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Depression among older adults with diabetes mellitus

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Synopsis

Depression is among the leading causes of decreased disability-adjusted life years in the world[1] and a serious public health problem.[2] Older adults with DM experience greater risk for comorbid depression compared to those who do not have DM.[3] Having DM increases the risk of subsequent development or recurrence of depression. Conversely, history of depression increases the risk for new onset DM.[4] As an unwanted co-traveler of DM, undetected, untreated or undertreated depression impinges an individual's ability to manage their DM successfully, hindering their adherence to treatment regime.[5] It also undermines the effectiveness of provider-patient communication and decays therapeutic relationships. Thus, in the context of caring for older adults with DM, comorbid depression presents special challenges and opportunities for clinicians. Moreover, recent studies have suggested that co-occurring depression and DM may accelerate cognitive decline, highlighting the importance of treating depression and DM. Several treatment modalities are available, which can be used to treat and manage depression in primary care settings: pharmaceutical, brief psychotherapeutic, behavioral and life style interventions, and combination therapies. An evidence-based health care delivery model is also available for treating depression in primary care settings. In this article, we summarize the clinical presentation of late-life depression, potential mechanisms of comorbidity of depression and DM, importance of depression in the successful management of DM, and available best practice models for depression treatment.

Keywords

Diabetes; Depression; Mood disorders; Aging; Collaborative Care

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Introduction

Diabetes mellitus (DM) is one of the most common chronic conditions among older adults. About 26.9%, or 10.9 million U.S. residents aged 65 years and older had diabetes in 2010.[6] Depressive disorders are serious chronic diseases that increase morbidity and mortality,[7] erode quality of life,[8] and increase medical expenditure. Depression and DM often co-occur. Data from a range of settings suggest that the prognosis of both DM and depression—in terms of severity of disease, complications, treatment resistance and mortality—is worse for either disease when they are co-morbid than when they occur separately. Comorbid depression in patients with DM is strongly associated with increased burdens of DM symptoms[9], poor self-management and treatment adherence[10], increase in health care services utilization and medical expenditures[11] and an increased risk of DM complications.[12] DM complications such as myocardial infarction, amputation or loss of vision can in turn precipitate or worsen depressive episodes. Yet, few studies have extensively examined the associations between depression and DM in the older adults populations. Also, recent studies have found that combination of DM and depression may increase the risk for dementia, suggesting increased brain toxicity.[13] The purpose of this review is to summarize the clinical presentation of late-life depression among older adults with DM, potential mechanisms of comorbidity of depression and DM, importance of depression in the successful management of DM, and available best practice models for depression treatment.

Disease description

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. To be diagnosed with major depression, a patient must have depressed mood or anhedonia and at least 5 of the following 9 symptoms nearly every day for at least 2 weeks:

- Depressed mood
- Marked diminished interest/pleasure
- Sleep disturbance (increased or decreased sleep)
- Appetite disturbance (increased or decreased appetite; typically with weight change)
- Fatigue/loss or energy
- Diminished concentration or indecisiveness
- Feelings of worthlessness or excessive or inappropriate guilt
- Psychomotor retardation or agitation (a change in mental and physical speed perceived by other people)
- Recurrent thoughts of death or suicide (not just fear of dying)

They must also experience functional impairment related to these depressive symptoms.

Older adults, however, do not always present with the typical symptoms of depression. In particular, depressed or sad mood may be less evident or not even present. In these cases,

anhedonia may be better indicator for depression.[14,15] Depressed older adults may experience sleep disturbances (sleeping too much or too little) or changes in appetite (eating too much or too little). Decrease in self-efficacy, motivation, and ability to participate in self-care may also indicate underlying depressive symptoms. Signs of such symptoms can be subtle. Older adults may reply with "I don't know" to simple questions, decline to participate in physical, speech or occupational therapy, and feeling negative or hopeless about treatments offered. Some may easily give up tasks during these therapies. Older adult who experience loss of self-worth or sense of loneliness due to depression, may complain "nobody needs me," or "I feel I am just in everyone's way." The symptoms of late-life depression are often attributed to normal aging, grief, physical illness or dementia and providers and patients miss important opportunities to initiate treatment for what is an treatable health problem.[16]

