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Older Adults with Severe, Treatment-Resistant Depression: “I got my mother back.”

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Abstract

Depression is one of the most common, disabling, and costly conditions encountered in older primary care patients. Using the case of a 69-year-old woman who struggled with prolonged depression and comorbid medical illnesses, this article summarizes effective strategies for detection and treatment of late-life depression. Clinicians should screen older patients for depression using a standard rating scale, initiate effective treatment such as antidepressant medications or evidence-based psychotherapies, and carefully follow for improvement of depression symptoms. Patients who are not improving should be considered for psychiatric consultation and additional treatments such as electroconvulsive therapy (ECT). Several changes in treatment are often needed before patients achieve remission, and maintenance treatment and relapse prevention planning can reduce the risk of relapse. Evidence-based collaborative programs, in which primary care providers work closely with special mental health providers, following a measurement-based treatment-to-target approach have been shown to be significantly more effective than usual primary care.

The Patient's Story

In early 2001, Mrs B, then a 69-year-old retired cafeteria worker, developed a severe depressive episode. At the time, she was married, and was the primary caretaker for a son suffering from leukemia. A few months earlier, she had developed asthma-like symptoms (later diagnosed as gastroesophageal reflux disease, causing wheezing), which were treated with corticosteroids. She developed a corticosteroid-induced psychosis with visual hallucinations, reported that she had “never felt better in her life” and called people in the middle of the night. Her psychotic and manic symptoms resolved after discontinuing corticosteroids and by March 2001, she felt “depressed 24 hours a day.” She had “lost all interest in things.” Her concentration was poor, making it difficult for her to read a newspaper or follow television programs. She became increasingly disabled; unable to make

even simple decisions and ultimately unable to get out of bed. Although she had worked in food services for many years, her daughter recalled, “She couldn't even fry an egg.”

She became increasingly anxious with related physical symptoms, including trouble swallowing, choking sensations, nausea, and vomiting. She reported being “in constant fear,” worrying that she was never going to get well. She had thoughts of death and suicide but no specific plan to end her life.

She slept poorly, and experienced severe appetite loss, with a 50-pound weight loss over 18 months. During this period, treatments with several antidepressant and anxiolytic medications proved unsuccessful. Her condition deteriorated and she had the first of what became several psychiatric hospitalizations. Her then psychiatrist recommended a course of electroconvulsive therapy (ECT) but her husband opposed this recommendation. Mrs B was discharged, additional medications were substituted and added, but she did not improve. Approximately 6 months after the onset of her depression, Mrs B's husband died unexpectedly. She was readmitted for a second time in December 2001, for a 50-day inpatient stay, again treated with a variety of medications without much improvement. In March 2002, after this second hospitalization, Mrs B's family arranged for her to live in an assisted living facility because she was too disabled to live at home or with family. Mrs B was readmitted for a third time for a 90-day inpatient stay, during which she had 8 ECTs, ending in the summer of 2002. She was judged to have a partial response with better appetite and interest. Still on several antidepressant medications, she was discharged to weekly outpatient psychotherapy.

Nonetheless, she remained depressed, stating “My days are hell.” She was independently able to carry out some ADLs, but still needed help in virtually all IADLs. In September 2002, her daughter took her to a university-based department of psychiatry, where she was seen by Dr F. At the time of her initial evaluation by Dr F, she was on bupropion SR 100 mg orally twice daily, mirtazapine 15 mg orally at bedtime, quetiapine 100 mg orally at bedtime, alprazolam 0.5 mg orally 3 times daily, and temazepam 30 mg orally at bedtime as needed. Dr F saw her every 2 to 4 weeks for several months. She increased the bupropion to 3 times daily, but saw little response.

In November 2002, she was admitted for a 35-day stay on an inpatient psychiatric unit. Dr F recommended electroconvulsive therapy. Her family strongly supported this recommendation and Mrs B consented. Upon admission, Mrs B's medical history included a hiatal hernia with gastroesophageal reflux disease, osteoporosis, and non-insulin dependent diabetes mellitus. Mrs B reported one prior episode of depression and anxiety. Her family history included a grandfather who had been in a mental hospital, a brother with depression and anxiety, and a sister with anxiety. She had recently lost her husband and her son.

Physical examination was essentially normal. She scored 26/30 points on the Mini Mental Status Examination, missing 4 points on “serial sevens.” She exhibited limited eye contact, depressed mood, and restricted and tearful affect. She had no psychotic symptoms and no thoughts of harming herself or others. Routine laboratory testing including electrolytes, blood counts, thyroid function tests, B12, and folate were normal.

