

Late-life depression with comorbid cognitive impairment and disability: nonpharmacological interventions

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Abstract: Less than half of older adults with depression achieve remission with antidepressant medications, and rates of remission are even poorer for those with comorbid conditions. Psychosocial interventions have been effective in treating geriatric depression, either alone or better yet, in combination with antidepressant medications. Traditional strategies for nonpharmacological treatment of late-life depression do not specifically address the co-occurring cognitive impairment and disability that is prevalent in this population. Newer therapies are recognizing the need to simultaneously direct treatment efforts in late-life depression towards the triad of depressive symptoms, cognitive dysfunction, and functional disability that is so often found in geriatric depression, and this comprehensive approach holds promise for improved treatment outcomes.

Keywords: geriatric depression, dementia, functional impairment, psychotherapy

Introduction

Depression is a devastating illness for patients and their families. Although efficacious treatments for late-life major depression are available,^{1,2} depression in older adults is underdiagnosed and undertreated,^{3–5} particularly in primary care settings.^{6,7} Although the treatment of late-life depression with antidepressant medication appears to be increasing, disparities exist regarding who receives such treatment.⁸ When treated with pharmacotherapy alone, fewer than half of older adults with major depression achieve remission.^{9–12} Rates of remission are even lower in cognitively impaired, disabled older adults, where these comorbid issues complicate treatment adherence and other elements essential to success. As a result, psychosocial interventions are particularly important for the treatment of depressed older adults with comorbid cognitive impairment (CI) and disability. This review will address the complex relationship of depression, CI, and disability and will provide an overview of currently available psychosocial interventions for geriatric depression, with attention to promising therapies that incorporate more comprehensive approaches for the most vulnerable depressed, cognitively impaired, disabled elders.

The triad of late-life depression, CI, and disability

Maturation changes in the brain may increase vulnerability for the development of late-life depression¹³ and have etiological significance for declines in cognition and daily functional skills. Cerebrovascular changes, whether due to aging or disease, can compromise the neural connectivity of frontal systems. These alterations, including

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connections with the limbic system, have been hypothesized to increase vulnerability for depression and contribute to the manifestation of executive dysfunction associated with late-life depression.^{9,14} Vascular insults need not be large to affect these neural systems. Large-scale epidemiological studies have found evidence that otherwise asymptomatic white matter changes on neuroimaging are associated with mild CI in older adults.^{15–17} Cognitive compromise and disability can foster nonadherence and interfere with treatment efforts in depressed older adults. Additional evidence suggests that CI is associated with poor and slower response to antidepressant medications.^{9,18,19}

CI in late-life depression

Cognitive compromise associated with late-life depression can present anywhere along a continuum from mild CI to a frank dementia. A mood disturbance in an older adult can initially present as subjective cognitive complaints. Likewise, the existence of depression can exacerbate previously existing cognitive difficulties. In community-dwelling residents, the combination of impaired cognition and depressive symptoms doubles in frequency at 5-year intervals beyond age 70; combined depression and cognitive dysfunction are present in 25% of individuals aged 85 years or older.²⁰ There is ample evidence that the presence of comorbid cognitive deficits is associated with reduced treatment responsiveness in late-life depression.^{18,21–24}

The relationship of late-life depression and CI is complex. Late-life depression often is accompanied by executive dysfunction, which manifests as reduced planning, initiation, organization, and sequencing.^{25–27} Cognition can be affected in terms of new learning,²⁸ visuospatial skills,^{29,30} and reduced psychomotor speed.³¹ Cognitive deficits may persist in depressed older adults even after depression remits.^{32–34} The presence of a dementing disorder in and of itself can increase the risk of depression.³⁵ Conversely, the presence of depressive symptoms in cognitively intact older adults predicts subsequent cognitive decline.³⁶ There is evidence that training in speed-of-processing skills is associated with less incidence of depression at follow-up,^{37,38} improved health-related quality of life,³⁹ and self-rated health,⁴⁰ whereas training in reasoning skills is associated with improved ability to perform instrumental activities of daily living.⁴¹

Research has noted cognitive differences between early-onset and late-onset late-life depression. Individuals with late-onset depression (ie, first depressive episode occurring at 60 years or older) exhibit more impairment

in overall cognitive deficits and in memory and executive dysfunction than those with early-onset depression.^{33,42,43} Furthermore, late age of depression onset is associated with the development of dementia in nondemented depressed older adults.⁴⁴

Disability in late-life depression

The World Health Organization conceptualizes disability as an overarching term that contains three types of dysfunction: compromised body function or structure, impairment in activity, and cessation in participation.⁴⁵ In most studies, disability or functional impairment is concerned with problems in any one or all three of these areas. The relationship of depression and disability is bidirectional with empirical evidence suggesting that late-life depression promotes disability, and likewise, disability increases the risk of depression.⁴⁶ Depression leaves older adults vulnerable to disability regardless of the presence of medical illness.^{47–50} In those who are already medically compromised, depression can increase the chances of disability, independent of the severity of the medical illness.⁴⁹ This predisposition toward depression is evident in older psychiatric patients,^{49,51–53} medical inpatients,⁵⁴ primary care patients,⁵⁵ and older community-dwelling residents.⁵⁶ The course of disability parallels the course of depression in that disability scores improve as a reflection of improvement in depression over time.^{57,58} Studies have not found significant differences between early-onset and late-onset depression in terms of disability.^{42,43} Although depression promotes disability, clinical intuition and empirical evidence argue that the reverse is also true; disability fosters depression.