The majority of older adults with clinically significant depressive symptoms do not meet standard diagnostic criteria for major depression or dysthymic disorder.[17,18] Patients in this group fall short of meeting diagnostic criteria for major depression because of fewer or limited duration of depression symptoms. Nonetheless, studies suggest that these patients carry similar disease burden: poorer health outcomes, functional impairment, and higher health utilization and treatment costs.[19-21] Moreover, these patients are at very high risk for subsequently developing major depression and may also develop suicidal ideation.[22-24]

Although depression can be successfully treated,[25] many older adult suffer from a chronic or recurrent depression.[26] In a prospective study about courses of major depression, approximately 85% of individuals who recover from depression experience recurrence within 15 years.[27] Findings meta-analyses of chronic depression in primary care and community sample suggests that about one in three depressed older adults experience chronic and persist course.[28,29] Depressed patients with DM are at greater risk for a chronic course of depression or less complete recovery.[30] Such chronicity, in turn, makes it more difficult for older adults and their family caregivers to optimally self-manage DM.

In the older adults with DM, depressive symptoms may be overlooked because they are assumed to be due to concurrent DM and other medical illnesses. Many of the symptoms of depression such as lower energy, fatigue, loss of appetite, and sleep disturbance are also associated with DM. Thus differentiating stress related to DM self-management and depression can be challenging.[31] Somatic complaints may suggest presence of depression, especially if they are out of proportion to underling physical disorders.[32] Only 25-30% of primary care patients present with purely affective or cognitive symptoms of depression.[33]

Risk factors

Risk factors for developing depression after age 65 are similar to those in younger individuals and include being female, unmarried, low socioeconomic status, having chronic physical illness, social isolation, a history of depression, and a family history. The risk of major depression increases up to three-fold if a first-degree relative has the illness.[34] Additional risk factors that are particularly important in older adults include loss and grief,[35] social isolation or limited social support,[36] high degrees of family conflict,[37,38] and care-

taking responsibilities.[39] Other risk factors that increase the likelihood of depression in the medically ill elderly include presence of cognitive impairment, age greater than 75, active alcohol abuse, and lower educational attainment.[40-49] Table 1 summarized the risk factors for depression in older adults.

Protective factors

Strong and supportive social context has been identified as a protective factor. A compelling body of evidence has shown that social support decreases the risks for depression[50,51] and for depression relapse,[52] increases adherence to depression treatment, [53,54] and improves treatment outcomes. Social support may have positive effects on psychological wellbeing independent of whether or not individuals are exposed to stress.[55,56] Social support may also promote wellbeing through modulation of neuro-endocrine response to stress.[57]

Social activities, such as volunteering suggested to have positive effect on depression outcomes in older adults.[58] Studies have also suggested that religion and spirituality may play an important part in many older adults' lives and social connectedness and support are an important part of organized religion.[59] Religion may allow older adults to experience life as meaningful despite losses and challenges and, thereby, reduce the risk of depression. It is also possible that the positive effect of religion on mental health is mediated by the social connectedness and the social support derived from taking part in religious activities.

Prevalence/Incidence

Depression is one of the most common mental disorders in late-life.[60] About one in four U.S. resident projected to experience major depression by age 75.[61] In community settings, about 5% of adults aged 65 and older meet research diagnostic criteria of major depression,[62,63] with rates of subsyndromal, clinically significant depression estimated at 8% -16%.[64] The rates of geriatric depression increase to 12-30% in institutional settings, and up to 50% for residents in long-term care facilities.[65,66] Approximately 5-10% of older adults seen in primary care settings have clinically significant depression.[67]

Variations in prevalence in late-life depression across racial/ethnic group are rarely examined and existing literature present mixed findings. However, given that differences in diabetes prevalence exist by racial/ethnic group, these may be important to appreciate. Cross-sectional and longitudinal epidemiological study showed that Non-Hispanic White and Latino older adults have higher rates of depression.[68-70] A longitudinal population study of community-dwelling Hispanic older adults showed approximately 9% of sample met the criteria for lifetime diagnosis of major depression, while 24% of sample reported minor depression.[70] The prevalence of depression in African American is generally lower than their White counterparts.[71]