Mrs B was seen by geriatric, cardiology, and anesthesia consultants and deemed an acceptable candidate for ECT. She began the ECT in December 2002, receiving 12 treatments at 2- to 3-day intervals. She reported some short-term memory loss between treatments but cognitive testing revealed no significant long-term changes in memory. Over the next 4 weeks, her mood, appetite, and activity level gradually improved and she was discharged to live with her sister-in-law. With outpatient maintenance ECT and medication management, her depression continued to improve over the ensuing 2 months and she was able to live independently at home again.

Mrs B's post-hospital ECT course was complicated by chest pain, which required emergent hospitalization and percutaneous transluminal coronary angioplasty and stent placement. While recuperating, maintenance ECT was discontinued for 2 months and the patient's depression again worsened. ECT was restarted, with the patient on aspirin, clopidogrel, and atenolol. One month after restarting ECT, Mrs B's mood improved. Over the next 9 months, her depression completely resolved and she was able to resume complete self-care. ECT was discontinued and Mrs B continued on maintenance antidepressant medications. She also pursued psychotherapy to deal with long-term difficulties related to her childhood and marriage and with bereavement related to losing her son and her husband.

Perspectives

Mrs B, her daughter, and Mrs B's psychiatrist, were interviewed by a Care of the Aging Patient editor in April and May 2011.

Mrs B: It was couple years when I didn't know anything about what was happening... I didn't eat, I got real sad. I don't remember any of this. They say that I was very, very depressed.

Mrs B's daughter: What she doesn't remember ... it's a blessing. Think about depression, who'd want to remember it?

Dr F: She was severely depressed...she was not functioning....being dependent in all IADLs... at age 69, who, before the depression was completely independent in everything.

Methods

We searched MEDLINE for English language articles on the epidemiology and treatment of late-life depression published between January 1995 and June 2012. This paper focuses on evidence from meta-analyses and randomized controlled trials (see online for a full description).

Results of Evidence Review: Evidence and Clinical Strategies

Epidemiology of late-life depression

Depression is one of the most common mental disorders in late-life¹. Two to 5% of community dwelling adults aged 65 years and older meet diagnostic criteria for major depression^{2, 3}. Up to 10% of older adults seen in primary care⁴ and 30-50% of those in institutional and long-term care facilities clinically significant depression^{5, 6}. When it is not

successfully treated, depression becomes a persistent problem in as many as 40% of older adults^{7, 8}. Rates of chronic depression are particularly high in individuals with chronic medical illnesses⁹. Yet, depression can be successfully treated, restoring patients to a high quality of life¹⁰.

Mrs B had several risk factors for depression^{11, 12} (e.g. being female, personal or family history of depression, loss and grief, care-taking responsibilities, comorbid medical conditions) and several risk factors associated with poor response to depression treatment (e.g. high initial symptom severity and chronicity, comorbid anxiety and somatic symptoms, a family history of mood disorders, and a history of childhood abuse and neglect).

Screening

The U.S. Preventive Services Task Force (USPSTF) found at least fair evidence that screening adults for depression improves health outcomes and that benefits outweigh harms (B rating), and recommends screening for depression if practices have systems in place to assure accurate diagnosis, effective treatment, and follow-up¹³. Based on these recommendations, the Centers for Medicare & Medicaid Services (CMS) recently determined to cover annual screening for depression for Medicare beneficiaries in primary care settings with staff-assisted depression care supports (see resources).

Brief depression screening tools (see resources) are available and can be easily administered by office staff or physicians during a primary care visit. A simple question ‘Do you often feel sad or depressed?’ can be a good starting point. The Patient Health Questionnaire-2 (PHQ-2)¹⁴ asks patients about depressed mood and anhedonia. To address possible ‘false negatives,’ clinicians can ask additional questions to patients who appear depressed, who have difficulty engaging in care, or whose functional impairment seems inconsistent with objective medical illness. A positive screen for depression should trigger further investigation such as an interview supported by the 9-item Patient Health Questionnaire (PHQ-9)¹⁵, which systematically explores the 9 DSM-IV¹⁶ symptoms of major depression. A score of 10 or greater on the PHQ-9 indicates an elevated level of depressive symptomatology and increased risk of clinically significant depression. Both PHQ-2 and PHQ-9 have good sensitivity (83% and 88% respectively) and specificity (92% and 88% respectively) for detecting depressive disorders^{14,15}.