Depression is projected to be the second leading cause of disability worldwide by 2020.⁵⁹ Disability resulting from medical or neurological illnesses is associated with increased risk for a first-onset depressive disorder.^{47,60} In addition to factors such as bereavement, sleep disturbances, and prior depression, disability is an important risk factor for depression in older adults.⁶¹ In homebound elders, chronic and new-onset functional impairment are associated with increased risk for depression.⁶⁰ Disability in the form of an increased risk of falls is associated with depression in later life.^{62,63} Severity of depression, degree of CI, and medical burden explain less than 40% of the variance in disability, implying that disability is a broader dimension of health status than each of these factors alone.⁵¹

The relationship of depression and disability becomes even more complex in the presence of CI. On the one hand, the effect of late-life depression on disability may be

independent of concomitant changes in cognitive status.⁶⁴ On the other hand, depression may contribute to disability in part due to the CI that often accompanies late-life depression. CI contributes to disability in late-life depression even after controlling for the effects of severity of depression. Deficits in executive functioning (eg, planning, organizing, initiating, and shifting) are independently associated with impairment in instrumental activities of daily living, such as bill paying, doing housework, and taking medication in both demented and nondemented elders.^{52,53} Furthermore, cognitive deficits have the greatest effect on daily functioning in nursing home residents even after controlling for psychiatric symptoms of depression, delusions, and behavioral disturbances.⁶⁵ There is also evidence that cognitive deficits, particularly impairments in problem solving and memory, mediate the effect of depression on disability.⁶⁶

Limited efficacy of antidepressant medication in depressed, cognitively impaired, older adults

Despite evidence that pharmacotherapy is efficacious in the acute treatment of late-life depression, this is not the case for those older adults with CI.⁶⁷ Antidepressant medications bring to remission fewer than 40% of elderly depressed patients who have some degree of CI.⁹⁻¹² Cognitive deficits, in particular measures of executive dysfunction such as reduced information processing speed, have been associated with slow and/or poor response to antidepressant treatment in this population.^{18,21-24}

The effects of the triad on patients and caregivers

Depression, CI, and disability contribute to increased medical and psychiatric morbidity and mortality.^{9,68-73} This triad also contributes to patient suffering, decreased quality of life, impairment in social and interpersonal functioning, and even leads to early nursing home placement.⁷⁴⁻⁷⁶ Caregivers of these individuals suffer similar consequences, such as decreased quality of life, medical and psychiatric morbidities,⁷⁶⁻⁷⁹ as well as increased risk of mortality.⁸⁰ Similarly, caregivers of nondemented cognitively impaired older adults report increased burden and psychiatric morbidity.^{54,77,81-83} Family caregivers of depressed older adults without CI experience burden to a similar degree as caregivers of dementia patients.⁸⁴ As a result, late-life depression has deleterious consequences not only for depressed older adults but also for those who provide direct care to these individuals.

Psychosocial interventions in late-life depression

Health care policy restructuring is placing greater demands on the use of treatment interventions that can be empirically supported. Using the criteria for evidence-based treatments set forth by the Committee on Science and Practice of the Society for Clinical Psychology (Division 12) of the American Psychological Association, several psychosocial interventions can be defined as evidence-based: behavioral therapy (BT), cognitive BT (CBT), cognitive bibliotherapy, problem-solving therapy (PST), brief psychodynamic therapy, and reminiscence therapy.⁸⁵ Using more focused criteria, Mackin and Arean⁸⁶ identified CBT (including PST), brief psychodynamic therapy, and to some extent reminiscence therapy as evidence-based interventions for late-life depression.

Although not without limitations, meta-analyses have been helpful in drawing conclusions on the current state of psychosocial interventions for late-life depression. Cuijpers et al⁸⁷ analyzed 25 randomized studies and found that these treatments had a moderate to large mean effect size. This meta-analysis reported no significant differences in the effects among psychological interventions (ie, CBT, BT, reminiscence therapy, interpersonal psychotherapy [IPT], PST, and others), no significant difference in effect of antidepressant medication vs psychological intervention, and a significantly larger effect of combined antidepressant and psychological intervention than antidepressant medication alone. In another meta-analysis that included nonrandomized studies but accounted for quality of study, Pinquart et al⁸⁸ reported that CBT and reminiscence therapy had large effects, whereas most of the remaining psychosocial interventions had moderate effects.

Cognitive behavioral therapy

CBT in its various forms focuses on the interplay between thoughts, feelings, and behaviors. CBT emphasizes the identification of emotions and monitoring mood in relation to thoughts and behaviors. Cognitive aspects of the treatment involve identifying maladaptive and negative thinking patterns in depressed individuals, evaluating these thoughts in terms of their irrationality, and challenging and restructuring these thoughts in such a way as to be more adaptive and less depressive. Behavioral aspects of the treatment involve activating the patient via activity scheduling, evaluating patients' expectations of their ability to accomplish tasks and activities successfully and/or to experience enjoyment in activities, and using positive reinforcement of desired

behaviors.⁸⁹⁻⁹¹ In the treatment of late-life depression, CBT has been significantly effective in reducing symptoms of depression when compared with a nontreatment control group.⁹²⁻⁹⁷ When compared with other active treatments, CBT was as good as other psychotherapies at treating depression,^{92,98-100} was superior or equivalent in maintaining treatment gains,^{98,101} and when used in combination with an antidepressant medication, was more effective in reducing depressive symptoms than either CBT or antidepressant treatment alone.¹⁰² More recent studies have continued to support CBT as an effective treatment.^{103,104}