Minority older adults are less likely to be diagnosed with or treated for depression than their white counterparts.[72,73] These health service disparities in minority populations become increasingly complicated when considering cultural beliefs and attitudes towards depression care. Culture influences how individuals experience and express depression.[74,75] Minority patients from certain ethnic groups may express their depression somatically than

psychologically.[33,76] Such somatic presentations may reduce the recognition of depression by primary care providers or leads to the perception of a patient as 'difficult.'[77] Some minorities may also have less faith in the biological etiology of depression, be more skeptical about antidepressant use, and show stronger preferences for counseling than their White counterparts.[78,79] When pharmaceutical treatment is the only available option, minority older adults may be less likely to engage in treatment and more likely to be non-adherent. The present primary care systems that focus primarily on pharmacological treatment without considering the unique barriers faced by ethnic and racial minority populations may not affect the pattern of disparities observed.[80]

Scant information on the cross-national prevalence of late-life depression is available. A report from a World Health Organization concluded that older adults in developed countries had relatively low average depression rates of 2.6% while those in developing countries had an average rate almost three times higher (7.5%).[81] The rapid increase in diabetes across the world, particularly in developing countries,[82,83] indicate that these international discrepancies are critical to understand.

Among older adults with DM, depression is highly prevalent.[84] Up to 30% of individuals with DM have a significant number of depressive symptoms and 12 to 18% meet diagnostic criteria for major depression.[3,85] Patients with DM experience significantly higher rates of depression compared with their age- and gender-matched counterparts.[84] A meta-analysis of ten studies showed that the prevalence of depression was significantly higher in patients with DM compared with those without (17.6 vs. 9.8%).[84] The prevalence of depression was higher in females with diabetes (23.8%) compared with males (12.8%); however, the odds ratio for depression in patients with Type 2 DM compared with those without was higher in males (OR = 1.9, 95% CI 1.7-2.1) than females (OR = 1.3, 95% CI 1.2-1.4).

Depression and mortality in individuals with DM

Based on several meta-analyses, depression is associated 1.5- to 2.6-fold increase of mortality among individuals with in DM.[7,86,87] Few studies have examined if treating depression may decrease mortality among individuals with depression. Data from a large clinical trial of collaborative late-life depression treatment program in primary care setting (PROSPECT) showed that evidence-based treatment of depression can reduce mortality rates among those with DM (adjusted hazard ratio 0.49, 95% CI: 0.24-0.98).[88] Another study of all cause mortality with same sample also found that patients with major depression in intervention practice were 24% less likely to have died, compared to depressed older adults in usual primary care practices.[89]

Underlying mechanisms of comorbidity of depression and DM

Katon[90] proposed a complex bidirectional relationship between depression and type 2 DM (Figure 1). Depression early in adult life is a risk factor for subsequent development of DM.[91] The increased risk of DM in patients with depression has been hypothesized to be the result of maladaptive health risk behaviors associated with depression such as smoking, obesity and lack of physical exercise[90] as well as psychobiologic factors such as increased cortisol levels, increased inflammatory factors[92] and insulin resistance.[93]

On the other hand, DM may increase risk of depression or worsen the depression symptoms due to increased symptom burden, DM complications causing functional impairment and decreased quality of life, as well as vascular brain changes secondary to DM. Comorbid depression has been found to impair the ability to perform self-care activities necessary to control DM by affecting memory, energy level, and executive function.[94-96] Lack of self-care and the psychobiologic changes associated with comorbid depression may explain why individuals with comorbid depression experience increased risk of macro- and micro-vascular complications[12] and dementia.[13]