Major Depression in Older Adults

Mrs B experienced all of the DSM-IV symptoms of major depression (Box 1): depressed mood, difficulty concentrating and making decisions, feelings of guilt, lack of energy, psychomotor retardation, poor sleep, poor appetite and significant weight loss, and thoughts of death or suicide. Unlike Mrs B, not all older adults fit this typical picture of depression¹⁷. Depressed mood may be less evident and some older adults do not report feeling sad at all¹⁸. In such patients, anhedonia and the absence of positive affect may be better indicators of depression. Patients with anhedonia and at least four of the remaining DSM-IV symptoms still meet criteria for major depression¹⁹. In addition to these ‘core symptoms’ of major depression, patients may present with high levels of anxiety and somatic symptoms^{20, 21}, concerns about cognitive impairment and physical disability²². Depressed older adults may

find it hard to participate in physical and social activities and in medical treatments such as physical therapy. Expressions such as “I just can't do this” or “nothing will help me” can be signs of decreased motivation, self-efficacy or hopelessness. Statements such as “I am not needed” or “I am in everyone's way” may indicate feelings of low self-worth or loneliness.

Evaluation

All depressed older adults should be asked about thoughts of harming themselves. If positive, clinicians should inquire about specific plans, develop a treatment plan that ensures the patient's safety and consider consultation with a mental health specialist. There is no evidence that inquiries about the self-harm increase the risk of suicide. Depressed older adults should also be asked about a history of mania, a time when they may have experienced rapid thoughts or speech, excess energy or activity, a reduced need for sleep, or behaviors that others thought were excessive or risky. Patients with bipolar disorder commonly present in a clinician's office in the depressive phase of the disorder. Taking a careful history of manic symptoms is important because treatment with antidepressants can exacerbate bipolar disorder and treatment with mood stabilizing medications such as Lithium is indicated instead. Clinicians should also explore the patient's day-to-day functioning because it would be easy to miss the profound level of functional impairment that can occur in older adults with severe depression.

A thorough history and physical examination should focus on medical conditions such as neurological illnesses that may contribute to or worsen depression. Cognitive screening is important to identify impairments that may be related to depression, delirium or dementia. Box 3 lists factors suggesting that cognitive deficits may be related to depression rather than dementia. In patients without a prior history of cognitive impairment, effective treatment of depression may improve cognitive functioning, although cognitive impairment first presenting in the context of depression may also be a sign of early dementia. Persistent cognitive deficits after treatment of depression should be evaluated to rule out dementia. Patients should be asked about new medications such as interferon or corticosteroids, about the use of alcohol, prescription sedatives, hypnotics, opioids, or illicit drugs which can exacerbate depressive symptoms.

Grief and bereavement are important factors to consider in late-life depression. Mrs B experienced grief and bereavement related to the losses of her son and husband. Grieving individuals may experience sorrow, emptiness, numbness, guilt, anger, and sadness. With time, these feelings gradually ease and individuals accept the loss. Major depression on the other hand is pervasive and persistent, and it can impair an older person's ability to overcome feelings of grief and move forward. Mrs B was suffering from a major depressive episode in addition to grief. She noted later that she was not able to grieve properly and to cope with her losses until she had received effective treatment for depression.

Management

Several treatment options are available for late-life depression: antidepressant medications, psychotherapy, or a combination. Other options include exercise programs and

electroconvulsive therapy (ECT). Figure 1 summarizes key steps in the management of late-life depression.

In selecting specific treatments, clinicians should discuss available treatment options and explore prior experiences with treatments, preferences and concerns with patients and family members. Individual preferences about depression treatment are strongly associated with treatment adherence and outcomes²³. A conceptual model called the ‘cycle of depression (Figure 2)’ can help clinicians explain how symptoms of depression may be related to one another and how specific treatments can address these symptoms. Mrs B, for example, reported multiple life stressors, physical symptoms and poor sleep, which led to her feeling tired and unable to concentrate the next day. She became increasingly inactive, and began to feel progressively depressed and hopeless, a “vicious cycle” that she could not escape from. Treatments may be aimed at the various ‘components’ of depression. For example, medications may target somatic symptoms, sleep, and energy. Brief counseling strategies such as behavioral activation can help with the inactivity often associated with depression, and psychotherapy can help address negative thoughts and help the patient learn strategies to solve current and future life problems.

Patients whose depression has remitted should have a relapse prevention plan that summarizes early warning signs for depression, maintenance treatments such as medications, and other strategies to reduce the risk of relapse (e.g., regular physical activity or pleasant activities). They should also be reassessed for recurrence of depressive symptoms with a screening tool such as the PHQ-9 on future visits.