Problem-solving therapy

Often considered a form of CBT, PST has garnered evidence as an effective treatment for late-life depression. PST consists of a structured format through which depressed older adults learn specific skills to enhance problem-solving abilities and, through successful resolution of problems, decrease depression. Problem-solving skills training consists of identifying and defining a problem, generating alternative solutions, analyzing positive and negative consequences of solutions, and carrying out a solution and subsequently evaluating the outcome.¹⁰⁵ In depressed older adults, PST was superior to reminiscence therapy and a wait-list control group¹⁰⁶ and was more effective than supportive therapy.^{35,107} Studies comparing PST with treatment as usual in primary care¹⁰⁸ and home care^{109,110} continue to support the usefulness of PST for depression in older adults.

Reminiscence therapy

Reminiscence therapy is a long-standing treatment modality that has been used to address depression in older adults. Based on Erikson's psychosocial developmental theory reminiscence therapy emphasizes the review of life and identification of meaning and purpose in one's life. This is done through a process of inspection of one's life through memories, focusing on both positive and negative experiences, and developing perspective. Reminiscence therapy, with its emphasis on personal experiences and history, lends itself to the older adult context. Studies have found that reminiscence therapy has been more effective than nonpsychotherapy social services¹¹¹ and nontreatment conditions.^{106,112-115} However, its effectiveness compared to other active interventions remains questionable.^{116,117}

Brief psychodynamic therapy

Psychodynamic therapy, particularly in its brief form, has empirical findings that support its effectiveness in

treating late-life depression. Brief psychodynamic therapy focuses on the identification of conflicts and unconscious processes, often originating from early developmental stages. Brief psychodynamic therapy encourages the development of insight and gives importance to the relationship and interactions of the therapist and client. As with other psychotherapies, more research is required to determine brief psychodynamic therapy's robustness as a treatment (eg, in comparison to or combination with antidepressant medication).

Interpersonal psychotherapy

Another intervention often cited in the late-life depression literature is IPT. IPT focuses on interpersonal problems in four areas: role transitions, interpersonal role conflicts, grief, and interpersonal skills deficits.¹¹⁸ IPT appears to have clinical utility in treating late-life depression¹¹⁹ and potential in combination with antidepressant medication.¹²⁰ More recent analyses have indicated that maintenance IPT is not as effective as supportive clinical management in sustaining gains made in health-related quality of life,¹²¹ but it may lower the risk of recurrence of major depression in older adults who have lower cognitive functioning.¹²² Although it remains a promising treatment for depression in later life, IPT continues to lack the empirical requisites for addition to the evidence-based intervention listing.^{86,123}

Need for tailored nonpharmacological interventions for late-life depression

Most psychosocial interventions for the acute treatment of geriatric major depression focus on "young-old" (average age of 65-70 years), cognitively intact, ambulatory older adults who can follow outpatient treatment.⁸⁶ Clearly, this is only a subsample of the population who are in need. Homebound, rural, and low-income older adults may not have the same access to effective interventions for depression as those living in situations more conducive to receiving traditional psychotherapeutic treatment.⁸⁶ Furthermore, interventions may not be available or appropriate for ethnically and culturally diverse populations. Factors such as comorbid illness can also serve as a barrier for treatment. Evidence suggests that depressed older adults with comorbid physical illness and CI experience reduced intervention effectiveness,⁸⁸ which argues for a strong need for new evidence-based psychosocial interventions to help depressed older adults with CI and disability. Studies have not indicated significant treatment remission differences between early-onset and

late-onset depression,¹²⁴ although older adults who had an early-onset depression may be slower to remit.¹²⁵

Targeting the triad

A small number of studies have started to address the triad of late-life depression, CI, and disability. These are adaptations of the traditional forms of psychosocial therapies for late-life depression that accommodate CI and disability, both by what is targeted in treatment and by how treatment is executed. Another important adaptation is the inclusion of family members and caregivers in the treatment.

Psychosocial interventions for depressed older adults with mild cognitive deficits

Two interventions have been successfully adapted for depression in older adults with mild CI: PST^{35,107} and IPT.¹²⁶ PST was adapted for depressed older adults with mild executive dysfunction, and recent data suggest that it is efficacious in reducing depression and disability in this population.^{35,107} IPT was modified for depressed older adults with mild CI (IPT-CI) by including the systematic incorporation of concerned caregivers into the treatment process, with joint patient–caregiver sessions to promote better understanding, communication, and respect.^{126,127} In addition, IPT-CI helps both the older adult and his or her caregiver through their role transitions that result from cognitive deficits and functional limitations.

Psychosocial interventions for depressed, disabled older adults with moderate to severe cognitive dysfunction

In patients with more moderate to severe cognitive compromise, there can be a spectrum of neuropsychiatric features. These include depressive symptoms and other behavioral impairments that can be addressed by psychosocial interventions. The following psychosocial interventions have been proposed for the treatment of major depression in advanced CI, including dementia.

