely to have a subsequent episode of major depression, which is the definition of recurrent depression. An episode of major depression severe enough to require hospitalization or complicated by suicidal ideation is more likely to be followed by recurrence even when stringent criteria for remission attain.

In primary care settings, where the HAM-D may be less familiar, response and remission may be assessed though serial administrations of the PHQ-9 without having to calculate percentage change from baseline. As shown in Table 1.2, a 5-point decline indicates a response. Patients scoring 5 or less have achieved remission (Oxman, 2003). The score can be used as an objective measure, beyond the clinician's global impression of change, to discuss prognosis and the subsequent course of treatment. For the sake of convenience, the PHQ-9 may be administered by phone without sacrificing validity. Indeed, telephone administration may be less embarrassing (Allen, Cull, & Sharpe, 2003) and a more effective means of reducing mental health disparities among members of disadvantaged minority groups (Pickett et al., 2014b).

The balance of this chapter overviews the various ways in which depression can present in older people and their clinical implications.

Depressive Conditions Other Than Major Depression

What follows is meant to help the reader navigate the scientific literature, which at times addresses the categorical entity of depressive disorders but also examines the dimensional conditions in which depressive symptoms are more or less present but do not reach the threshold of a disorder. Definitions of "subclinical," "subsyndromal," "minor," and "submajor" depression are confusing, with various investigators using DSM criteria and/or structured diagnostic interviews and symptom severity scores to characterize symptomatic individuals. DSM-5 describes three "other specified depressive disorders" that are not the aftermath of a major mood or psychotic disorder. Recurrent brief depression is defined by episodes that occur at least monthly with depressed mood plus four other criteria of a major disorder but do not last the requisite 2 weeks. Short-duration depressive episode contains the same symptom count but lasts from 4 to 13 days. Depressive episode with insufficient symptoms is defined by the presence of depressed mood, but with only one other criterion symptom of a major disorder, which lasts for 2 weeks. The utility of these designations for older adults and the providers who care for them remains to be determined.

In contrast, "minor depression," which appears in the appendix to DSM-IV (American Psychiatric Association, 1994), uses the same list of symptoms as major depression but requires only depressed mood plus one other symptom to meet criteria. Subsyndromal depression is generally used to distinguish persons whose number or duration of depressive symptoms does not conform to criteria for minor depression. Dysthymic disorder (persistent depressive disorder in DSM-5), defined as depressed mood plus one of eight other DSM criteria present most of the day more days than not over 2 or more years, is often included. However, each designation is associated with as much as a fivefold risk for the subsequent development of a major depressive episode (Lyness et al., 2007) as well as increased use of health services even without progression to a major disorder (Pickett et al., 2014a). These entities may be the prodrome for, or the residue of, a major depressive episode. They also represent a dimension of both symptom severity and duration. Nonetheless, a substantial number of patients in each category will experience a spontaneous remission of symptoms with no intervention. Self-assessed poor health, perceived lack of social support (Lyness et al., 2006), symptom severity, and general assessment of functioning (Lyness et al., 2009)

may be the simplest, most reliable measures to predict the subsequent development of major depression. As a result, patients whose symptoms meet the definitions for these entities may be among the most logical population for interventions to prevent the onset and disability of major depressive disorders (see Chapter 9).

Psychotic Depression

Patients with psychotic depression, more appropriately described as delusional depression, have sustained irrational beliefs (delusions) in association with depressed mood. These delusions are often plausible. Psychotic depression should be suspected when the irrational belief focuses on somatic symptoms or around fears of a serious physical condition when there is no medical evidence to support the belief despite adequate examinations. Patients with somatic delusions visit multiple specialists and obtain repeated testing to identify problems that they "know" exist rather than for the purpose of seeking relief from persistent somatic "worries." The presence of delusions in association with major depression is not recognized in 25% of cases (Andreescu, Mulsant, & Peasley-Miklus, 2007). The careful assessment of depressed patients for the plausibility of their concerns would presumably reduce this rate.