Pharmacological management—In primary care, treatment commonly starts with an antidepressant medication, but clinicians should also consider non-pharmacologic treatment options as alternatives or in addition to medication management. More than 20 antidepressant medications have been approved by the FDA for treatment of depression in older adults, Table 1 lists commonly used antidepressants. Older adults may require lower doses of medications than younger patients because of changes in pharmacokinetics (e.g., decreased renal or hepatic clearance) or drug-drug interactions. On the other hand, medication doses should be titrated upwards to full adult doses in patients who experience partial responses without substantial side effects. Older adults may be more sensitive to certain medication side effects (e.g., the anticholinergic effects of tricyclic antidepressants). Recent meta-analyses^{24, 25} conclude that newer generations of antidepressants such as SSRIs and SNRIs are often preferred to older medications such as tricyclic antidepressants because of their more tolerable side effect profile.

A recent AHRQ report comparing second generation antidepressants²⁶ found no evidence that specific medications are more effective than others, leaving the choice of individual medications up to physicians and patients. When choosing antidepressant medication, patient's and family members' treatment history, patient's treatment preferences, side effect profile, safety in overdose, drug-drug interactions, availability and cost of medication should be discussed with the patient. In Mrs B's case, for example, bupropion is not likely to help with her anxiety and might even exacerbate this problem and SNRIs or SSRIs may exacerbate her problems with nausea and vomiting. A drug like mirtazapine may help with

her depressive symptoms, insomnia, and loss of appetite and weight loss. For most older adults, maintenance treatment with antidepressants (usually for at least 2 years) can substantially reduce the risk of depression relapse compared to placebo²⁷.

Nonpharmacological options for depression treatment include psychotherapy and exercise programs (Table 2). These approaches can be used alone or in combination with antidepressants. A meta-analysis study of 89 controlled studies (pooled observation=5,328 older adults) concluded that psychotherapy and medication did not show strong differences in effect sizes (effect sizes ranged from 0.62 for pharmacotherapy to 0.83 for psychotherapy studies) and recommended that the choice of treatment should be based on other criteria, such as contraindications, treatment access or patients preferences^{28, 29}.

Psychotherapy—Data from IMPACT study showed that older adults find various types of psychological services acceptable and more patients prefer psychotherapy (57%) over medications (43%)³⁰. Recent meta-analyses show that several psychotherapeutic treatments are effective for late-life depression^{31, 32}: cognitive behavioral therapy (CBT)^{28, 33}, interpersonal therapy (IPT)³⁴, and problem solving treatment (PST)³⁵. Briefer strategies such as Activity Scheduling and Behavioral Activation (BA) may also be useful³⁶⁻³⁸. Maintenance treatment with a combination of psychotherapy and antidepressants has been associated with fewer relapses than either treatment alone³⁹. Although such treatments can be effectively provided to older adults in primary care^{40, 41}, they are not widely available in most primary care settings today and we encourage primary care providers(PCPs) to develop relationships with mental health specialists who can offer such treatments or to train a staff member in the clinic to provide evidence-based psychotherapies.

Exercise—Several RCTs and a recent meta-analysis have found that exercise can be effective treatment or treatment adjunct for late-life depression^{42, 43}. It can be challenging, however, to engage severely depressed patients in exercise programs. Everyday physical activities (e.g. walking, taking stairs) and light housework such as gardening may be a good start. For fragile elders, low intensity exercises using a chair or wheelchair can build strength and improve a sense of self-efficacy.

Electroconvulsive Treatment (ECT)—ECT is an important and viable treatment option for severely depressed older adults. In Mrs B's case, two courses of ECT were required to improve her depression. ECT should be strongly considered for patients who have severe, persistent depression that does not respond to several trials of pharmacological or psychotherapy and/or puts patient at high risk of harm (e.g. severe weight loss, malnutrition, refusal of food or suicidal ideation). Poor tolerance or limited response to medications and a history of successful treatment with ECT are also indications for ECT. Data from the 1993 Healthcare Cost and Utilization Project suggested that the likelihood of receiving ECT was greater for individuals 65 years of age and older (21%)⁴⁴.

Physical side effects of ECT are usually short lived and can be treated with medications. They include nausea, headache, jaw pain, or muscle aches. Other adverse effects related to ECT include an increased risk of falls. Serious morbidity and mortality from ECT are low with an estimated complication rate of less than 1%. Even medically frail patients usually

tolerate ECT well^{45, 46}. However, increased blood pressure and cardiopulmonary events can occur during the seizure or in the immediate peri-ECT period, making adequate preoperative evaluation essential. Patients with coronary heart disease may experience ischemic events during seizures, a time of increased cardiac activity and oxygen demand⁴⁷. Unstable cardiopulmonary disease, recent intracranial surgery, an intracranial mass with raised intracranial pressure, unstable vascular aneurysm, recent cerebral hemorrhage or stroke, or pheochromocytoma are contraindications for ECT. Mrs B's ECT had to be interrupted until her coronary heart disease was stabilized.

