Published in final edited form as:

Maturitas. 2014 October ; 79(2): 147–152. doi:10.1016/j.maturitas.2014.05.026.

Late-life depression in the primary care setting: Challenges, collaborative care, and prevention

Charles A. Hall^a and Charles F. Reynolds III^{b,*}

^aUniversity of Pittsburgh School of Medicine, United States

^bNIMH Center for Late Life Depression Prevention and Treatment, University of Pittsburgh School of Medicine and Graduate School of Public Health, United States

Abstract

Late-life depression is highly prevalent worldwide. In addition to being a debilitating illness, it is a risk factor for excess morbidity and mortality. Older adults with depression are at risk for dementia, coronary heart disease, stroke, cancer and suicide. Individuals with late-life depression often have significant medical comorbidity and, poor treatment adherence. Furthermore, psychosocial considerations such as gender, ethnicity, stigma and bereavement are necessary to understand the full context of late-life depression.

The fact that most older adults seek treatment for depression in primary care settings led to the development of collaborative care interventions for depression. These interventions have consistently demonstrated clinically meaningful effectiveness in the treatment of late-life depression. We describe three pivotal studies detailing the management of depression in primary care settings in both high and low-income countries. Beyond effectively treating depression, collaborative care models address additional challenges associated with late-life depression. Although depression treatment interventions are effective compared to usual care, they exhibit relatively low remission rates and small to medium effect sizes.

Several studies have demonstrated that depression prevention is possible and most effective in at-risk older adults. Given the relatively modest effects of treatment in averting years lived with disability, preventing late-life depression at the primary care level should be highly prioritized as a matter of health policy.

© 2014 Published by Elsevier Ireland Ltd.

*Corresponding author at: Western Psychiatric Institute and Clinic, 3811 O'Hara Street, 758 Bellefield Towers, Pittsburgh, PA 15213, United States. Tel.: +1 412 246 6426; fax: +1 412 246 5991. ReynoldsCF@upmc.edu, korzondm@upmc.edu (C.F. Reynolds-III).

Contributors

Dr. Reynolds and Mr. Hall prepared and approved the final manuscript.

Conflicts of interest statements

Charles Hall reports no conflicts of interest.

Competing interests

None declared.

Provenance and peer review

Commissioned and externally peer reviewed.

Keywords

Late-life depression; Collaborative care; Depression prevention; Treatment of depression; Primary care

1. Clinical presentation and challenges in the primary care setting: introduction

Depression is among the leading causes of illness-related disability and is projected to be the greatest contributor to disease burden in 2030 in high-income countries [1]. Estimated depression prevalence rates among aging populations range between 1 and 3% in the community and 6 and 9% in primary care (PC) settings [2]. Given the prevalence of late-life depression (LLD), and the preference of older adults to seek out treatment in PC settings [3], it is important to recognize the challenges surrounding the diagnosis and treatment of LLD faced by primary care physicians (PCP's). Additionally, one should understand the evidence-based strategies designed to mitigate these challenges.

This review aims to: (1) characterize the clinical presentation of LLD and the challenges often encountered by the primary care physician (PCP); (2) provide the rationale for the development of collaborative care models and present three pivotal studies highlighting their effectiveness in treating depression; and (3) describe relevant literature in LLD prevention.

2. Associated risks

Recognition of LLD is paramount as its consequences can be life threatening. Depression increases the risk for first-ever stroke and myocardial infarction [4], and increases mortality in patients with coronary heart disease [5] and various forms of cancer [6]. Depression has been identified as a risk factor for all-cause dementia including both vascular dementia and Alzheimer's disease [7]. Depression remains *the* major risk factor for suicide in old age. Indeed, older adults successfully attempt suicide at higher rates than any other age group and these rates continue to rise in many countries. Even after suicide is accounted for, LLD is associated with increased rates of mortality [8].

