Depression in older adults: Diagnosis and management

Once late-life depression has been detected and assessed, psychotherapy and pharmacotherapy are both options for treating this common mental health problem.

ABSTRACT: Late-life depression is a major mental health problem that challenges clinicians and will remain so as the population of British Columbians older than 65 continues to grow. Late-life depression contributes to adverse functional, social, and medical outcomes, and can interfere with treatment for medical problems such as stroke. An effective approach to this treatable disorder includes recognition of risk factors, detection, and assessment. The Geriatric Depression Scale and the Cornell Scale for Depression in Dementia can assist in diagnosis, while both psychotherapy and pharmacotherapy are options for management. When psychotherapies are compared, the strongest evidence for effectiveness has been found for cognitive behavioral therapy, problem-solving therapy, and interpersonal therapy. When pharmacotherapies are compared, efficacy is similar for different classes of antidepressants and adjuvant medications but side effect profiles differ and must be taken into account to avoid adverse events. Patients with severe clinical features of late-life depression, including suicidal ideation and psychosis, should be referred to mental health services.

Late-life depression (LLD) is defined as a depressive disorder occurring in a patient older than 60 years, although the onset and definition of cutoff may vary.1 The impact of clinical depression in older adults can be significant, and choosing effective psychotherapeutic and pharmacological management options can be challenging.

Impact

As the most common mental health problem in older adults, LLD exerts a profoundly deleterious effect on patients, their families, and their communities.2 The proportion of the population in British Columbia older than 65 is predicted to rise from 16.4% in 2013 to between 23.9% and 27.0% by 2038.3 An increasing number of patients will be presenting with LLD in future.

In a community study of adults older than 60 from rural and urban centres, 27.0% complained of depressive symptoms, with 4.0% complaining of more severe symptoms and 0.8% meeting criteria for a major depressive episode.4 A more recent community-based study yielded a prevalence rate of 11.2% for combined symptoms of major and minor depression.5 Older adults in institutions have demonstrated even higher rates. One study showed that 12.0% to 45.0% of hospitalized patients experienced depressive symptoms,6 and 12.4% of nursing home residents met criteria for major depression.7

LLD leads to significant distress and is associated with several adverse outcomes. Functional impairment from the illness may overwhelm caregivers and lead to placement in a care facility. LLD may also interfere with treatment for other common geriatric medical problems such as stroke, Parkinson disease, and cognitive disorders. Impaired motivation further limits rehabilitation efforts and worsens outcomes.2

LLD is a risk factor associated with increased nonsuicide mortality in older adults.8,9 LLD is also associated with suicide in older adults. According to Statistics Canada, 19.0% of Canada’s 3890 suicide victims in 2009 were older than 60. Older men have a higher suicide rate than older women and are a particularly high-risk group. In addition, geriatric

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patients may use more lethal suicide methods, with data from 2009 showing 26.0% of victims over 60 died by firearm, compared with 12.0% of those aged 15 to 39.10

**Detection and assessment**

Detection of late-life depression is more effective when predisposing and precipitating risk factors are considered. Predisposing factors include previous clinical depression, physical and chronic disabling illnesses (e.g., cerebrovascular illness), problematic substance use (including multiple medications and alcohol), and persistent sleep difficulties. Psychosocial predisposing risk factors include female gender, personality traits such as dependency, being widowed or divorced, being socially disadvantaged, lacking social support, and having caregiving responsibilities for others with significant illness.2

Precipitating risk factors for LLD include recent bereavement, change of residence (e.g., from house to nursing home), and adverse life events (e.g., loss, separation, financial crisis, declining health, marital problems). Recently bereaved patients should be screened for LLD and a clinical determination should be made regarding depression based on the patient’s history and the cultural norms for the expression of distress after loss.11

Help-seeking behaviors suggestive of LLD include persistent complaints of pain, headache, fatigue, insomnia, gastrointestinal distress, weight loss, and multiple diffuse symptoms. There may be frequent calls and visits to the family practitioner and high utilization of services.12 In hospital, the presence of LLD should be considered when patients have undergone coronary artery bypass graft surgery, myocardial infarction, stroke, or hip fracture, and when patients experience delayed recovery or refuse treatment or discharge. In the care facility, LLD should be considered when patients present with apathy, withdrawal, isolation, failure to thrive, agitation, and delayed rehabilitation. In older patients with both LLD and physical illness, somatic symptoms are strongly associated with depression.13