Despite the paucity of randomized evidence for ECT in elderly populations⁴⁸, literature suggests that ECT is safe and effective in acute treatment of late-life depression^{49, 50}. Patients who improve with ECT are at high risk for relapse^{50, 51} and maintenance treatment with ECT or appropriate pharmacotherapy is highly recommended to reduce this risk^{52, 53}. Maintenance ECT (ranging from weekly to monthly) has been found to be safe and effective in depressed older adults⁴⁶. Mrs B's ECT was started on an inpatient basis and followed-up with outpatient maintenance ECT for almost one year. ECT is available in most academic medical centers and in many hospitals with inpatient psychiatric units. Clinicians should consult a psychiatrist who specializes in this procedure when considering ECT for their patients.

Patients immediately after ECT may awaken with varying degrees of confusion that resolves within hours of treatment. Anterograde amnesia, which can occur after ECT, will usually resolve within 4-8 weeks of stopping ECT. Memory for events during the time shortly before or during ECT may not be fully recovered. Older adults with cognitive impairment from dementia may be at increased risk for cognitive side effects. On the other hand, depression can contribute to cognitive impairment and cognition may improve after successful ECT for depression. A recent review of 27 studies concluded that studies have mixed results, but except for a deterioration in information processing speed during a course of ECT, there is negligible deterioration in the cognition of older adults who receive ECT⁵⁴.

Other Treatment Considerations

Minimize adverse effects: first, do no harm

Mrs B's daughter: My mom was on so much medication it was unbelievable. I think I counted from May until October that she had been on between maybe 50 and 60 different kinds of medications.

All depression treatments have potential adverse effects, especially in medically ill older adults who are on multiple medications. A careful review of all medications is recommended before starting new medications. Discontinuing medications that do not appear helpful or simplifying complex medication regimens can reduce side effects and improve medication adherence and thus effectiveness.

Measure outcomes and treat to target

Systematic tracking of depression severity with rating scales such as the PHQ-9 can help address clinical inertia which is a frequent barrier to improvement and suggest when it is time for treatment adjustments or a specialty consultation⁵⁵. As many as 50-70% of depressed patients will not improve with initial treatment and need adjustments such as medication changes and/or addition of psychotherapy⁵⁶. With systematic treatment adjustments, the majority of patients who fail an initial antidepressant trial eventually improve⁵⁷.

Patients with persistent depression despite multiple courses of antidepressant medications and psychotherapy like Mrs B should be reevaluated for potential contributors to persistent depression (Box 4) and considered for referral to a geriatric psychiatrist.

Overcome barriers to care

A clear and consistent message of hope is an important step to keeping patients engaged even if initial treatments are not immediately effective. Stigma can be a formidable barrier to depression care and clinicians should emphasize that depression is not a sign of personal weakness or simply a part of ‘normal aging’^{58, 59}. Common fears about losing autonomy⁶⁰ and concerns about treatments (e.g. becoming addicted to antidepressant medications) should be addressed as well as cultural and individual variations in the presentation of depression and in treatment preferences.

Clinicians should pay particular attention to populations at high risk for not receiving depression care. These include older adults who are poor, less educated, from ethnic minority groups, or with low social support⁶¹⁻⁶⁴. Older men are also less likely to receive depression care⁶⁵.

Include family caregivers

Engaged and active family members and caregivers can play critical roles, especially when an older adult's ability to advocate for oneself is decreased due to depression. Family members can facilitate adherence to treatment^{66, 67} and improve depression outcomes⁶⁸⁻⁷⁰. Dr. F reported, for example, that “*the buy-in from the family*” for ECT was instrumental for successful treatment of Mrs. B.

Translate evidence into clinical practice—Mrs B's long journey to recovery from depression is not unique. System barriers to effective depression care include a fragmented health care system where PCPs and mental health providers cannot collaborate effectively, limited availability of mental health specialists, especially for evidence-based psychotherapies⁷¹, and a lack of systematic approaches for detecting and managing depression in primary care⁷².