3. Clinical presentation of LLD

LLD refers to older adults whose mood disorder presented either in earlier life or is now present for the first time in late-life. The diagnostic criteria for major depression are identical for both older and younger patients. However, LLD includes some features that make it unique among mood disorders. First, LLD tends to have a more chronic course including transient recoveries and frequent relapses. LLD is often accompanied by cognitive impairment, dementia and other chronic medical conditions. Finally, a myriad of social factors commonly experienced in late-life such as bereavement may influence the identification and treatment of LLD.

3.1. Medical burden

LLD is often accompanied by significant medical burden and disability. In fact, as the number of health conditions and their attendant disability increases, so does MDD prevalence [9]. Depressed older adults are more likely to have poor treatment adherence for medical conditions such as diabetes and cardiovascular disease [10].

Compared to non-depressed elders, those with LLD had nearly twice the number of doctor's appointments, spent nearly twice as many days in the hospital over the expected length of stay and were almost twice as likely to receive five or more medications [11,12].

The preponderance of medical conditions seen in late-life may help explain why PCP's identify less than half of LLD cases [13]. Many symptoms (ex. fatigue and sleep disturbance) of medical conditions in late-life mimic depressive symptoms. Additionally, PCP's are more likely to be presented with less severe and vague symptom profiles which may further obscure depressive symptoms.

The extent of medical comorbidity in those with LLD impacts treatment efficacy. In a study of maintenance pharmacotherapy for LLD, participants with fewer and less severe coexisting medical illness showed lower rates of recurrent episodes of major depression than those with more numerous and severe coexisting medical illness [14].

3.2. Cognitive impairment

Cognitive impairment may complicate the identification and treatment of LLD. Cognitive impairment often develops after the onset of mood symptoms, and has been detected in 40–60% of non-demented individuals with LLD [7]. These impairments often persist after treatment and symptom remission [7]. The deficits are seen across various cognitive domains, namely, executive function and information processing speed [15].

3.3. Treating late-life depression and cognitive impairment

Treating depression in the context of cognitive impairment can be challenging. In a study of recently remitted older adults with depression, donepezil and maintenance antidepressant therapy was compared to placebo and maintenance antidepressant therapy. The donepezil group temporarily improved global cognition and showed a lower rate of conversion to frank dementia, but was more likely to experience recurrent major depression compared with the placebo group [16]. Therefore, the risk of increased recurrence of depression must be weighed against the benefit of reduced rate of dementia conversion when using cholinesterase inhibitor augmentation to treat LLD with mild cognitive impairment.

A meta-analysis [17] investigated the efficacy of antidepressants for the treatment of depression in patients with both depression and dementia. Two of the seven studies in the meta-analysis found antidepressants to be more effective than placebo, the other five did not. It is still unclear whether antidepressants are effective in the treatment of depression in patients with dementia, but the weight of the evidence is that antidepressant pharmacotherapy in dementia does not “beat” placebo in terms of response rates.

4. Social context

In addition to significant medical burden, social factors may complicate the presentation and prognosis of LLD. For example, individuals with LLD and lower SES have more morbidity and mortality compared to those with LLD and higher SES [18]. Furthermore, those with low SES tend to respond poorly to antidepressant therapy [19].

4.1. Gender

Gender can influence the clinical presentation of LLD. Older women suffer from depression at twice the rate of older men. Possible reasons for this disparity are economical disadvantages, increased isolation, more medical morbidity and higher rates of disability [20]. Men may be more likely than women to present with symptoms of anger, irritability, anhedonia, withdrawal and apathy and less likely to complain of sadness or psychological symptoms [21].

4.2. Ethnicity

Special considerations may be helpful to clinicians evaluating patients from diverse ethnic groups. For example, depressive disorders are underdiagnosed and undertreated among Black Americans and Latinos [22]. Somatization of psychological distress has been observed in Korean and Chinese elders. Among Chinese-Americans the view that depression brings dishonor and shame to one's family was thought to deter help seeking.

4.3. Bereavement and caregiver stress

Bereavement, a frequently experienced and highly stressful event in later life may be complicated by episodes of major depression. Losing a loved one may also be preceded by strenuous and extended care giving. Bereavement and stressful care giving both have the potential to increase mortality and initiate or exacerbate depression [23].