While DM and depression independently associated with memory and cognitive impairment,[97-99] recent clinical epidemiological studies found that concurrent DM and depression may have synergistic negative effect on brain health, posing greater risk for developing dementia and Alzheimer's disease.[13] There are several biological mechanisms that can explain such a toxic effect of the DM and depression combination on brain health. First, DM and depression are risk factors for cardiovascular and cerebrovascular diseases (e.g., vascular dementia and Alzheimer's disease). Concurrent DM and depression may increase risk for cardiovascular and cerebrovascular events in additive fashion.[13] Secondly, depression is associated with dysregulation of the hypothalamic-pituitary axis,[100,101] which increases glucocorticoid production, and impairs negative feedback. Hypercortisolemia is associated with metabolic syndrome—a risk factor for vascular dementia and Alzheimer's disease.[102-104] Finally, chronic or recurrent depression is associated with hippocampal atrophy.[105,106]

The temporal relationship between depression and DM has not been fully established. Existing evidence suggests that the association between history of depression and subsequent development of DM is stronger than that between history DM and subsequent development of depression.[107] Several prospective epidemiological studies have found that having depression increased risk for developing DM subsequent years by 1.62-to 2.52-fold: Demakakos and colleagues[108] analyzed data of 6,111 individuals who reported not having doctor-diagnosed DM at baseline in 2002-2003 and concluded that, after adjusting for several demographic and clinical characteristics, individuals who had greater depressive symptomatology at baseline experienced 1.62-fold increased risk for developing DM in the subsequent 45.8 months. In another longitudinal study of community-residing adult population by Camethon et al, after adjusting for age, race, and gander, the adjusted risk of developing DM in subsequent years are 2.52-fold higher among those with greater depressive symptoms than those with low depressive symptoms.[109] A prospective epidemiological study of 1,715 residents of Baltimore Catchment area showed that having major depressive disorder was associated with more than 2-fold increase in risk (adjusted odds ratio: 2.23; 95% CI 0.90-5.55) for developing DM in the subsequent 13 years.[110] However, this was not statistically significant.

Having DM increases the risk for developing depression subsequently. A meta-analysis of 11 epidemiological studies concluded that individuals who had Type 2 DM without depression at baseline experienced 1.24-fold increased risk (95% CI 1.09-1.40) for subsequently developing or recurring depression in subsequent years.[111] Data from the study of 5,201 multi-racial participants of Women's Health Across the Nation (SWAN) concluded

that having DM increase the odds for developing DM in the subsequent 2 years by 2.8-fold (95% CI: 1.2-6.4) among depressed African American Women.[91] Therefore, older adults with diabetes should be considered at higher risk for future depression.

Prevention and early treatment

Prevention and early treatment of depression matter to providers who treat individuals with DM for several reasons. First, as mentioned earlier, having depression may increase the risk for subsequently developing DM. Thus, prevention and early treatment of depression may lower the incidence of DM. Second, having comorbid depression decreases individuals' ability to successfully self-manage DM and increases likelihood for poor DM outcomes. Thirdly, depression is treatable and several treatment approaches are developed for primary care settings. In a recent clinical trial with 247 older adults[112] suggests that both problem solving therapy for primary care (PST-PC) and coaching in health dietary practices could effectively reduce the incidence of major depression in older adults, including in older black adults with high BMI. Despite the fact that black participants in the trial carried a greater risk for depression than did their white counterparts – including obesity –the interventions were equally effective in reducing the incidence of major depression from an expected rate of 20-25% over 2 years to only 8-9%, in both black older adults and white older adults. Thus, given the challenges of treating prevalent depression in people living with both depression an DM mellitus, especially in minority populations –where stigma represents an important barrier, it seems particularly important to develop depression prevention strategies that utilize, variously, active coping strategies and life style interventions that promote health and protective factors.

The U.S. Preventive Services Task Force 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-up.[113] Based on these recommendations, the Centers for Medicare & Medicaid Services recently determined to cover annual screening for depression for Medicare beneficiaries in primary care settings with staff-assisted depression care supports.

Treatment strategies

In managing DM, clinicians use several clinical data to establish a baseline and treatment goals – e.g. fasting serum glucose level and HgA1C. The same stepped, measurement-based treatment principles can be applied to treating depression: establishing a baseline; setting clinical and functional goal for depression; and assessing patient's progress accordingly. Figure 2 illustrates one of widely used clinical guidelines for depression treatment.