Models of care in which PCPs and mental health specialists collaborate effectively, have gained significant momentum nationally and internationally and are supported by a robust efficacy and effectiveness literature⁷³⁻⁷⁵. In such programs, a depression care manager (typically a nurse, social worker, or psychologist) works closely with the patient's PCP to

provide education, support treatment adherence, and track treatment effectiveness. Care managers may coach patients in pleasant events scheduling and behavioral activation, support antidepressant medications prescribed by a PCP, or offer evidence-based psychotherapies such as PST⁴⁰ or IPT⁷⁶. A designated psychiatrist regularly reviews patients who are not improving and provides treatment recommendations to the PCP. The IMPACT model (Improving Mood: Promoting Access to Collaborative Treatment for Late-life Depression) was demonstrated in a large RCT to more than double the effectiveness of usual care for depression, improve patient functioning, and to reduce long-term health care costs⁷⁷.

Conclusions

Within a few months of completing her second course of ECT, Mrs B was living back in her home. She was going to church regularly, played cards with friends, made lunches for people, and attended her grandson's sports events. She entertained 32 people in her home for her daughter's 50th birthday party and her daughter reported that this was the happiest she had ever seen her mother. At age 78, nine years after developing severe depression, Mrs B continues on one antidepressant medication (venlafaxine) to prevent a relapse. She lives independently, drives, is socially active and enjoys her life.

Mrs B: Every Thursday night, I go out with my friends to eat. On Friday nights, I play cards. We have a card club, there's 10 of us: 5 guys and 5 women. My girlfriend and I go to all the local basketball and football games and volleyball games. I go to church. I like to go grocery shopping, though I don't like to put the groceries away...

Even severe depression in late-life can be treated in most cases. Patients, family members, and clinicians should be prepared to systematically pursue treatment until an effective approach is found.

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Box 1: Diagnostic criteria for major depression (adapted from DSM-IV ¹⁶)

1. Depressed mood
2. Marked diminished interest or pleasure (anhedonia)
3. Sleep disturbance (insomnia or hypersomnia)
4. Appetite or weight disturbance (markedly increased or decreased appetite and / or weight) when not dieting
5. Persistent fatigue or loss of energy
6. Diminished ability to concentrate or indecisiveness
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Psychomotor retardation or agitation (obvious change in mental and physical speed perceived by other people)
9. Recurrent thoughts of death or suicide (not just fear of dying)

Note: To meet criteria for a major depressive episode, a patient must have 1 of the 2 core symptoms (depressed mood or anhedonia) and at least 5 of these 9 symptoms nearly every day for at least 2 weeks. They must also experience functional impairment related to these depressive symptoms and the symptoms should not be due to bipolar disorder or a mixed episode (with depressive and hypomanic symptoms), medications, a drug of abuse, or a medical condition (e.g., hypothyroidism).

Box 2: "Red flags" for consideration of depression

Irritability

Agitation/anxiety/excessive worrying

Excessive or unexplained somatic complaints

Concerns about cognitive impairment

Decreased problem-solving capacity

Excessive guilt

Social withdrawal

Alcohol or substance abuse

Statements such as: "I just can't do this" "Nothing will help me" "I am not needed" "I am in everyone's way"

Box 3: Factors that suggest cognitive impairment may be related to depression

- Depressed affect/mood
- Neurovegetative signs such as poor energy, appetite, or sleep
- Long response latency
- Frequent responses of “I don't know”
- Little effort; quick to give up
- Slow speech and movements
- Errors of omission rather than errors of commission
- Patient is concerned about cognitive difficulties. “I think I am getting Alzheimer's. I cannot remember things.”
- Movements, writing, and speaking may be slow but no clear signs of aphasia, apraxia, or agnosia.
- Greater similarity to subcortical dementias, such as Parkinson Disease

Box 4: Factors to consider in the evaluation of patients with persistent depression

- Wrong Diagnosis (eg, does the patient have bipolar disorder?)
- Comorbid psychiatric disorders (eg, dementia, posttraumatic stress disorder)
- Untreated or ineffectively treated chronic pain
- Insomnia
- Alcohol or substance abuse
- Medical problems or medications that may cause or worsen depression
- Severe psychological or social stressors
- Problems with treatment adherence
- Insufficient dose / duration of treatment
- Side effects
- Initial treatments may have been appropriate but are simply not effective