Generally, the diagnosis of LLD can be made using *DSM-5* criteria. However, contextual challenges must be considered. The criterion “markedly diminished interest or pleasure” may overlap with or be confused with the apathy of dementia (classified as major neurocognitive disorder in *DSM-5*) or another neurological illness. Loss of weight or appetite can also be caused by physical illness or major neurocognitive disorder. Sleep disturbance may be a result of physical illness, chronic pain, or the use of substances such as opioids. Psychomotor retardation, fatigue, and anergia can be caused by physical or neurological illness. Feelings of worthlessness and suicidal ideation may be attributable to end-of-life issues.

Two screening tools for LLD can assist in diagnosis. The Geriatric Depression Scale (GDS), a validated questionnaire for self-rated assessment, is available in a 30-item long-form and a 15-item short-form version. The long form uses an 11-point cutoff score for diagnosing depression and the short form a 7-point cutoff score.14,15 The GDS is available free online in a variety of languages. Unfortunately, its reliability diminishes with increasing cognitive impairment,16 in which case the Cornell Scale for Depression in Dementia (CSDD) is preferred.17 The CSDD relies on an interview with a family member or caregiver as well as with the patient, and is validated for use in patients with or without dementia.

A complete assessment for LLD requires:

- Reviewing *DSM-5* diagnostic criteria for late-life depression11 and assessing the patient for depression using appropriate screening tools.
- Performing a physical examination and ordering laboratory investigations to identify any medical problems that could contribute to or mimic depressive symptoms (e.g., hypothyroidism, anemia).
- Determining severity of condition, including presence of psychosis or catatonia.
- Assessing suicide risk.
• Identifying any comorbid psychiatric and medical illnesses.
• Identifying any personal or family history of mood disorder.
• Reviewing current medications, allergies, and substance use.
• Reviewing current stresses and life situation.
• Assessing level of functioning/disability.
• Considering support system, family situation, and personal strengths.
• Reviewing results from Mini-Mental State Exam and any other tests for cognitive function.
• Reviewing collateral information.

Management
Once late-life depression has been diagnosed, management options can be considered. There is good evidence to support the use of psychotherapy or pharmacotherapy alone, and the two in combination. For milder forms of LLD, psychotherapy may be recommended as a stand-alone treatment, with the addition of pharmacotherapy if required. For moderate severity LLD, antidepressant treatment is recommended, with the addition of psychotherapy if required. For severe LLD, antidepressant treatment and referral to mental health services are recommended.

Psychotherapy
Although studies have established that psychotherapy is an effective treatment for LLD, the magnitude of the effect found varies with the type of control group used. Few trials of psychotherapeutic modalities have used control groups receiving supportive therapy, which includes attention, education, reassurance, and monitoring of symptoms, despite the fact that this therapy is associated with considerable change and control groups receiving supportive therapy may be the best for assessing nonspecific factors common to all psychotherapies.18

A literature review of psychological interventions for late-life depression found psychotherapy to be moderately effective.19 The interventions studied were cognitive behavioral therapy (CBT), problem-solving therapy (PST), interpersonal therapy (IPT), reminiscence and life review therapy, and brief psychodynamic therapy.

Cognitive behavioral therapy is based on the theory that a patient’s interpretation of situations affects mood and behavior. In treatment, the patient identifies maladaptive or distorted cognitions and learns to challenge these to reduce the intensity of emotion and problematic behavior. A number of meta-analyses reported large effects when groups receiving CBT for LLD were compared with control groups, but demonstrated no difference between CBT and other psychological treatments. CBT for LLD appeared to be effective when wait-listed patients were used as controls, but was not shown to be superior to other forms of treatment.19

Problem-solving therapy is a form of CBT that involves teaching the patient to identify problems, brainstorm solutions, implement a solution, and evaluate its effectiveness. Five studies reviewing PST for LLD in patients not taking antidepressants found significant reductions in symptoms in PST subjects compared with subjects in other groups: wait-list control, treatment-as-usual, reminiscence therapy, supportive therapy, and community-based psychotherapy. PST also appeared to be effective for those with depression and executive dysfunction.19