CBT for early stage dementia

CBT has been adapted for depressed older adults with mild stages of dementia, but no efficacy data are available.¹²⁸ The CBT-mild dementia protocol is 16–20 sessions long and includes a comprehensive neuropsychological battery to assess the cognitive deficits and the cognitive strengths of the patient. The treatment consists of behavioral activation and the incorporation of memory aids (eg, notepads and audio taping of sessions), as well as the cognitive components

of examination of the evidence for and against a specific condition, listing the pros and cons of situations, and experimenting with new attitudes and cognitions in stressful situations.¹²⁸

Problem adaptation therapy

Problem adaptation therapy (PATH) is a relatively new 12-week home-delivered intervention specifically developed to treat late-life major depression presenting with significant CI (including mild to moderate dementia) and disability.^{129,130} PATH focuses on the patients' ecosystem, which involves the patient, the caregiver, and the home environment. PATH utilizes PST as its basic framework to promote adaptive functioning and integrates environmental adaptation tools (PATH tools), including calendars, checklists, notepads, signs, and timers, to bypass the functional and behavioral limitations of these patients. Finally, willing and available caregivers participate in treatment when the patient cannot utilize problem-solving skills, employ environmental adaptations tools, and engage in pleasurable activities. Preliminary efficacy data suggest that PATH is effective compared with a control condition of home-delivered supportive therapy in reducing both depression and disability.¹²⁹

Behavioral treatment for depression in moderate to severe dementia

A behavioral treatment developed by Teri et al¹³¹ focused on teaching caregivers strategies aimed at increasing patients' pleasant events or aiding them with problem-solving skills. In a controlled clinical trial, this behavioral intervention was useful in reducing depressive symptoms in older adults with major or minor depression and moderate to severe dementia, with symptom reduction maintained at 6-month follow-up. Another finding of this study was that caregivers of those receiving behavioral interventions experienced significant reduction in depression compared with those in the control groups. This behavioral approach is the recommended intervention for older adults with depression who are in the more moderate to severe stages of dementia.

Conclusion

Clinicians should be aware of the complexities of geriatric depression and how problems with cognitive and physical functioning play a role in the presentation of depressive symptoms. Effective interventions for geriatric depression should recognize the older adult's potential limitations in key areas of cognitive functioning, such as information processing, organization, and memory, that may impact

engagement in therapy and following through of treatment plans. Consideration of the individuals' mobility and their ability to independently manage health behaviors and routines is essential to the success of the intervention. Treating depressive symptoms in isolation of the patients' cognitive and physical limitations risks slower or less-effective reduction in depressive symptoms; however, targeting the triad of depression, CI, and disability provides a concerted effort to help patients adapt and cope up with their problems, promoting successful outcomes for depression treatment. Although evidence for such multi-faceted approaches to treatment is nascent, large-scale studies and further intervention development are currently underway. Given the high prevalence of depression in older adults, establishing more effective treatments is vital to improving geriatric mental health and quality of life for patients and their families.