4.4. Treating bereavement-related depression

Identifying bereavement-related depression has implications for treatment. A double-blinded placebo-controlled study assessing behavioral and pharmacological interventions for bereavement-related depression found nortriptyline and interpersonal therapy (IPT) in combination was significantly more effective at inducing remission than either nortriptyline alone or placebo [24].

4.5. Stigma

Those with LLD often do not perceive a need for mental health care services. Stigma often prevents acknowledgment of symptoms, proper medication adherence and was found to be a fundamental reason why older-adults do not seek treatment and discontinue treatment within PC settings [25].

5. Collaborative care interventions: the need for collaborative care

The development of collaborative care models for depression was originally stimulated by findings suggesting that over half of the mental health treatment for LLD is delivered in the

PC setting [26]. They were also developed to address many of the challenges facing PCP's such as the inadequate use of antidepressants and psychotherapy [27] as well as poor treatment adherence rates [27].

5.1. Overview of pivotal research

It is increasingly recognized that depression, like other chronic diseases with a relapsing and recurring course, responds favorably to collaborative care treatment models. Studies of collaborative care models generally share four characteristics: scheduled patient follow-ups, enhanced inter-professional communication; a structured management plan; and a multi-professional approach to patient care including case managers (CM's). CM's are often trained nurses, social workers, or psychologists who coordinate between specialty mental health providers and the PC team. In the case of the MANAS trial described below, they are lay health counselors (LHC's) from local communities. CM's often assist PCP's in prescribing antidepressants, oversee patients as they receive pharmacological interventions and provide psychosocial interventions including psychotherapy.

Below we describe three pivotal state-of-the-art studies detailing treatment of depression in PC settings in both the high and low-income world. Each compares a collaborative care intervention group to an enhanced usual care group. Usual care was enhanced because participants were informed of their diagnosis and encouraged to follow-up with their PCP. Many studies of collaborative care models (ex. PROSPECT and MANAS) utilize cluster randomization where the unit of randomization is the practice setting, not the research participant (Table 1).

5.2. Improving mood-promoting access to collaborative treatment (IMPACT) [28]

The IMPACT study was conducted across 18 PC clinics and seven sites of various patient populations in the USA. Participants were age 60 years and older and met diagnostic criteria for MDD or dysthymia. Exclusion criteria were substance abuse, psychosis, high suicide risk, cognitive impairment and current depression treatment. Participants were randomized to a usual care group or a stepped care intervention group. In step 1 of the intervention, patients met with their CM and would choose to be treated with either antidepressants or problem solving therapy (PST) for 6–8 sessions. If a patient did not respond to treatment in 8–12 weeks, step 2 would follow. In step 2 a patient would be offered the treatment (antidepressant or PST) they forewent in step 1. If an antidepressant was chosen in step 1 patients were given the alternative to try a different antidepressant. If symptoms persisted, step 3 commenced in which antidepressants and PST were used in combination. Beyond step 3, a final treatment option included referral for electroconvulsive therapy or specialty mental health care. Patients received monthly sessions over the course of one year and were followed an additional year after the completion of the primary outcomes study.

At 1 year, 45% of intervention patients had a 50% or greater reduction in depressive symptoms from baseline compared with 19% of usual care participants. Compared with usual care, intervention participants had lower depression severity, received depression treatment at greater rates, and were more satisfied with their depression care. The intervention group also reported less functional impairment and greater quality of life

compared to usual care participants. Significant differences in depression symptomatology favoring the intervention group remained after one year of the completion of the original IMPACT study [29].

5.3. Prevention of suicide in primary care elderly: collaborative trial (PROSPECT) [30]

PROSPECT is a multisite clinical trial aimed at treating and reducing suicidal ideation in elderly PC patients. PROSPECT was conducted using a broad patient population in 20 PC practices across the north-eastern US. Participants were age 60 or older and met diagnostic criteria for either major or minor depression. Individuals were excluded if cognitively impaired or were taking monoamine oxidase inhibitors. Participants were randomized to either intervention or usual care. PCP's worked with an algorithm based treatment protocol to prescribe SSRI's as first-line treatment for depression. IPT was administered by the CM to participants who either requested IPT or refused pharmacotherapy.