Various treatment options are available for late-life depression: antidepressant medications, psychotherapy, or a combination. Other options include exercise programs or other life-style modifying interventions and electroconvulsive therapy (ECT). Several meta-analyses showed that combination therapy is more efficacious than monotherapeutic approaches in treating and in preventing relapse.[114-117] In a recent meta-analysis of 14 RCTs of intervention for depression among patient with diabetes, all treatments have shown to be

effective in reduction of depressive symptoms (g=−0.51, 95% CI: −0.63, −0.39).[118] The pooled effect size was large in psychotherapeutic interventions combined with diabetes self-management education (g= −0.58, 95% CI −0.77, −0.39); and pharmacological treatment showed moderate pooled effect size (g=−0.47; 95% CI −0.67 to −0.27).[118] Unlike major depression, subsyndromal depressive conditions have a relatively small evidence base regarding treatments; existing data suggest that available therapies have modest effect sizes when compared to usual care or placebo.[16,119,120]

Targeting interventions for patients with minor and subsyndromal depression may prove useful as both primary and secondary prevention strategies and clinicians should watch such patients carefully because of the high risk of worsening depression, especially if patients have experienced prior episodes of major depression. Psychosocial treatments may be more helpful than medications for older adults with less severe forms of depression.[121]

Treatment delivery model for comorbid depression and DM

To date, more than 40 randomized controlled trials have established a robust evidence base for an approach called ’collaborative care models (also called integrated care models).[122-125] Recently, several trials of collaborative care model have documented the effectiveness of treating comorbid depression and DM[125,126] (e.g., PATHWAY[126]) and comorbid depression, and DM and/or coronary heart disease (TEAMcare[127]). In such programs, a depression care manager (usually a nurse or clinical social worker) supports medication management prescribed by PCPs through patient education, close and proactive follow-up, and brief, evidence-based psychosocial treatments such as behavioral activation or problem solving treatment in primary care. The care manager may also facilitate referrals to additional services as needed. A psychiatric consultant regularly (usually weekly) reviews all patients in the care manager’s caseload who are not improving as expected and provides focused treatment recommendations to the patient’s PCP.[122,128-130]

Tools for assessing and tracking depression

Several tools for assessing depression severity are available and can be easily administered by office staff or physicians during a clinic care visit. The most frequently used tool is the 9-item Patient Health Questionnaire (PHQ-9)[131], which systematically explores the 9 DSM-IV[132] 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. PHQ-9 have good sensitivity and specificity (both about 88%) for detecting depressive disorders.[133,131]

Pharmacological management

Approximately 80% of antidepressant prescribed in the U.S. is prescribed in primary care settings. More than 20 antidepressant medications have been approved by the FDA for treatment of depression in older adults. Newer generations of antidepressants such as SSRIs and SNRIs have more tolerable side effect profile compared to tricyclic antidepressants (TCAs).[134,135] Comparing second generation antidepressants, studies found no evidence that specific medications are more effective than others.[136] Thus, physicians may discuss the choice of medication with patients and their family. Because of the changes in

pharmacokinetics (e.g., decreased renal or hepatic clearance), older adults may require lower doses of medications than their younger counterparts. Furthermore, considering high rates of multimorbidity and polypharmacy among older adults, drug-drug interactions are particular concern in this population. On the other hand, medication doses should be titrated upwards to full adult doses in patients who experience partial responses without substantial side effects. Table 2 summarizes common antidepressant medications.

Psychological management

Older adults patients with depression tend to prefer psychotherapy over medications.[137] Several psychotherapeutic modalities are effective for late-life depression[138-140]: cognitive behavioral therapy (CBT),[121,141] interpersonal therapy (IPT),[142] problem solving treatment (PST),[143] and Behavioral Activation and Pleasant Activity Scheduling (BA).[144-146] A recent meta-analysis of 44 studies comparing psychotherapies and control conditions,[140] concluded that the overall effect size of psychotherapy over control group were g = 0.64 (95% CI: 0.47-0.80). Although such treatments can be effectively provided to older adults in primary care,[147,148] they are not widely available in most primary care settings today and we encourage clinicians 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 brief psychotherapies. Table 3 summarizes brief- and evidence –based psychotherapeutic approaches that can be easily administered in the primary care context and by nurses, social workers, or other licensed psychotherapists.