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Disclosure

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References

- Hollon S, Jarrett R, Nierenberg A, Thase M, Trivedi M, Rush AJ. Psychotherapy and medication in the treatment of adult and geriatric depression: which monotherapy or combined treatment? *J Clin Psychiatry*. 2005; 66(4):455–468.
- Baldwin R, Anderson D, Black S, et al. Guideline for the management of late-life depression in primary care. *Int J Geriatr Psychiatry*. 2003; 18(9):829–838.
- Charlson M, Peterson J. Medical comorbidity and late life depression: what is known and what are the unmet needs? *Biol Psychiatry*. 2002; 52(3):226–235.
- Goldman LS, Nielsen NH, Champion HC. Awareness, diagnosis, and treatment of depression. *J Gen Intern Med*. 1999;14(9):569–580.
- Charney D, Reynolds C, Lewis L, et al. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. *Arch Gen Psychiatry*. 2003; 60(7):664–672.
- Harman JS, Brown EL, Have TT, Mulsant BH, Brown G, Bruce ML. Primary care physicians attitude toward diagnosis and treatment of late-life depression. *CNS Spectr*. 2002;7(11):784–790.
- Uebelacker L, Wang P, Berglund P, Kessler R. Clinical differences among patients treated for mental health problems in general medical and specialty mental health settings in the National Comorbidity Survey Replication. *Gen Hosp Psychiatry*. 2006;28(5):387–395.
- Blazer D, Hybels C, Fillenbaum G, Pieper C. Predictors of antidepressant use among older adults: have they changed over time? *Am J Psychiatry*. 2005;162(4):705–710.
- Alexopoulos G, Kiosses D, Heo M, Murphy C, Shanmugham B, Gunning-Dixon F. Executive dysfunction and the course of geriatric depression. *Biol Psychiatry*. 2005;58(3):204–210.
- Lyketsos C, Olin J. Depression in Alzheimer's disease: overview and treatment. *Biol Psychiatry*. 2002;52(3):243–252.
- Lyketsos C, DelCampo L, Steinberg M, et al. Treating depression in Alzheimer disease: efficacy and safety of sertraline therapy, and the benefits of depression reduction: the DIADS. *Arch Gen Psychiatry*. 2003;60(7):737–746.
- de Vasconcelos Cunha UG, Rocha F, de Melo R, et al. A placebo-controlled double-blind randomized study of venlafaxine in the treatment of depression in dementia. *Dement Geriatr Cogn Disord*. 2007;24(1):36–41.
- Tiemeier H. Biological risk factors for late life depression. *Eur J Epidemiol*. 2003;18(8):745–750.
- Alexopoulos GS, Meyers BS, Young RC, Campbell S, Silbersweig D, Charlson M. 'Vascular depression' hypothesis. *Arch Gen Psychiatry*. 1997;54(10):915–922.
- de Leeuw FE, de Groot JC, Achten E, et al. Prevalence of cerebral white matter lesions in elderly people: a population based magnetic resonance imaging study. The Rotterdam Scan Study. *J Neurol Neurosurg Psychiatry*. 2001;70(1):9–14.
- Lopez O, Jagust W, Dulberg C, et al. Risk factors for mild cognitive impairment in the Cardiovascular Health Study Cognition Study: 2. *Arch Neurol*. 2003;60(10):1394–1399.
- Breteler MM, van Swieten JC, Bots ML, et al. Cerebral white matter lesions, vascular risk factors, and cognitive function in a population-based study: the Rotterdam Study. *Neurology*. 1994;44(7):1246–1252.
- Kalayam B, Alexopoulos GS. Prefrontal dysfunction and treatment response in geriatric depression. *Arch Gen Psychiatry*. 1999;56(8): 713–718.
- Alexopoulos GS, Meyers BS, Young RC, et al. Executive dysfunction and long-term outcomes of geriatric depression. *Arch Gen Psychiatry*. 2000;57(3):285–290.
- Arve S, Tilvis RS, Lehtonen A, Valvanne J, Sairanen S. Coexistence of lowered mood and cognitive impairment of elderly people in five birth cohorts. *Aging (Milano)*. 1999;11(2):90–95.
- Sneed J, Roose S, Keilp J, Krishnan KRR, Alexopoulos G, Sackeim H. Response inhibition predicts poor antidepressant treatment response in very old depressed patients. *Am J Geriatr Psychiatry*. 2007; 15(7):553–563.
- Potter G, Kittinger J, Wagner HR, Steffens D, Krishnan KRR. Prefrontal neuropsychological predictors of treatment remission in late-life depression. *Neuropsychopharmacology*. 2004;29(12):2266–2271.
- Story T, Potter G, Attix D, Welsh-Bohmer K, Steffens D. Neurocognitive correlates of response to treatment in late-life depression. *Am J Geriatr Psychiatry*. 2008;16(9):752–759.
- Simpson S, Baldwin RC, Jackson A, Burns AS. Is subcortical disease associated with a poor response to antidepressants? Neurological, neuropsychological and neuroradiological findings in late-life depression. *Psychol Med*. 1998;28(5):1015–1026.
- Lockwood K, Alexopoulos G, van Gorp W. Executive dysfunction in geriatric depression. *Am J Psychiatry*. 2002;159(7):1119–1126.
- Butters MA, Becker JT, Nebes RD, et al. Changes in cognitive functioning following treatment of late-life depression. *Am J Psychiatry*. 2000; 157(12):1949–1954.
- Goodwin GM. Functional imaging, affective disorder and dementia. *Br Med Bull*. 1996;52(3):495–512.
- Hart RP, Kwentus JA, Hamer RM, Taylor JR. Selective reminding procedure in depression and dementia. *Psychol Aging*. 1987;2(2):111–115.
- Boone KB, Lesser IM, Miller BL, et al. Cognitive functioning in older depressed outpatients: relationship of presence and severity of depression to neuropsychological test scores. *Neuropsychology*. 1995; 9(3):390–398.
- Lesser IM, Boone KB, Mehringer CM, Wohl MA, Miller BL, Berman NG. Cognition and white matter hyperintensities in older depressed patients. *Am J Psychiatry*. 1996;153(10):1280–1287.
- van Ojen R, Hooijer C, Bezemer D, Jonker C, Lindeboom J, van Tilburg W. Late-life depressive disorder in the community. 1. The relationship between MMSE score and depression in subjects with and without psychiatric history. *Br J Psychiatry*. 1995;166(3): 311–315,319.