Participants assigned to intervention were more likely to receive antidepressants and or psychotherapy and experienced greater than twice the reduction in suicidal ideation over 24 months. Response to treatment, defined as a 50% reduction in depressive symptoms, occurred earlier (month 4) in the intervention group and continued to increase in months 18 and 24. Participants in the intervention group with major depression were more likely to achieve remission compared to the usual care group at months 4 (26.6 vs. 15.2%), 8 (36% vs. 22.5%), and 24 (45.4% vs. 31.5%). No advantages were seen in individuals with minor depression in the intervention group [31].

5.4. MANAS: lay health counselor led collaborative stepped care intervention [32]

MANAS was a stratified cluster randomized controlled trial aimed at developing an intervention for common mental disorders in PC settings in Goa, India. Participants were age 18 and older and had no cognitive or communication difficulties that would interfere with the clinical interview. Participants screened positive for common mental disorders by yielding a score of >5 on the 12-item general health questionnaire. Diagnostic categorization and severity of mental disorders were evaluated using a structured clinical diagnostic interview for use by the LHC. Clinical sites included 12 public primary healthcare facilities and 12 private general practitioners and were randomized to either the intervention or usual care groups. Participants were randomized to either the stepped-care intervention or a usual care group. The intervention included LHCs, individuals with no background in healthcare from Goa, who completed a 2-month training program. Step 1 of the intervention included psychoeducation. This included symptom education, strategies to reduce symptoms, and encouragement to discuss symptoms with their doctors and social support network. Participants who did not respond to step 1 or who were severely ill at first consultation moved to step 2. Step 2 included the use of an antidepressant prescribed by a PCP or IPT administered by the LHC. Participants who remained unwell or who were non-adherent moved to step 3. Step 3 utilized antidepressants and IPT in combination. Participants who did not respond to step 3 or who were at significant risk for suicide at any time were referred to mental health specialist. It must be noted that IPT was not found to be culturally acceptable and therefore, LHC's improvised to deliver an abbreviated form consisting of some components of the initial phases of IPT.

Among participants attending public facilities, the intervention had the strongest impact at all time points. There was a 30% decrease in the prevalence of common mental disorders among those with baseline ICD-10 diagnoses. A similar effect was seen among the subgroup of intervention participants with depression. Suicide attempts and plans showed a 36% reduction over 12 months among baseline ICD-10 cases. Strong effects were observed on days out of work and psychological morbidity, and modest effects on overall disability. In contrast, among participants attending private facilities, there was little evidence of impact of the intervention on any outcome [33].

5.5. Additional evidence supporting collaborative care interventions

Collaborative care interventions for LLD have comparable treatment effectiveness compared to specialty practices. The PRISM-E study compared the effectiveness of integrated care models to specialty mental health referrals in the treatment of LLD. Greater symptom severity reduction was observed in the specialty referral group, however, remission rates and number of symptoms reduced were equal between the two groups. [34]

Collaborative care interventions have not only been effective at treating depression. They have been shown to reduce mortality. In a long term follow-up analysis of the PROSPECT study participants with MDD in the intervention group were 24% less likely to die compared to individuals with MDD in the usual care group [35].

Collaborative care models have been shown to mitigate ethnic and economical disparities. Several studies have consistently found that the benefits of collaborative care vs. usual care for minorities and those living in poverty are equal or greater to that of Whites and middle-class populations [36].

Collaborative care models have been successfully implemented into non-research practice settings with cost effectiveness and treatment outcomes equal to that of the IMPACT study [37]. A meta-analysis reviewing 37 trials of depression collaborative care found that collaborative care interventions had antidepressant adherence rates twice that of usual care over the first six months and favorable treatment outcomes that persisted for up to five years [38].