Electroconvulsive Treatment (ECT)

ECT is an important and viable treatment option for severely depressed older adults. ECT should be strongly considered for patients who have severe, persistent depression that does not respond to several trials of antidepressant medications or psychotherapy and/or puts patient at high risk of harm (e.g. severe weight loss, malnutrition, refusal of food, suicidal ideation). Poor tolerance or limited response to medications and a history of successful treatment with ECT are also indications for ECT. Rates of ECT use in depressed adults vary substantially.[149,150] Older adults are more likely to receive ECT than younger adults, African Americans are less likely to receive ECT than Whites and individuals with poor health insurance or living in rural areas are also less likely to receive ECT.[149]

Summary/Discussion

DM and depression is frequently comorbid in older adult patients. Considering the negative synergistic effects on range of health outcomes resulted by comorbid depression and DM, prevention and early treatment of comorbid depression are a critical component of successful health management in older adult patients with DM.

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Key Points

1. Depression is highly prevalent in the general population and increases the risk for type 2 DM 2.
2. Comorbid depression and DM is associated negative health outcomes, such as accelerated cognitive decline and increased mortality.
3. Depression impinges the patient and the family caregiver's ability to effectively manage DM, decreases adherence to treatment, and undermines successful physician-patient relationship
4. Effective models for treating comorbid depression and DM exists and some components of these models are implementable in individual clinics.

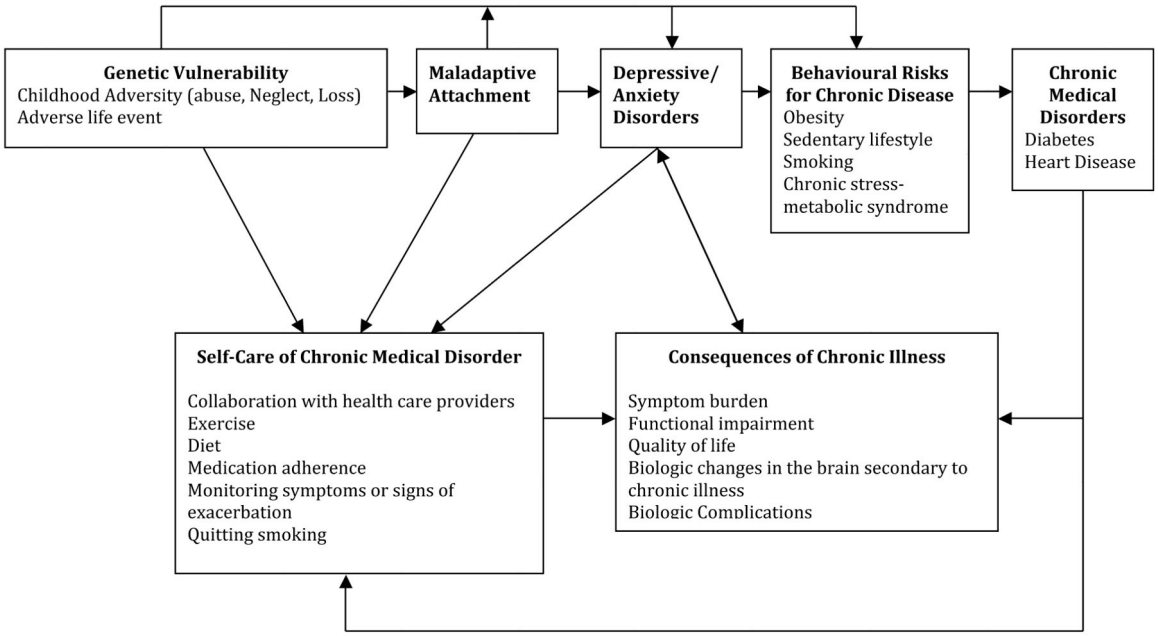

Figure 1. A conceptual model of interaction between major depression and medical illness

Reproduced from Katon, Wayne J. "Clinical and Health Services Relationships between Major Depression, Depressive Symptoms, and General Medical Illness." Biological Psychiatry 54, no. 3 (2003): 216-26.