Interpersonal therapy is a structured, time-limited treatment based on the premise that onset and recurrence of depression is related to interpersonal relationships. IPT focuses on grief, interpersonal conflicts, role transitions, and interpersonal deficits. Patients use techniques to explore, clarify, and express feelings, and to change behavior. IPT is effective in combination with pharmacotherapy, but further research is needed to determine if this psychotherapy is effective as a stand-alone treatment for LLD. Two studies showed IPT and treatment-as-usual were equally effective on measures of depression severity. However, at 6-month follow-up both studies found greater improvement in the IPT groups compared with the treatment-as-usual groups.19

Reminiscence and life review therapy is an intervention based on Erikson’s psychosocial stages of development. Unstructured reminiscence therapy focuses on reviewing positive life events to enhance well-being. Structured reminiscence typically covers the entire life span and is used to evaluate both positive and negative events with the goal of reframing and integrating them. Although meta-analyses of this treatment for LLD found moderate effect, many of the studies were of poor quality and significant heterogeneity in the application of the intervention rendered comparison difficult. Structured reminiscence therapy demonstrated greater improvement than unstructured reminiscence on the Beck Depression Inventory, but was found to be less effective than PST.19

Brief psychodynamic therapy is based on the theory that past conflicts between a caregiver and an older relative are reactivated in the caregiving situation and lead to difficulty with separating caregiver emotions and needs from those of the relative. Studies have found brief psychodynamic therapy to be as effective as CBT for treating community-dwelling older adults with LLD. Results from a subsequent study comparing brief
psychodynamic therapy and CBT in a depressed caregiver group indicated psychodynamic therapy was no different than CBT and confirmed that further research is required. Overall, the strongest evidence for effectiveness has been found for cognitive behavioral therapy, problem-solving therapy, and interpersonal therapy. Most studies large enough to determine a stable effect of treatment for LLD are limited by a focus on ambulatory, middle- to high-income older adults, suggesting that more research is needed.

Pharmacotherapy
While response rates to antidepressants are similar in younger and older patients, physiological changes with aging, polypharmacy, and comorbidities all increase the risk of adverse drug reactions occurring. This means the rule “start low, go slow” applies, with the understanding that older patients may require full adult doses in order to achieve response (defined as a 50% reduction in symptoms on a validated depression scale) or remission (defined as absence of depression on a validated depression scale), and the rule may need to be expanded to “start low, go slow, but go” since many older adults receive subtherapeutic doses or are treated for inadequately short periods. A systematic review found that depressed patients in residential care facilities have a modest response to antidepressant medications, but otherwise there is a dearth of evidence to guide treatment in residential care patients or those with significant frailty or medical comorbidity.

Although different classes of antidepressant medications for LLD should be started at half the normal adult dose and then increased within 1 week if tolerated. Subsequently, doses should be titrated up regularly until there is a noticeable clinical response, maximum dose is reached, or side effects limit further increases. The aim should be to reach average therapeutic dose within 4 weeks. A change of medication should be considered if there is no response after 4 weeks on maximum dose. If there is only partial response after 8 weeks, options include switching to or adding on an alternative antidepressant (preferably of a different class). Some add-on options include lithium, amantadine, another antidepressant, or psychotherapy. Physicians without comfort or experience using multiple agents should consider referral to a specialist or use the strategy of switching. When adding on a second antidepressant, clinicians must monitor for serotonin syndrome. Full remission of symptoms should be the goal of treatment. Following remission of a first episode of LLD, patients should be maintained on a full therapeutic dose of medication for at least 1 year. If pharmacotherapy is discontinued, it should be done gradually over months with close monitoring. Patients who respond but do not achieve full remission should be maintained on therapy indefinitely with ongoing effort to achieve full resolution. Patients who have had more than two episodes of LLD or had particularly severe episodes should also continue on indefinite antidepressant treatment if tolerated.