32. Bhalla R, Butters M, Becker J, et al. Patterns of mild cognitive impairment after treatment of depression in the elderly. *Am J Geriatr Psychiatry*. 2009;17(4):308–316.
33. Kohler S, Thomas AJ, Barnett NA, O'Brien JT. The pattern and course of cognitive impairment in late-life depression. *Psychol Med*. 2010;40(4):591–602.
34. Nebes R, Pollock B, Houck P, et al. Persistence of cognitive impairment in geriatric patients following antidepressant treatment: a randomized, double-blind clinical trial with nortriptyline and paroxetine. *J Psychiatry Res*. 2003;37(2):99–108.
35. Alexopoulos G, Raue P, Aren P. Problem-solving therapy versus supportive therapy in geriatric major depression with executive dysfunction. *Am J Geriatr Psychiatry*. 2003;11(1):46–52.
36. Rosenberg P, Mielke M, Xue Q-L, Carlson M. Depressive symptoms predict incident cognitive impairment in cognitively healthy older women. *Am J Geriatr Psychiatry*. 2010;18(3):204–211.
37. Wolinsky F, Mahncke H, Vander Weg MW, et al. The ACTIVE cognitive training interventions and the onset of and recovery from suspected clinical depression. *J Gerontol B Psychol Sci Soc Sci*. 2009;64(5):577–585.
38. Wolinsky F, Vander Weg MW, Martin R, et al. The effect of speed-of-processing training on depressive symptoms in ACTIVE. *J Gerontol A Bio Sci Med Sci*. 2009;64(4):468–472.
39. Wolinsky F, Unverzagt F, Smith D, Jones R, Wright E, Tennstedt S. The effects of the ACTIVE cognitive training trial on clinically relevant declines in health-related quality of life. *J Gerontol B Psychol Sci Soc Sci*. 2006;61(5):S281–S287.
40. Wolinsky F, Mahncke H, Vander Weg MW, et al. Speed of processing training protects self-rated health in older adults: enduring effects observed in the multi-site ACTIVE randomized controlled trial. *Int Psychogeriatr*. 2010;22(3):470–478.
41. Willis S, Tennstedt S, Marsiske M, et al. Long-term effects of cognitive training on everyday functional outcomes in older adults. *JAMA*. 2006;296(23):2805–2814.
42. Gallagher D, Ni Mhaolain A, Greene E, et al. Late life depression: a comparison of risk factors and symptoms according to age of onset in community dwelling older adults. *Int J Geriatr Psychiatry*. 2010;25(10):981–987.
43. Janssen J, Beekman ATF, Comijs H, Deeg DJH, Heeren T. Late-life depression: the differences between early- and late-onset illness in a community-based sample. *Int J Geriatr Psychiatry*. 2006;21(1):86–93.
44. Alexopoulos G, Kelly R. Research advances in geriatric depression. *World Psychiatry*. 2009;8(3):140–149.
45. World Health Organization. Disabilities. 2010. Available from: <http://www.who.int/topics/disabilities/en/>. Accessed May 26, 2010.
46. Kennedy GJ. The dynamics of depression and disability. *Am J Geriatr Psychiatry*. 2001;9(2):99–101.
47. Bruce ML, Hoff RA. Social and physical health risk factors for first-onset major depressive disorder in a community sample. *Soc Psychiatry Psychiatr Epidemiol*. 1994;29(4):165–171.
48. Patten SB. Long-term medical conditions and major depression in the Canadian population. *Can J Psychiatr*. 1999;44:151–157.
49. Steffens DC, O'Connor CM, Jiang WJ, et al. The effect of major depression on functional status in patients with coronary artery disease. *J Am Geriatr Soc*. 1999;47(3):319–322.
50. Ng T-P, Niti M, Fones C, Yap K, Tan W-C. Co-morbid association of depression and COPD: a population-based study. *Respir Med*. 2009;103(6):895–901.
51. Alexopoulos GS, Vrontou C, Kakuma T, et al. Disability in geriatric depression. *Am J Psychiatry*. 1996;153(7):877–885.
52. Kiosses DN, Alexopoulos GS, Murphy C. Symptoms of striatofrontal dysfunction contribute to disability in geriatric depression. *Int J Geriatr Psychiatry*. 2000;15(11):992–999.
53. Kiosses DN, Klimstra S, Murphy C, Alexopoulos GS. Executive dysfunction and disability in elderly patients with major depression. *Am J Geriatr Psychiatry*. 2001;9(3):269–274.
54. McCusker J, Cole M, Ciampi A, Latimer E, Windholz S, Belzile E. Major depression in older medical inpatients predicts poor physical and mental health status over 12 months. *Gen Hosp Psychiatry*. 2007;29(4):340–348.
55. Noël P, Williams J, Untzer J, et al. Depression and comorbid illness in elderly primary care patients: impact on multiple domains of health status and well-being. *Ann Fam Med*. 2004;2(6):555–562.
56. Forsell Y, Jorm AF, Winblad B. Association of age, sex, cognitive dysfunction, and disability with major depressive symptoms in an elderly sample. *Am J Psychiatry*. 1994;151(11):1600–1604.
57. Ormel J, von Korff M, van den Brink W, Katon W, Brilman E, Oldehinkel T. Depression, anxiety, and social disability show synchrony of change in primary care patients. *Am J Public Health*. 1993;83(3):385–390.
58. von Korff M, Ormel J, Katon W, Lin EH. Disability and depression among high utilizers of health care. A longitudinal analysis. *Arch Gen Psychiatry*. 1992;49(2):91–100.
59. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997;349(9064):1498–1504.
60. Weinberger M, Raue P, Meyers B, Bruce M. Predictors of new onset depression in medically ill, disabled older adults at 1 year follow-up. *Am J Geriatr Psychiatry*. 2009;17(9):802–809.
61. Cole M, Dendukuri N. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am J Psychiatry*. 2003;160(6):1147–1156.
62. Sheeran T, Brown E, Nassisi P, Bruce M. Does depression predict falls among home health patients? Using a clinical-research partnership to improve the quality of geriatric care. *Home Healthc Nurse*. 2004;22(6):384–389.
63. Turcu A, Toubin S, Mourey F, D'Athis P, Manckoundia P, Pfitzenmeyer P. Falls and depression in older people. *Gerontology*. 2004;50(5):303–308.
64. Li L, Conwell Y. Effects of changes in depressive symptoms and cognitive functioning on physical disability in home care elders. *J Gerontol A Bio Sci Med Sci*. 2009;64(2):230–236.
65. Schultz S, Ellingrod V, Turvey C, Moser D, Arndt S. The influence of cognitive impairment and behavioral dysregulation on daily functioning in the nursing home setting. *Am J Psychiatry*. 2003;160(3):582–584.
66. Gallo JJ, Rebok GW, Tennstedt S, Wadley VG, Horgas A. Linking depressive symptoms and functional disability in late life. *Aging Ment Health*. 2003;7(6):469–480.
67. Rajji T, Mulsant B, Lotrich F, Lokker C, Reynolds C. Use of antidepressants in late-life depression. *Drugs Aging*. 2008;25(10):841–853.
68. Reynolds CF III, Alexopoulos GS, Katz IR, Lebowitz BD. Chronic depression in the elderly: approaches for prevention. *Drugs Aging*. 2001;18(7):507–514.
69. Unützer J, Patrick D, Marmon T, Simon G, Katon W. Depressive symptoms and mortality in a prospective study of 2,558 older adults. *Am J Geriatr Psychiatry*. 2002;10(5):521–530.
70. Lenze E, Sheffrin M, Driscoll H, et al. Incomplete response in late-life depression: getting to remission. *Dialogues Clin Neurosci*. 2008;10(4):419–430.
71. Roberts R, Knopman DS, Geda YE, Cha RH, Roger VL, Petersen RC. Coronary heart disease is associated with non-amnesic mild cognitive impairment. *Neurobiol Aging*. 2010;31(11):1894–1902.
72. Cacciatori F, Gallo C, Ferrara N, et al. Morbidity patterns in aged population in southern Italy. A survey sampling. *Arch Gerontol Geriatr*. 1998;26(3):201–213.
73. Ganguli M, Dodge H, Mulsant B. Rates and predictors of mortality in an aging, rural, community-based cohort: the role of depression. *Arch Gen Psychiatry*. 2002;59(11):1046–1052.
74. Pratt L, Brody DJ. Depression in the United States household population 2005–2006. *NCHS Data Brief*. 2008;7:1–8.
75. Kales H, Chen P, Blow F, Welsh D, Mellow A. Rates of clinical depression diagnosis, functional impairment, and nursing home placement in coexisting dementia and depression. *Am J Geriatr Psychiatry*. 2005;13(6):441–449.