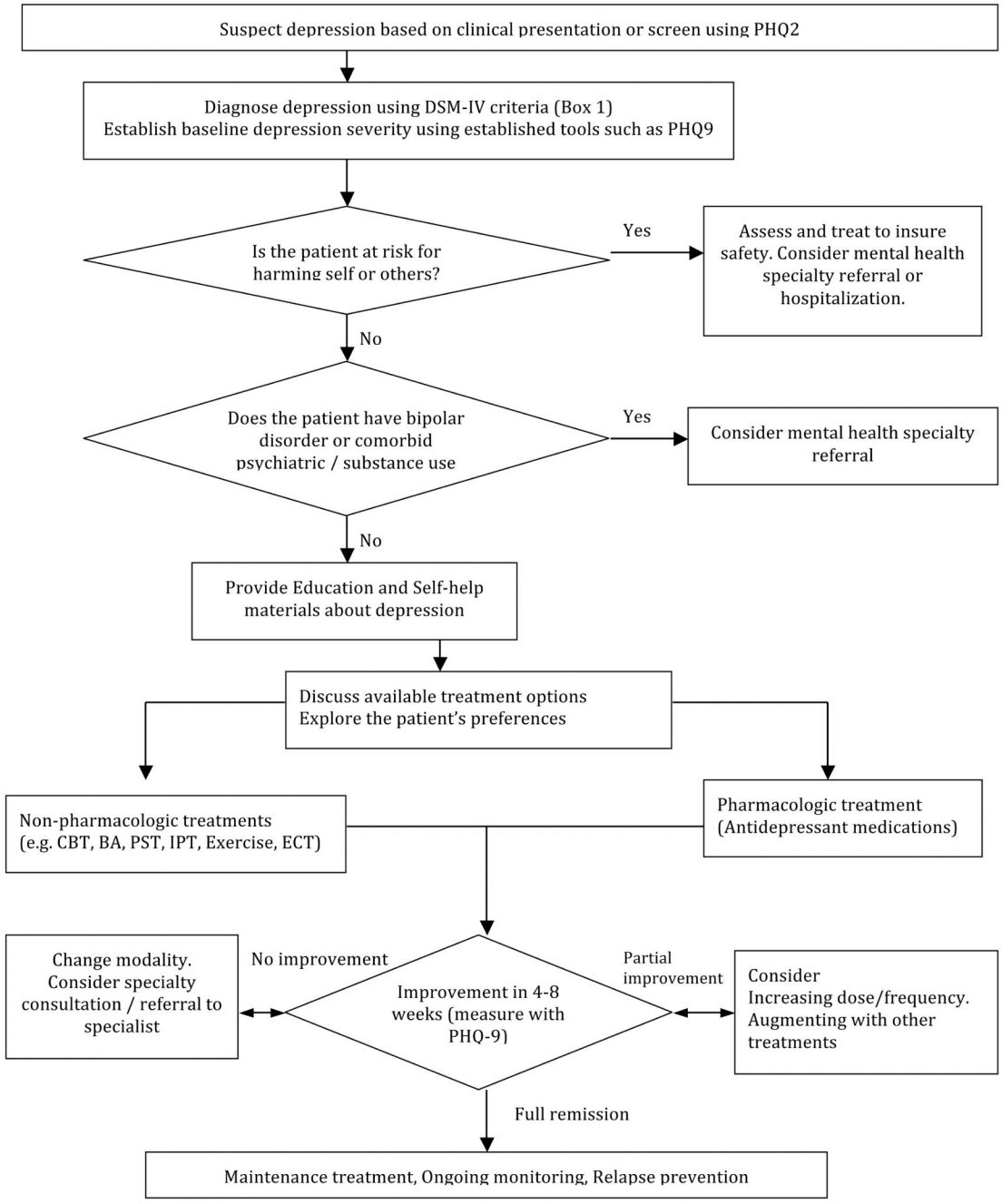

Figure 2.
Algorithm for Screening and Treating Depression in Primary Care Setting