Differential Diagnosis

Due to the obsessional yet plausible quality of the delusions, obsessive–compulsive disorder may seem a reasonable possibility. The difference between obsessive rumination and delusional thinking can be difficult to distinguish (DeBattista & Lembke, 2008). Body Dysmorphic disorder with psychosis, which is characterized by an irrational belief that one's physique is seriously flawed despite obvious evidence to the contrary, may also complicate the diagnostic consideration. Hypochondriasis is a common feature of delusional depression, misdirecting the diagnostician to a somatoform (somatic symptoms disorder in DSM-5) rather than a mood disorder. The distinction is important because body dysmorphic disorder responds to monotherapy with a selective serotonin reuptake inhibitor (SSRI; Phillips, 2004). Difficulty concentrating, deficits in executive function, and subjective complaints of impaired cognition suggestive of dementia are frequently seen. The occurrence of depression with hallucinations but not delusions in older adults suggests structural

brain diseases, or bipolar or schizoaffective disorder. Other symptoms of a major depressive disorder may not be so prominent or severe, further distracting the practitioner from the correct diagnosis. Differentiating schizoaffective disorder from psychotic depression may also be difficult because of the inability to reliably differentiate the sequence of symptom emergence, and establish the presence of psychosis prior to depression (Rothschild et al., 2006).

Bipolar Depression

Occurring in approximately 0.5% of the U.S. population, type II bipolar disorder is characterized by recurrent major depressive episodes interspersed with periods of hypomania (Mitchell, Wilhelm, & Parker, 2001). Hypomania is defined as a disturbance in which mood is persistently and abnormally elevated, irritable, or expansive for at least 4 days' duration. Associated symptoms include grandiosity or inflated self-regard, decreased need for sleep, loquaciousness or pressured speech, flight of ideas, racing thoughts, distractibility, agitation, increased goal-directed activity, and pursuit of pleasures with high self-destructive potential. The symptoms represent an unequivocal, uncharacteristic, and socially disruptive change in behavior. The absence of psychosis and severe social impairment and the duration of symptoms for less than 1 week distinguish hypomania from the mania of type I bipolar disorder.

Because the social disruption may be minimal, and some of the symptoms may even seem beneficial, past episodes of hypomania may have been ignored or dismissed by the patient and family. Major depressive episodes also occur in type I bipolar disorder, in which the occurrence of one or more manic episodes is the distinguishing diagnostic feature. And there are mixed states in which criteria for both mania and major depression are present. As a result the term "bipolar depression" spans the spectrum of bipolar disorders. This broad, rather heterogeneous definition may explain why the array of proven treatments, especially for older patients, remains limited.

Among older adults with bipolar disorder, mania is a more frequent cause of hospitalization than depression (Sajatovic et al., 2005), but depression may account for more disability (Sachs et al., 2007). Worse, the results of present treatment for older adults with bipolar disorders are not remarkably better than those recorded prospectively from 1959 to 1985 (Angst & Presig, 1995). Indeed, few older persons with the

disorder experience a full functional recovery despite symptom remission. Perlis et al. (2006a) prospectively assessed potential predictors of recurrent mood disturbance among 858 symptomatic patients ages 15 and older who subsequently recovered from an episode of bipolar illness. Of persons followed for up to 2 years, nearly half experienced a recurrence. And depressive episodes were twice as frequent as manic ones. The proportion of days depressed or anxious in the preceding year as well as residual symptoms of depression or mania at recovery predicted a subsequent depressive episode. Proportion of days with elevated mood in the preceding year, as well as residual symptoms of mania, were associated with a shorter time to the recurrence of a manic, mixed, or depressive episode. Impairments in cognitive speed and executive dysfunction (Gildengers et al., 2007; Murphy et al., 1999) and changes in subcortical brain structures are common (McDonald et al., 1991), further reducing the chances of return to full function.