A number of studies have applied collaborative care approaches to the treatment of depression in chronic medical illnesses: diabetes [39], cancer [40], stroke [41] and post-coronary artery bypass grafting surgery [42]. These studies all found significant improvements in care quality and depression management compared to usual care. A recent study evaluating collaborative care in depression and other chronic illnesses found that participants in the intervention group had significant improvements in glycated hemoglobin levels, LDL-cholesterol levels, systolic blood pressure and depressive symptoms compared to the usual care group at one year [43].

6. Depression prevention in late-life

Prevention of LLD deserves considerable effort because of its contributions to disability, morbidity, and mortality. The literature suggests that depression prevention in later life may

be most effective when prevention is indicated. For example, it may be best to target older adults who have risk factors for depression such as stroke, macular degeneration, small social networks or subthreshold symptoms [44,45].

A report from Amsterdam evaluated indicated prevention in Dutch primary-care patients above age 75. 170 individuals with subthreshold depression or anxiety were followed. Having not yet met diagnostic criteria for their respective disorders, they were randomized to either a preventive stepped-care intervention or usual care. The intervention consisted of four sequential steps, each lasting three months in duration: watchful waiting, cognitive behavioral therapy-based bibliotherapy, PST, and referrals to PC if an antidepressant was needed. At the conclusion of the study it was found that the incidence of major depressive episodes and anxiety disorders was reduced by half over a one-year follow-up period. Thus 24% of participants randomized to usual care experienced the onset of major depressive episodes or anxiety disorders compared with 11% of individuals assigned to the stepped-care intervention [46]. These effects were found to be cost effective [47] and were maintained over a period of two years [48].

A recent study assessed the efficacy of PST for preventing MDD in older black and white adults with subsyndromal depressive symptoms. PST was compared to a culturally acceptable active control condition – coaching in healthy lifestyles (DIET). Compared to previously published rates of incident major depression in persons with subsyndromal symptoms, both PST and DIET were found to be potentially effective in protecting participants with subsyndromal symptoms from developing MDD over two years [49].

A recent meta-analysis of 32 randomized controlled trials examining the effects of preventive interventions in participants without diagnosed depression, found a 21% decrease in incidence over 1–2 years in prevention groups compared to control groups [50].

From a public health perspective, depression prevention is needed to preempt episodes of major depression in those with known risk factors and those who are mildly symptomatic, thereby mitigating the burden of depression's illness-related disability.

7. Conclusion

Evidence supports the importance of screening for depression in older adults because of its prevalence and risk for increased morbidity and mortality. Many factors both biological and psychosocial influence the variability in both the clinical presentation and response to LLD treatments. Collaborative care interventions for LLD have better response rates than usual care, even when the latter is enhanced by feedback to PCP's. However, the advantages of collaborative care interventions over usual care are moderate, not large. This underscores the need for referral to mental health specialists for patients who have not responded to treatment fully.

Because of factors including modest treatment effects, stigma and excess medical burden, efforts to prevent depression in at risk older adults is critical. Substantial evidence exists that indicated prevention can significantly reduce depression incidence rates.

Acknowledgments

Charles F. Reynolds III, MD reports receiving pharmaceutical support for NIH-sponsored research studies from Bristol-Myers Squibb, Forest, Pfizer, and Lilly; receiving grants from the National Institute of Mental Health, National Institute on Aging, National Center for Minority Health Disparities, National Heart Lung and Blood Institute, Center for Medicare and Medicaid Services (CMS), Patient Centered Outcomes Research Institute (PCORI), the Commonwealth of Pennsylvania, the John A Hartford Foundation, National Palliative Care Research Center (NPCRC), Clinical and Translational Science Institute (CTSI), and the American Foundation for Suicide Prevention; and serving on the American Association for Geriatric Psychiatry editorial review board. He has received an honorarium as a speaker from MedScape/WEB MD. He is the co-inventor (Licensed Intellectual Property) of Psychometric analysis of the Pittsburgh Sleep Quality Index (PSQI) PRO10050447 (PI: Buysse). Supported by the National Institutes of Health through Grant Numbers P60 MD000207; P30 MH090333; UL1RR024153, UL1TR000005; and the UPMC Endowment in Geriatric Psychiatry.