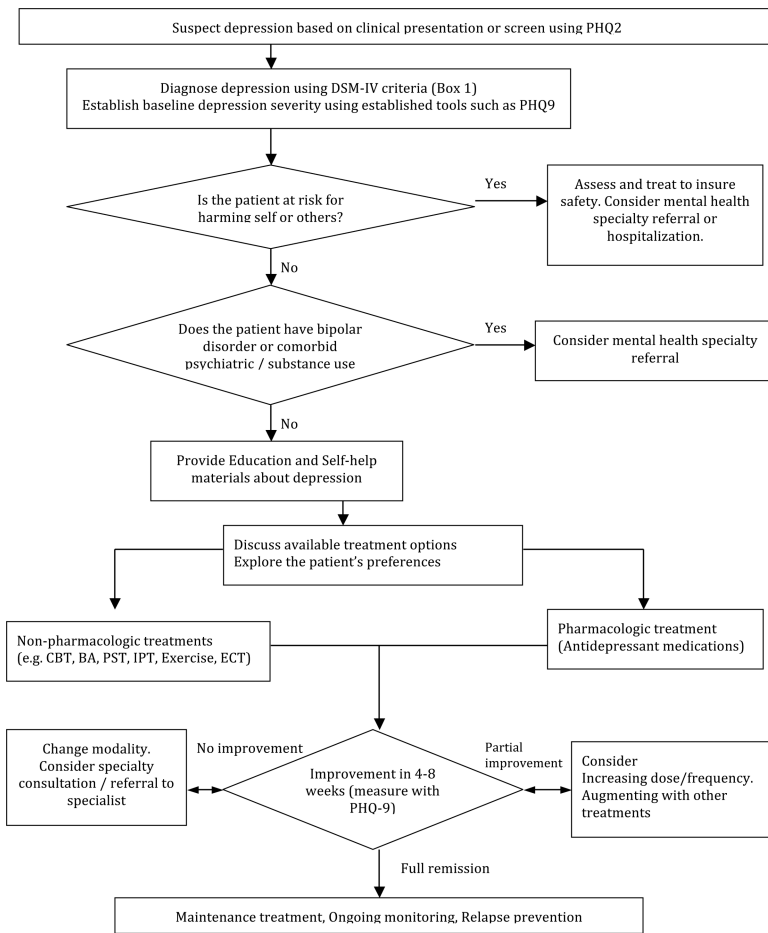


Figure 1.
Flowchart of late-life depression treatment.

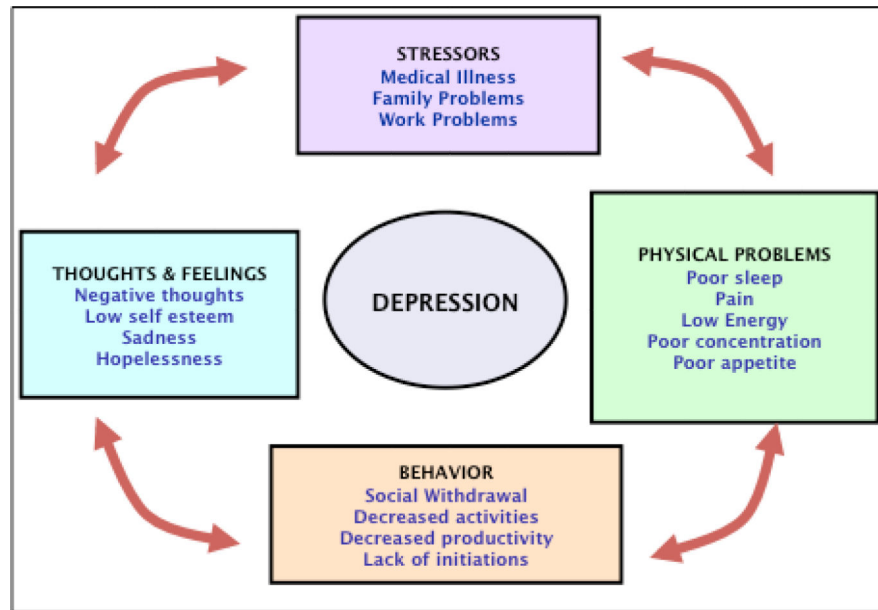


Figure 2. The ‘Cycle of Depression.’ This conceptual model can help clinician explain how symptoms of depression may be related to one another and discuss treatment options aimed at the various ‘components’ of depression with patients.