Vascular Depression

Two groups, led by Krishnan (Krishnan, Doraiswamy, & Clary, 2001) and Alexopoulos (Alexopoulos et al., 1997), have described major depressive episodes occurring after age 55 associated with white matter changes on magnetic resonance images of the brain and executive dysfunction on measures of neuropsychological performance. White matter, in the center of the brain, allows communication to and from gray matter, the information-processing areas, and other parts of the body. As many as 50% of older adults experiencing a major depressive episode may have subcortical white matter changes (Krishnan et al., 2004). These patients are also more likely to have heart disease, hypertension, and diabetes. More important, executive dysfunction predicts delayed or absent response to antidepressant medication (Alexopoulos et al., 2008) and accelerates development of dementia (Alexopoulos et al., 2005b). Executive deficits may prevent the recovery of independence even when the mood disorder of a major depressive episode has fully remitted (Alexopoulos, Meyers, Young, et al., 2000).

Subsequently Alexopoulos and colleagues (2008) tested the hypothesis that depressed elders who fail to achieve remission have microstructural white matter abnormalities in cortico-striato-limbic networks. They used diffusion tensor imaging, a magnetic resonance imaging

(MRI) technique that displays the integrity of neural tracts connecting cortical and subcortical structures. This technique measures the extent to which water molecules in the brain exhibit diffuse (isotropic) versus directional (anisotropic) patterns of movement. The greater the diffusion tensor anisotropy, the greater the integrity and connectivity of the neural circuit or network. Lesser anisotropy is thought to represent disconnection between distributed cerebral networks. Among 23 older patients who had not achieved remission of depressive symptoms despite adequate dose and duration of antidepressant treatment, they found lower fractional anisotropy in multiple frontal limbic brain areas. The authors concluded that lower fractional anisotropy is associated with poor antidepressant response and may represent a neuroanatomical substrate that predisposes to geriatric depression.

However, the white matter changes and anisotropy associated with depression may convey other risks as well. In the Longitudinal Aging Study of Amsterdam, 2,965 adults with a mean age of 70 years and without a history of stroke were followed for 9 years or until the occurrence of a stroke. In participants with prior heart disease, but not in those without, clinically relevant depressive symptoms at baseline (hazard ratio [HR] 2.18; 95% CI 1.17–4.09) and the severity (range 0–60; HR 1.08; 95% CI 1.02–1.13) and chronicity (HR 3.51; 95% CI 1.13–10.93) of symptoms during follow-up were associated with stroke. The investigators concluded that symptoms of depression at baseline as well as their severity and persistence were associated with subsequent stroke (Wouts et al., 2008). I say more about white matter brain changes in the next chapter.

Mixed Anxiety–Depression

Older adults may have clinically significant symptoms of both depression and anxiety, yet not meet formal criteria for either a depressive or anxiety disorder (unspecified depressive disorder in DSM-5). This syndrome of mixed anxiety and depression is associated with impaired social function, exacerbated disability due to physical illness, suicidality, and poor prognosis. The severity profile may shift back and forth from more anxious to more depressed, with one profile masking the presence of the other and making diagnosis difficult. For example, hallmark symptoms of anxiety disorders such as avoidance and realization that

symptoms are out of the norm or "excessive" may not be readily apparent to the older person.

Avoidance rationales may seem reasonable on the surface, but upon examination are maladaptive. These include (1) excessive checking of financial records, medications, blood pressure, or the well-being of family members; (2) failure to accept assistive devices or home care services or to purchase needed items out of exaggerated concern for costs or loss of independence; (3) refusing to engage in socially supportive activities or family events out of fear of being perceived as "stupid" or "old" or burdensome; and (4) hoarding. Interestingly, fear of falling exists along with anxiety symptoms, but like the behaviors listed above does not seem excessive to the affected older adult. However, the word *excessive* may not conform to the older patient's perceptions. Asking "compared to others your age . . ." or "how much time do you spend worrying about . . ." may give a more telling picture of preoccupation and counterproductive consequences. Similarly, younger persons with phobias are more likely to acknowledge the irrationality of their fears. In contrast, "uncontrollability" distinguishes older but not younger patients who meet criteria for generalized anxiety disorder compared to those with subclinical anxiety. Clinic-based studies find little prevalence of anxiety disorders in the absence of comorbid depression (major depressive disorder with anxious distress in DSM-5) in contrast to community-based samples, in which discrete anxiety disorders do appear.