Funding information

Supported by the National Institutes of Health through Grant Numbers: NIMH 5R25MH054318; P30MH090333; UL1RR024153, UL1TR000005; and the UPMC Endowment in Geriatric Psychiatry.

References

- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med.* 2006; 3:e442. [PubMed: 17132052]
- Unutzer J, Katon W, Sullivan M, et al. Treating depressed older adults in primary care: narrowing the gap between efficacy and effectiveness. *Milbank Q.* 1999; 77:225–256. [PubMed: 10392163]
- Klap R, Unroe KT, Unützer J. Caring for mental illness in the United States: a focus on older adults. *Am J Geriatr Psychiatry.* 2003; 11(September–October (5)):517–524. [PubMed: 14506085]
- Valkanova V, Ebmeier KP. Vascular risk factors and depression in later life: a systematic review and meta-analysis. *Biol Psychiatry.* 2013; 73(March (5)):406–413. [PubMed: 23237315]
- Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom Med.* 2004; 66(November–December (6)): 802–813. [PubMed: 15564343]
- Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med.* 2010
- Diniz BS, Butters MA, Albert SM, et al. Late-life depression and risk of vascular dementia and Alzheimer's disease: systematic review and meta-analysis of community-based cohort studies. *Br J Psychiatry.* 2013; 202(May (5)):329–335. [PubMed: 23637108]
- Schulz R, Drayer RA, Rollman BL. Depression as a risk factor for non-suicide mortality in the elderly. *Biol Psychiatry.* 2002; 52:205–225. [PubMed: 12182927]
- Lyness JM, Niculescu A, Tu X, et al. The relationship of medical comorbidity and depression in older, primary care patients. *Psychosomatics.* 2006; 47(September–October (5)):435–439. [PubMed: 16959933]
- Clechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med.* 2000; 160:3278–3285. [PubMed: 11088090]
- Luber MP, Hollenberg JP, Williams-Russo P, et al. Diagnosis, treatment, comorbidity, and resource utilization in patients in a general medical practice. *Int J Psychiatry Med.* 2000; 30(1):1–13. [PubMed: 10900557]
- Alexopoulos GS, Buckwalter K, Olin J, et al. Comorbidity of late life depression: an opportunity for research on mechanisms and treatment. *Biol Psychiatry.* 2002; 52(September (6)):543–558. [PubMed: 12361668]
- Mitchell AJ, Rao S, Vaze A. Do primary care physicians have particular difficulty identifying late-life depression? A meta-analysis stratified by age. *Psychother Psychosom.* 2010; 79(5):285–294. [PubMed: 20616623]
- Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. *N Engl J Med.* 2006; 354(March (11)):1130–1138. [PubMed: 16540613]