SSRIs (e.g., citalopram, escitalopram, paroxetine, sertraline), selective norepinephrine reuptake inhibitors (e.g., venlafaxine), bupropion, moclobemide, and mirtazapine are all commonly used and well tolerated by older patients. A 2014 guideline update from the Canadian Coalition for Seniors’ Mental Health recommends SSRIs, venlafaxine, mirtazapine, bupropion, and duloxetine as first-line agents for depressed long-term care residents. In general, these drugs share a side effect profile characterized by constipation, diarrhea, nausea, insomnia, somnolence, and sexual dysfunction. There is variation, however, in the frequency of adverse events from agent to agent. TCAs are not recommended as...
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First-line agents for LLD in spite of being well studied in older patients. This is due to side effects such as postural hypotension, cardiac conduction abnormalities, and anticholinergic effects. When a TCA is used as a second-line agent, an electrocardiogram and postural blood pressure measurement should be obtained before starting the drug and before dose changes. Likewise, blood level monitoring is recommended. Nortriptyline and desipramine are preferred agents because of their lower associated anticholinergic burden compared with other TCAs. A risk exists for hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), meaning that serum sodium levels should be checked 1 month after treatment with an SSRI or a selective norepinephrine reuptake inhibitor. A review of antidepressant-induced SIADH showed greater risk from SSRIs and venlafaxine than from mirtazapine and TCAs. There was insufficient information to draw conclusions on bupropion, duloxetine, and monoamine oxidase inhibitors. Clinicians should check sodium levels sooner if symptoms of hyponatremia develop or if there are risk factors such as old age, female sex, diuretic use, low body mass index, or low baseline plasma sodium level. SSRIs have also been shown to increase risk of gastrointestinal bleeding and should be used with caution in those at higher risk for this (e.g., patients taking nonsteroidal anti-inflammatory drugs or with a history of peptic ulcers). It is generally recommended that older patients avoid fluoxetine because of the long half-life and avoid paroxetine because of the anticholinergic burden.

Citalopram and escitalopram can be associated with QT interval prolongation. In patients over 65, clinicians must be cautious with citalopram doses above 20 mg and escitalopram doses above 10 mg, and exercise care regarding concurrent QT-prolonging medications. An electrocardiogram is indicated before starting these medications and should be repeated if there is concern.

Additional agents for LLD have been studied since publication of the Canadian Coalition for Seniors’ Mental Health guidelines. Vortioxetine is a multimodal serotonergic agent that has synergistic antidepressant and antianxiety effects. Interestingly, it has shown benefit to cognition in animal models. A single randomized, double-blind, placebo-controlled study of the drug for LLD has shown significantly greater rates of response and remission compared with placebo, as well as improvement on cognitive measures.

Duloxetine and desvenlafaxine are both approved selective norepinephrine reuptake inhibitors in Canada. Duloxetine has antidepressant, antianxiety, and central pain inhibitory effects and is well tolerated by older patients, with placebo-controlled trials suggesting effectiveness in LLD. A recent randomized, double-blind study of duloxetine for LLD failed to confirm antidepressant efficacy in older patients but did suggest it, and also confirmed beneficial effects for managing pain in LLD. Desvenlafaxine still has no published studies examining its efficacy in geriatric patients.

Atypical antipsychotics such as risperidone, olanzapine, quetiapine, aripiprazole, ziprasidone, asenapine, lurasidone, and clozapine may be useful as adjuvant medications for LLD, particularly in cases of treatment-resistant depression. Of these, aripiprazole, risperidone, and quetiapine (as a monotherapy) for LLD have been studied. These agents all carry a risk of side effects, including extrapyramidal symptoms, falls, sedation, weight gain, dyslipidemia, and diabetes, and should be used with caution. Health Canada has also published a black box warning that states treatment with atypical antipsychotic medication is associated with an increased risk of all-cause mortality in older patients with dementia.

Full remission of symptoms should be the goal of treatment.
Referral
Patients with severe LLD should be referred to mental health services, possibly emergently, and started on medication. Severe clinical features include presence of suicidal ideation, psychosis, rapid functional or physical deterioration (poor intake, metabolic derangement), and comorbid disorders, including substance misuse. Electroconvulsive therapy may be indicated in these cases. Patients with treatment-resistant depression should also be referred to mental health services.

Summary
The impact of clinical depression in older adults can be significant. Predisposing risk factors include previous clinical depression and disabling illness. Precipitating risk factors include recent bereavement and change of residence. A complete assessment for late-life depression involves performing a physical examination and using a validated screening tool such as the Geriatric Depression Scale. Both psychotherapy and pharmacotherapy may be considered. Studies have found cognitive behavioral therapy, problem-solving therapy, and interpersonal therapy to be effective. While SSRIs may be a superior first choice for treatment, other classes of antidepressant and other adjuvant medications may be options. When choosing a medication, additional considerations include possible side effects, patient preference, and cost. Patients with severe depression should always be referred to mental health services.

Competing interests
None declared.

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