Further complicating the recognition of anxiety symptoms is their co-occurrence with medical conditions. Panic attacks due to angina or the hypoxemia of chronic obstructive pulmonary disease may be directly due to physiological processes yet still lead to agoraphobia. Corticosteroids and other medications can be anxiety provoking yet be accompanied by disability in excess of expectations. In summary, practitioners should be vigilant for symptoms of anxiety, not to stigmatize the genuine fears associated with the patient's physical condition or prognosis, but rather to detect the presence of a disorder whose diagnosis may justify intervention and promote autonomy. There are several antidepressant medications approved for the treatment of anxiety (see Table 3.1) that are preferred over benzodiazepines. Psychotherapies for depression and anxiety can be hybridized to address both (see Chapter 4 and Tables 4.1 and 4.2). Note that offering an intervention to an anxious person is bound to provoke anxiety. The presence of supportive family is invaluable not only to substantiate the diagnosis but also to assist with acceptance of the treatment (Mohlman et al., 2012).

Affective Syndrome of Alzheimer's Disease

Depressive symptoms are the most common neuropsychiatric manifestation of dementia. Depression is thought to be a risk factor for development of dementia, a symptom of dementia, and a separate diagnostic entity that can represent recurrence of a comorbid disorder (Kennedy & Kastenschmidt, 2010). As a result, efforts to characterize as well as treat depression in the dementias including Alzheimer's disease have been extensive. One expert group (Olin et al., 2002) described an affective syndrome of dementia captured by depressed mood, loss of positive affect, or loss of pleasure in activities plus two additional criteria, all lasting a minimum of 2 weeks. Additional symptoms included social isolation or withdrawal, disruption in sleep or appetite, psychomotor retardation, agitation, fatigue, loss of energy, irritability, feeling worthless, hopeless, or guilty, and morbid preoccupation (death, suicide).

However, in cross-sectional data from persons with dementia in the Cache County study (Lyketsos et al., 2001), apathy was the most common neuropsychiatric symptom, followed by depressed mood, agitation, aggression, and irritability. Depressed mood was more prevalent in vascular dementia. Hallucinations and delusions did not cluster with apathy, irritability, or depressed mood. The most common neuropsychiatric symptom profile was an affective syndrome characterized by apathy, depression, and irritability in more than a quarter of the sample. In another population-based study, motivation-related symptoms (disinterest, low energy, poor concentration) rather than mood disturbances were more prevalent. Notably there was no correlation between the presence of depressive symptoms and the patient's awareness of cognitive deficit (Berger et al., 1999). The Depression in Alzheimer's Disease Study (DIADS) enrolled patients meeting criteria for either a major depressive disorder or minor depression, or the less severe affective syndrome. Patients underwent a randomized, placebo-controlled trial of sertraline (Drye et al., 2011). Although participants on average achieved a 50% reduction in depressive symptoms, there was no statistically significant difference between sertraline and placebo. Nor was there a difference in outcomes based on major or minor depression status. But this is not to say that the depressive symptoms so prevalent in dementia are beyond intervention. Rather, behavioral management techniques taught to caregivers can have measureable and lasting benefits, as shown in chapter on psychotherapy. The hope offered caregivers by both the drug and placebo arms in DIADS may have had a genuine therapeutic effect that was not illusory.

Conclusion

Depression in late life may present as a disorder, a transient emotional state, or a symptom associated with a physical disorder or medication. The challenge is: What to do? The array of interventions, including reassurance and watchful waiting, follows in subsequent chapters. Table 1.4 briefly summarizes the forms of depression that practitioners may encounter. It is the presence of excess, potentially avoidable disability that compels intervention. More often than not, the promise of restoring function, and of preserving autonomy, is the determining factor in the patient's acceptance of treatment. For both the practitioner and the patient, it is a functional solution that is used to address the problematic definition of depression.