15. Butters MA, Whyte EM, Nebes RD, et al. The nature and determinants of neuropsychological functioning in late-life depression. *Arch Gen Psychiatry*. 2004; 61(June (6)):587–595. [PubMed: 15184238]
16. Reynolds CF 3rd, Butters MA, Lopez O, et al. Maintenance treatment of depression in old age: a randomized, double-blind, placebo-controlled evaluation of the efficacy and safety of donepezil combined with antidepressant pharmacotherapy. *Arch Gen Psychiatry*. 2011; 68(January (1)):51–60. [PubMed: 21199965]
17. Nelson JC, Devanand DP. A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *J Am Geriatr Soc*. 2011; 59(April (4)):577–585. [PubMed: 21453380]
18. Wilson KC, Chen R, Taylor S, et al. Socio-economic deprivation and the prevalence and prediction of depression in older community residents. The MRC-ALPHA study. *Br J Psychiatry*. 1999; 175(December):549–553. [PubMed: 10789352]
19. Cohen A, Houck PR, Szanto K, et al. Social inequalities in response to antidepressant treatment in older adults. *Arch Gen Psychiatry*. 2006; 63:50–56. [PubMed: 16389196]
20. Whooley MA, Browner WS. Association between depressive symptoms and mortality in older women Study of Osteoporotic Fractures Research Group. *Arch Intern Med*. 1998; 158(October (19)):2129–2135. [PubMed: 9801180]
21. Gallo JJ, Rabins PV, Lyketsos CG, et al. Depression without sadness: functional outcomes of nondysphoric depression in later life. *J Am Geriatr Soc*. 1997; 45(May (5)):570–578. [PubMed: 9158577]
22. Stockdale SE, Lagomasino IT, Siddique J, et al. Racial and ethnic disparities in detection and treatment of depression and anxiety among psychiatric and primary health care visits, 1995–2005. *Med Care*. 2008; 46(July (7)):668–677. [PubMed: 18580385]
23. Schulz R, O'Brien AT, Bookwala J, et al. Psychiatric and physical morbidity effects of dementia caregiving: prevalence, correlates, and causes. *Gerontologist*. 1995; 35(December (6)):771–791. [PubMed: 8557205]
24. Reynolds CF 3rd, Miller MD, Pasternak RE, et al. Treatment of bereavement-related major depressive episodes in later life: a controlled study of acute and continuation treatment with nortriptyline and interpersonal psychotherapy. *Am J Psychiatry*. 1999; 156(February (2)):202–208. [PubMed: 9989555]
25. Maidment R, Livingston G, Katona C. Just keep taking the tablets: adherence to antidepressant treatment in older people in primary care. *Int J Geriatr Psychiatry*. 2002; 17(August (8)):752–757. [PubMed: 12211126]
26. Regier DA, Goldberg ID, Taube CA. The de facto US mental health services system: a public health perspective. *Arch Gen Psychiatry*. 1978; 35(6):685–693. [PubMed: 306803]
27. Davidson JR, Meltzer-Brody SE. The under-recognition and under-treatment of depression: what is the breadth and depth of the problem? *J Clin Psychiatry*. 1999; 60(Suppl 7):4–9. [PubMed: 10326869]
28. Unützer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. *J Am Med Assoc*. 2002; 288(December (22)):2836–2845.
29. Hunkeler EM, Katon W, Tang L, et al. Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. *Br Med J*. 2006; 332(February (7536)):259–263. [PubMed: 16428253]
30. Bruce ML, Ten Have TR, Reynolds CF 3rd, et al. Reducing suicidal ideation and depressive symptoms in depressed older primary care patients: a randomized controlled trial. *J Am Med Assoc*. 2004; 291(March (9)):1081–1091.
31. Alexopoulos GS, Reynolds CF 3rd, Bruce ML, et al. Reducing suicidal ideation and depression in older primary care patients: 24-month outcomes of the PROSPECT study. *Am J Psychiatry*. 2009; 166(August (8)):882–890. [PubMed: 19528195]
32. Patel V, Weiss HA, Chowdhary N, et al. Effectiveness of an intervention led by lay health counsellors for depressive and anxiety disorders in primary care in Goa India (MANAS): a cluster