Table 1

Commonly used antidepressant for late-life depression

Medication	Starting dose	Common Therapeutic Doses	Half-life (hour)	Common side effects	Comments
SSRI (Selective serotonin-reuptake inhibitors):					
Fluoxetine	5 mg	10 – 40 mg once daily	70–80	Nausea, dyspepsia, anorexia, tremors, anxiety, insomnia, sexual dysfunction, jitteriness, hyponatremia	Risk of serotonin syndrome if combined with certain drugs. Very long acting.
Sertraline	12.5 mg	50 – 200 mg once daily	25–30	Loose stools, diarrhea	
Citalopram	10 mg	20 – 40 mg once daily	40–50		
Escitalopram	2.5 mg	10– 30 mg once daily	40–50		
Paroxetine	10 mg	20 – 50 mg once daily	10–20	Dry mouth, drowsiness, fatigue, weight gain	More anticholinergic side effects. High risk of discontinuation syndrome if drug stopped abruptly.
SNRIs (Serotonin-norepinephrine reuptake inhibitors)					
Venlafaxine XR	37.5 mg	75-225g once daily	5 –9	Nausea, drowsiness, fatigue, weight gain, hyponatremia, diastolic hypertension at higher doses	Risk of serotonin syndrome if combined with certain drugs. High risk of discontinuation syndrome if medication stopped abruptly.
Duloxetine	20 mg	20-60mg once daily	8 –17		
Other newer antidepressants					
Mirtazapine	15mg	15–45mg at bedtime	20 –40	Sedation, increased appetite / weight gain	No sexual side effects.
Bupropion SR	100mg	100-150 mg twice daily	15		No sexual side effects. Contraindicated in patients with seizures. Not recommended for patients with comorbid anxiety.
TCAs (Tricyclic antidepressants)					
Nortriptyline	10mg	50-125mg every night	18 –56	Sedation, weight gain, dry mouth, urinary retention, constipation, blurry vision, orthostatic hypotension, impairment of cardiac conduction	High risk in overdose: 10 days of typical daily dose may result in a fatal cardiac arrhythmia. Get baseline ECG and follow-up ECG at steady state or if new cardiac symptoms occur.
Desipramine	25mg	100-200mg once daily	12 –28	Fatigue Insomnia, agitation	Therapeutic blood levels range from 50 to 150 ng/mL

Table 2

Meta-analyses of non-pharmacologic treatment for late-life depression

Treatment type	Name of the studies	Efficacy*
Cognitive Behavioral Therapy (CBT): Challenge and change negative or dysfunctional thoughts, behaviors, and associated feelings.	5 RCTs (pooled N=153 older adults)	CBT more efficacious than waitlist control [WMD=9.85 (95% CI: -11.97, -7.73)]
Behavioral activation (BA): Increase pleasant activities and experiences of success to improve sense of self-efficacy, mastery, and mood.	16 RCTs (pooled N=780) (5 RCTs with older adults)	BA equally effective as cognitive therapy [PES=0.02 (95% CI: -0.21, 0.25)] Large effect size [MSE=0.87 (95% CI: 0.60-1.15)]
Mazzucchelli et al 2009 ³⁵	34 RCTs (pooled N=2,055) (5 RCTs with older adults)	BA more efficacious than control groups (waitlist or treatment as usual) [PES=0.74 (95% CI: 0.57, 0.97)]
Ekers et al 20 07 ³⁶	17 RCTs (pooled N=1,109) (3 studies with older adults)	BA more efficacious than control groups [SDM= -0.70 (95% CI: -1.00, -0.39)], brief psychotherapy [SDM=-0.66 (95% CI: -1.00, -0.12)], supportive therapy [SDM=-0.75 (95% CI: -1.37, -0.14)], and equal to CBT [SDM=-0.08 (95% CI: -0.14, -0.30)]
Problem solving therapy (PST): Increase understanding the link between depression and life problems. Teach a technique to resolve problems in a structured way. Provide positive experiences related to problem solving.	21 RCTs (pooled N=1,264) (2 studies with older adults)	PST significantly more efficacious in reducing depression symptom than supportive therapy and attention control group [SDM = .45 (p<.001)], likely be more effective than waitlist control group [SDM=2.38 (p=.09)]
Bell et al 20 09 ³³	13 RCTs (pooled N=2,199) (2 studies with older adults)	IPT was superior in efficacy to placebo [WMD=-3.57 (95% CI: -5.9, -1.16)] and significantly better than CBT [WMD=-2.16 (95% CI: -4.16, -0.15)].
Interpersonal psychotherapy (IPT): Develop interpersonal skills to help adapt to current interpersonal roles and situations.	13 RCTs (pooled N=1,264 older adults)	The majority of studies reported statistically significant improvement in exercise group compared to control group. No pooled effect sizes were provided
de Mello et al 2005 ³²	11 RCTs (pooled N=641 older adults)	
Exercise: Improve physical activity, fitness, resilience, sense of mastery.		
Sjosten et al 2006 ⁴⁰		
Blake et al 2009 ⁴¹		

* Studies have reported different outcomes measures for efficacy: WMD= weighted mean differences. MES= mean effect size. PES= pooled effect size. SMD= standardized mean difference