TABLE 1.4. Distinguishing Characteristics of Depressive Disorders and Syndromes

Disorder or syndrome	Criteria	Source
Major depressive disorder	Depressed mood or anhedonia, plus four other symptoms, almost every day for most of the day for at least 2 weeks, severe enough to cause a major change in personal function	DSM-5
Persistent depressive disorder (dysthymia in DSM-IV-TR)	Chronically depressed mood most days plus two additional symptoms, 2 years or more duration	DSM-5
Minor depression	Depressed mood plus one other symptom nearly every day for at least 2 weeks, severe enough to "represent a change from previous functioning"	DSM-IV
Subsyndromal, subclinical, submajor depression	No set definition; generally indicates the presence of depressive symptoms, but of insufficient duration, severity, or number to meet DSM-IV-TR criteria for major depressive disorder; often defined statistically on the basis of the diagnostic or symptom checklist instrument used in the study	Lyness et al. (2006)
Other specified depressive disorder	Recurrent brief depression; short-duration depressive episode; depressive episode with insufficient symptoms	DSM-5
Bipolar depression	Major depressive episodes in the context of prior episodes of hypomania (bipolar type II) or mania (bipolar type I)	DSM-5
Depression with anxious distress or with mixed features	Depressive disorder with significant symptoms of an anxiety disorder or bipolar I disorder in which mania and depression alternate over the period of a week	DSM-5
Depression due to other medical disorder	Major depressive episode caused by, rather than simply associated with, a physical illness (e.g., hypothyroidism) or treatment (e.g., interferon alpha)	DSM-5
Adjustment disorder with depressed mood	Disturbance in mood (depression, tearfulness, hopelessness) that follows within 3 months of a stressor and is excessively disruptive but self-limited to 6-month duration; not bereavement	DSM-5

(continued)

TABLE 1.4. *(continued)*

Disorder or syndrome	Criteria	Source
Complicated bereavement	Crippling grief that may meet criteria for major depressive disorder but includes (1) a sense of disbelief regarding the death, (2) anger, bitterness over the loss, (3) recurrent waves of painful yearning, (4) preoccupation with the loss, (5) intrusive thoughts related to the death, and (6) avoidance of situations and activities that remind the person of the loss	Shear et al. (2005)
Depression with psychotic features	Major depressive disorder accompanied by delusions, less often hallucinations; the delusional person may be preoccupied with somatic fears, guilt, or impoverishment	DSM-5
Affective syndrome of Alzheimer's disease	Depressed mood or "decreased positive affect or pleasure" (anhedonia) plus two additional symptoms of major depressive disorder; symptoms such as weight loss or social withdrawal should not simply be a manifestation of the dementia	Olin et al. (2002)
Late-onset depression	Major depressive episode with onset at age 55 or older	Alexopoulos et al. (1997)
Vascular depression	Depressive disorder associated with subcortical white matter brain changes due to diabetes, cardio-, or cerebrovascular disease	Alexopoulos et al. (1997); Krishnan et al. (2001)
Schizoaffective disorder	Symptoms of schizophrenia (hallucinations, delusions, incoherence, avolition) exist concurrently with major depression or bipolar disorder; symptoms of schizophrenia are present for at least 2 weeks in the absence of a mood disorder	DSM-5
Treatment-resistant depression	Various definitions but generally means at least one, more often two trials of antidepressant therapy at adequate dose and duration have failed to bring about remission	Carney & Freedland (2009)
Positive affect domain (lack thereof, including anhedonia)	Core feature of depressive and obsessive disorders suggested by the Research Domain Criteria initiative, and distinguished from "negative affect" domain, which includes fear, distress, and aggression	Stanislaw et al. (2010)

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