76. Alzheimer's Association. 2009 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2009;5(3):234–270.
77. Garand L, Dew M, Eazor L, DeKosky S, Reynolds C. Caregiving burden and psychiatric morbidity in spouses of persons with mild cognitive impairment. *Int J Geriatr Psychiatry*. 2005;20(6):512–522.
78. Schulz R, Martire L. Family caregiving of persons with dementia: prevalence, health effects, and support strategies. *Am J Geriatr Psychiatry*. 2004;12(3):240–249.
79. Schubert C, Boustani M, Callahan C, Perkins A, Hui S, Hendrie H. Acute care utilization by dementia caregivers within urban primary care practices. *J Gen Intern Med*. 2008;23(11):1736–1740.
80. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA*. 1999;282(23):2215–2219.
81. Bruce J, McQuiggan M, Williams V, Westervelt H, Tremont G. Burden among spousal and child caregivers of patients with mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2008;25(4):385–390.
82. Lu Y-F, Austrom M, Perkins S, et al. Depressed mood in informal caregivers of individuals with mild cognitive impairment. *Am J Alzheimers Dis Other Dement*. 2007;22(4):273–285.
83. Kurz X, Scuvee-Moreau J, Vernooij-Dassen M, Dresse A. Cognitive impairment, dementia and quality of life in patients and caregivers. *Acta Neurol Belg*. 2003;103(1):24–34.
84. Scazufca M, Menezes P, Almeida O. Caregiver burden in an elderly population with depression in São Paulo, Brazil. *Soc Psychiatry Psychiatr Epidemiol*. 2002;37(9):416–422.
85. Scogin F. Evidence-based psychotherapies for depression in older adults. *Clin Psychol Sci Pract*. 2005;12(3):222.
86. Mackin RS, Arean P. Evidence-based psychotherapeutic interventions for geriatric depression. *Psychiatr Clin North Am*. 2005;28(4):805–820, vii.
87. Cuijpers P, van Straten A, Smit F. Psychological treatment of late-life depression: a meta-analysis of randomized controlled trials. *Int J Geriatr Psychiatry*. 2006;21(12):1139–1149.
88. Pinquart M, Duberstein PR, Lyness JM. Effects of psychotherapy and other behavioral interventions on clinically depressed older adults: a meta-analysis. *Aging Ment Health*. 2007;11(6):645–657.
89. Laidlaw K, Thompson LW, Dick-Siskin L, Gallagher-Thompson D. *Cognitive Behaviour Therapy With Older People*. Chichester, England: John Wiley and Sons, Ltd; 2003.
90. Laidlaw K, Thompson LW. Cognitive behaviour therapy with depressed older people. In: Laidlaw K, editor. *Handbook of Emotional Disorders in Later Life: Assessment and Treatment*. New York, NY: Oxford University Press; 2008.
91. Moss KS, Scogin FR. Behavioral and cognitive treatments for geriatric depression: an evidence-based perspective. In: Gallagher-Thompson D, Steffen AM, Thompson LW, editors. *Handbook of Behavioral and Cognitive Therapies With Older Adults*. New York, NY: Springer; 2008:1–17.
92. Thompson LW, Gallagher D, Breckenridge JS. Comparative effectiveness of psychotherapies for depressed elders. *J Consult Clin Psychol*. 1987;55(3):385–390.
93. Campbell JM. Treating depression in well older adults: use of diaries in cognitive therapy. *Issues Ment Health Nurs*. 1992;13(1):19–29.
94. Blanchard MR, Waterreus A, Mann AH. The effect of primary care nurse intervention upon older people screened as depressed. *Int J Geriatr Psychiatry*. 1995;10:289–298.
95. Lichtenberg PA, Kimbarow ML, Morris P, Vangel SJ. Behavioral treatment of depression in predominantly African-American medical patients. *Clin Gerontol*. 1996;17(2):15.
96. Rokke PD, Tomhave JA, Jovic Z. The role of client choice and target selection in self-management therapy for depression in older adults. *Psychol Aging*. 1999;14(1):155–169.
97. Floyd M, Scogin F, McKendree-Smith N, Floyd D, Rokke P. Cognitive therapy for depression: a comparison of individual psychotherapy and bibliotherapy for depressed older adults. *Behav Modif*. 2004;28(2):297–318.
98. Gallagher DE, Thompson LW. Treatment of major depressive disorder in older adult outpatients with brief psychotherapies. *Psychother Theor Res Pract*. 1982;19(4):482–490.
99. Steuer JL, Mintz J, Hammen CL, et al. Cognitive-behavioral and psychodynamic group psychotherapy in treatment of geriatric depression. *J Consult Clin Psychol*. 1984;52(2):180–189.