- randomised controlled trial. *Lancet*. 2010; 376(December (9758)):2086–2095. [PubMed: 21159375]
33. Patel V, Weiss HA, Chowdhary N, et al. Lay health worker led intervention for depressive and anxiety disorders in India: impact on clinical and disability outcomes over 12 months. *Br J Psychiatry*. 2011; 199(December (6)):459–466. [PubMed: 22130747]
 34. Krahn DD, Bartels SJ, Coakley E, et al. PRISM-E: comparison of integrated care and enhanced specialty referral models in depression outcomes. *Psychiatr Serv*. 2006; 57(July (7)):946–953. [PubMed: 16816278]
 35. Gallo JJ, Morales KH, Bogner HR, et al. Long term effect of depression care management on mortality in older adults: follow-up of cluster randomized clinical trial in primary care. *Br Med J*. 2013; 346(June):f2570. [PubMed: 23738992]
 36. Arean PA, Ayalon L, Hunkeler E, et al. Improving depression care for older, minority patients in primary care. *Med Care*. 2005; 43(4):381–390. [PubMed: 15778641]
 37. Grypma L, Haverkamp R, Little S, et al. Taking an evidence-based model of depression care from research to practice: making lemonade out of depression. *Gen Hosp Psychiatry*. 2006; 28(2):101–107. [PubMed: 16516059]
 38. Gilbody S, Bower P, Fletcher J, et al. Collaborative care for depression: a cumulative meta-analysis and review of longer-term outcomes. *Arch Intern Med*. 2006; 166(21):2314–2321. [PubMed: 17130383]
 39. Ell K, Katon W, Xie B, et al. Collaborative care management of major depression among low-income, predominantly Hispanic subjects with diabetes: a randomized controlled trial. *Diab Care*. 2010; 33(4):706–713.
 40. Ell K, Xie B, Quon B, et al. Randomized controlled trial of collaborative care management of depression among low-income patients with cancer. *J Clin Oncol*. 2008; 26(27):4488–4496. [PubMed: 18802161]
 41. Williams LS, Kroenke K, Bakas T, et al. Care management of poststroke depression: a randomized, controlled trial. *Stroke*. 2007; 38(3):998–1003. [PubMed: 17303771]
 42. Rollman BL, Belnap BH, LeMenager MS, et al. Telephone-delivered collaborative care for treating post-CABG depression: a randomized controlled trial. *J Am Med Assoc*. 2009; 302(19):2095–2103.
 43. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with depression and chronic illnesses. *N Engl J Med*. 2010; 363(December (27)):2611–2620. [PubMed: 21190455]
 44. Smit F, Ederveen A, Cuijpers P, et al. Opportunities for cost-effective prevention of late-life depression: an epidemiological approach. *Arch Gen Psychiatry*. 2006; 63:290–296. [PubMed: 16520434]
 45. Robinson RG, Jorge RE, Moser DJ, et al. Escitalopram and problem-solving therapy for prevention of poststroke depression: randomized controlled trial. *J Am Med Assoc*. 2008; 299:2391–2400.
 46. van't Veer-Tazelaar PJ, van Marwijk HW, van Oppen P, et al. Stepped-care prevention of anxiety and depression in late life: a randomized controlled trial. *Arch Gen Psychiatry*. 2009; 66(March (3)):297–304. [PubMed: 19255379]
 47. van't Veer-Tazelaar P, Smit F, vanHout HP, van Oppen P, van derHorst H, et al. Cost-effectiveness of a stepped care intervention to prevent depression and anxiety in late life: randomised trial. *Br J Psychiatry*. 2010; 196:319–325. [PubMed: 20357310]
 48. van't Veer-Tazelaar PJ, van Marwijk HW, van Oppen P, et al. Prevention of late-life anxiety and depression has sustained effects over 24 months: a pragmatic randomized trial. *Am J Geriatr Psychiatry*. 2011; 19(March (3)):230–239. [PubMed: 21425519]
 49. Reynolds CF, Thomas SB, Morse JQ, et al. Early intervention to preempt major depression among older black and white adults. *Psychiatr Serv*. 2014 (in press).
 50. van Zoonen K, Burntrok C, Ebert DD, et al. Preventing the onset of major depressive disorder: a meta-analytic review of psychological interventions. *Int J Epidemiol*. 2014; 43(April (2)):318–329. [PubMed: 24760873]

Table 1

Comparison of study sample sizes, depression outcome variables, depression severities and numbers needed to treat

Study	<i>N</i>	Depression outcome variable	Depression severity	NNT
IMPACT	1,801	Hopkins symptom checklist-20	Major depression or dysthymia	At 12 months = 4 ^{<i>a</i>} At 18 months = 6 ^{<i>a</i>} At 24 months = 9 ^{<i>a</i>}
PROSPECT	598	Hamilton depression Rating Scale	Major or minor depression	At 24 months = 6 ^{<i>a</i>}
MANAS	2,796	Clinical Interview Schedule-Revised	Major depression	At 6 months = 8 ^{<i>b</i>}

N = number of randomized participants. NNT = Number needed to treat.

^{*a*}Treatment response was defined as a 50% reduction in depression outcome variable score.

^{*b*}Based on overall primary outcome: recovery from common mental disorders including depression via ICD-10.