Table 1

Risk Factors for Depression in Older Adults

Authors, year	Sample	Finding
Age		
Cole et al (2003)[152]	Age≥50	Meta-analysis of epidemiological studies. Pooled OR for depression associated with age: 1.2 (95% CI: 0.9-1.7)
Snowden (2008)[153]	Mixed age	Comprehensive review of epidemiological studies: Depression is as common in older age as in earlier life.
Being Female		
Cole et al (2003)[152]	Age≥50	Meta-analysis of epidemiological studies. Pooled OR for depression associated with being female: 1.4 (95% CI: 1.2-1.8)
Sonnenberg et al (2001)[154]	55≤Age≤85	A random, age and sex-stratified community sample of 3056 older Dutch people; Prevalence of depression in women was almost twice as high as in men.
Grief and Loss		
Zisook et al (1991)[155]	Mixed age	Major depression and anxiety disorders are common within the first year of the spouse's death: 29-58% meet criteria for major depression at one month, 24-30% at two months, and 25% at three months.
Cole et al (2003)[152]	Age≥50	Meta-analysis of epidemiological studies. Pooled OR for depression associated with recent bereavement: 3.3 (95% CI: 1.7-4.9)
Turkey et al (1999)[156]	Age≥70	The rate of syndromal depression in the newly bereaved was nearly nine times as high as the rate for married individuals, and the rate of depressive symptoms was nearly four times as high.
Social Isolation		
Cole et al (2003)[152]	Age≥50	Meta-analysis of epidemiological studies. Pooled OR for depression associated with living alone: 1.7 (95% CI: 0.6-4.7)
Prince et al (1998)[157]	Age≥65	Prospective epidemiological study. Lack of contact with friends was a direct risk factor but also modified the association between handicap and depression.
Cacioppo et al (2006)[158]	Age≥55	There is a reciprocal relationship between loneliness depressive symptomatology and over time
Cognitive impairment		
Cole et al (2003)[152]	Age≥50	Meta-analysis of epidemiological studies. Pooled OR for depression associated with recent bereavement: 2.1 (95% CI: 0.6-8.6)

Table 2

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):				Nausea, dyspepsia, anorexia, tremors, anxiety, insomnia, sexual dysfunction, jitteriness, hyponatremia	Risk of serotonin syndrome if combined with certain drugs.
Fluoxetine	5 mg	10 – 40 mg once daily	70-80		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)				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.
Venlafaxine XR	37.5 mg	75-225g once daily	5 – 9		
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)				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.
Nortriptyline	10mg	50-125mg every night	18–56	Fatigue	Therapeutic blood levels range from 50 to 150 ng/mL
Desipramine	25mg	100-200mg once daily	12–28	Insomnia, agitation	

Table 3

Efficacious non-pharmacologic treatments for late-life depression

Treatment type	Studies	Level of evidence	Comments
Cognitive Behavioral Therapy (CBT)	Gould et al 2012[159]	Meta-analysis of RCTs	CBT significantly more efficacious at reducing depressive symptoms Combination with pharmacotherapy more efficacious than CBT alone
	Cuijpers et al 2014[140]	Meta-analysis of RCTs	Older adults populations studies
Behavior activation (BA)	Cuijpers et al 2007[160]	Meta-analysis of RCTs	Mixed population studies Effect is weaker in older adults
	Ekers et al, 2014[161]	Meta-analysis of RCTs	Mixed population studies
	Samad et al[162]	Meta-analysis of RCTs	Older adults populations studies
Problem solving therapy (PST)	Bell et al 2009[163]	Meta-analysis of RCTs	Mixed population studies
Interpersonal psychotherapy (IPT)	Beekman et al 2006[164]	Pragmatic RCT	Older adults populations studies
Reminiscence (life review)	Bohlmeijer et al 2003[165]	Meta-analysis of RCTs	Older adults populations studies
	Pinquart & Forstmeier[166]	Meta-analysis of RCTs	Efficacious for broad range of outcomes, and therapeutic as well as preventive effects are similar to those observed in other frequently used interventions.