Depression represents the most common expression of distress in patients with serious and advanced illness. Depressive symptoms can be described along a continuum of severity, from occasional low mood to the development of clinical depression. Though prevalent, clinical depression remains underrecognized and undertreated in seriously ill patients. Undertreatment of clinical depression is especially concerning because it is associated with reduced quality of life for the patient and family caregivers, reduced autonomy, and increased suicidal ideation and desire for hastened death.

Professional and attitudinal barriers to diagnosis and treatment of depression include the belief that depression should be expected in advanced illness; a fear of overpathologizing end-of-life; concerns about adding symptom burden by prescribing psychotropic medication; and diagnostic difficulties due to overlap of neurovegetative symptoms in depression and advanced illness.

Prevalence
The prevalence of clinical depression in patients with advanced cancer ranges from 3% to 58%, based on the different thresholds of the assessment methodology used. Rates of depression for patients with cancer of the pancreas are 40% to 50%, and their suicide risk is 11 times higher than the general population. Reported rates of depression in children with cancer range between 10% and 14%.

Clinical depression is also reported in patients with non-cancer diagnoses, including end-stage renal disease, advanced heart failure, COPD, and end-stage AIDS.

Risk Factors
Common risk factors for depression in the seriously ill include a prior history of depression, poorly controlled pain, and existential and spiritual suffering. Metabolic and endocrinologic abnormalities are also associated with depression, as are several medications, including steroids, betablockers, and certain chemotherapy agents.

Assessment
Depression assessment methods include diagnostic classification systems, e.g., Diagnostic and Statistical Manual of Mental Disorders (DSM-5), and self-report screening.
Depression and Suicidality in the Seriously Ill

tools, e.g., Geriatric Depression Scale (GDS) and Hospital Anxiety and Depression Scale (HADS). Persistent low mood and decreased interest in previously valued activities are considered hallmarks of depression.

Somatic symptoms of depression include fatigue, decreased ability to concentrate, psychomotor retardation, hypersomnia, and weight loss. As these symptoms are also common manifestations of advanced illness, accurate diagnosis of depression in the seriously ill can be challenging. Endicott (1984) proposed replacing somatic symptoms with psychological symptoms to avoid overdiagnosing depression. Accordingly, weight loss is replaced by depressed appearance; insomnia or hypersomnia are replaced by social withdrawal and decreased talkativeness; fatigue and loss of energy are replaced by brooding, self-pity, and pessimism; diminished ability to concentrate is replaced by lack of reactivity.

Differential diagnoses for depression in the seriously ill include hypoactive delirium and grief reactions. Patients with hypoactive delirium typically experience reduced awareness of their surroundings, which is not generally present in depression. In grief reactions, mood typically fluctuates and the patient retains some ability to experience periods of emotional well-being. Additionally, self-esteem is generally not affected in grief reactions.

Suicidality

Depression increases the risk for suicidality in patients with serious illness. Known risk factors for suicidal ideation are depression and hopelessness, unmanaged pain and physical symptoms, cognitive dysfunction and delirium, poor social support, a prior history of psychiatric illness, prior suicide attempts, and spiritual and existential distress. The presence of suicidality should always be assessed in patients who are depressed. The clinician should assess the presence of a) suicidal ideation, b) suicidal plan, c) intent, and d) availability of means to carry out the suicidal plan. The most effective assessment strategy involves asking the patient clearly and directly whether they have been thinking about ending their lives. The concern that openly asking patients about suicidal ideation may actually trigger suicidal thoughts is not supported by evidence and should never prevent a clinician from conducting a thorough assessment. Based on the assessment, the clinician can determine the risk level and appropriate intervention for each patient.

General Management Considerations

The distress and hopelessness created by uncontrolled physical symptoms can mimic psychiatric illness, especially depression. Thus, the first step in the management of depression in patients who are seriously ill requires managing any uncontrolled symptoms, especially pain. Additionally, patients who present with guilt, ruminative thinking, hopelessness, anhedonia, and decreased quality of life should receive treatment for depression even if criteria for major depression are not fully met. The available evidence indicates that successful management of depression can decrease the desire for hastened death.

Pharmacological Management

There is a general lack of high quality evidence in pharmacological management of depression in patients who are seriously ill. However, a number of randomized trials and meta-analyses indicate the effectiveness of antidepressants. Antidepressants are chosen based on side-effect profile, available time for treatment, target symptom, and coexisting medical properties. SSRIs are generally considered first-line treatment because of a
more favorable side-effect profile. SNRIs can be particularly indicated in depressed patients who are also experiencing neuropathic pain. Tricyclics may be more effective for severely depressed patients, but have a less favorable side-effect profile. The use of stimulants can be appropriate to relieve depressive symptoms in patients with a prognosis of weeks. Improvement in mood and energy are possible within 24 to 48 hours.

**Psychological and Integrative Approaches**

Patients with serious illness diagnosed with depression should receive psychological interventions supported by evidence. The framework, type, and frequency of the intervention are determined by patient-related and illness-related factors. To illustrate, cognitive-behavioral therapy can effectively address depression-inducing cognitive styles, e.g., catastrophizing, in patients whose cognitive and emotional function allows active engagement in therapy.

Similarly, positive life-review-based approaches (e.g., Dignity Therapy) and meaning-oriented approaches (e.g., meaning-centered psychotherapy) can promote a sense of purpose and decrease depressive symptoms. Integrative medicine approaches, e.g., music therapy, can be part of the psychological treatment plan to ameliorate depression throughout the continuum of care, including advanced illness and end of life. It can decrease isolation and despair, and promote connectedness and hope.

**Bibliography**