100. Gallagher-Thompson D, Steffen AM. Comparative effects of cognitive-behavioral and brief psychodynamic psychotherapies for depressed family caregivers. *J Consult Clin Psychol*. 1994;62(3):543–549.
101. Gallagher-Thompson D, Hanley-Peterson P, Thompson LW. Maintenance of gains versus relapse following brief psychotherapy for depression. *J Consult Clin Psychol*. 1990;58(3):371–374.
102. Thompson LW, Coon DW, Gallagher-Thompson D, Sommer BR, Koin D. Comparison of desipramine and cognitive/behavioral therapy in the treatment of elderly outpatients with mild-to-moderate depression. *Am J Geriatr Psychiatry*. 2001;9(3):225–240.
103. Serfaty M, Haworth D, Blanchard M, Buszewicz M, Murad S, King M. Clinical effectiveness of individual cognitive behavioral therapy for depressed older people in primary care: a randomized controlled trial. *Arch Gen Psychiatry*. 2009;66(12):1332–1340.
104. Laidlaw K, Davidson K, Toner H, et al. A randomised controlled trial of cognitive behaviour therapy vs treatment as usual in the treatment of mild to moderate late life depression. *Int J Geriatr Psychiatry*. 2008;23(8):843–850.
105. Nezu AM, Nezu CM, Perri MG. *Problem-Solving Therapy for Depression: Theory, Research, and Clinical Guidelines*. Oxford: Wiley; 1989.
106. Arean PA, Perri MG, Nezu AM, Schein RL, Christopher F, Joseph TX. Comparative effectiveness of social problem-solving therapy and reminiscence therapy as treatments for depression in older adults. *J Consult Clin Psychol*. 1993;61(6):1003–1010.
107. Arean PA, Raue P, Mackin RS, Kanellopoulos D, McCulloch C, Alexopoulos GS. Problem-solving therapy and supportive therapy in older adults with major depression and executive dysfunction. *Am J Psychiatry*. 2010;167(11):1391–1398.
108. Arean P, Hegel M, Vannoy S, Fan M-Y, Unützer J. Effectiveness of problem-solving therapy for older, primary care patients with depression: results from the IMPACT project. *Gerontologist*. 2008;48(3):311–323.
109. Gellis Z, McGinty J, Horowitz A, Bruce M, Misener E. Problem-solving therapy for late-life depression in home care: a randomized field trial. *Am J Geriatr Psychiatry*. 2007;15(11):968–978.
110. Gellis ZD. Randomized controlled trial of problem-solving therapy for minor depression in home care. *Res Soc Work Pract*. 2008;18(6):596.
111. Serrano JP, Latorre JM, Gatz M, Montanes J. Life review therapy using autobiographical retrieval practice for older adults with depressive symptomatology. *Psychol Aging*. 2004;19(2):272–277.
112. Watt LM, Cappeliez P. Integrative and instrumental reminiscence therapies for depression in older adults: intervention strategies and treatment effectiveness. *Aging Ment Health*. 2000;4(2):166–177.
113. Fry PS. Structured and unstructured reminiscence training and depression among the elderly. *Clin Gerontol*. 1983;1(3):15.
114. Wang J-J. The effects of reminiscence on depressive symptoms and mood status of older institutionalized adults in Taiwan. *Int J Geriatr Psychiatry*. 2005;20(1):57–62.
115. Hsu Y-C, Wang J-J. Physical, affective, and behavioral effects of group reminiscence on depressed institutionalized elders in Taiwan. *Nurs Res*. 2009;58(4):294–299.
116. Klausner EJ, Clarkin JF, Spielman L, Pupo C, Abrams R, Alexopoulos GS. Late-life depression and functional disability: the role of goal-focused group psychotherapy. *Int J Geriatr Psychiatry*. 1998;13(10):707–716.
117. Stinson C, Kirk E. Structured reminiscence: an intervention to decrease depression and increase self-transcendence in older women. *J Clin Nurs*. 2006;15(2):208–218.

118. Hinrichsen GA, Clougherty KF. *Interpersonal Psychotherapy for Depressed Older Adults*. Washington, DC: American Psychological Association; 2006.
119. Mossey JM, Knott KA, Higgins M, Talerico K. Effectiveness of a psychosocial intervention, interpersonal counseling, for subdysthymic depression in medically ill elderly. *J Gerontol A Bio Sci Med Sci*. 1996; 51(4):M172–M178.
120. Reynolds CF III, Frank E, Perel JM, et al. Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: a randomized controlled trial in patients older than 59 years. *JAMA*. 1999;281(1):39–45.
121. Dombrovski A, Lenze E, Dew M, et al. Maintenance treatment for old-age depression preserves health-related quality of life: a randomized, controlled trial of paroxetine and interpersonal psychotherapy. *J Am Geriatr Soc*. 2007;55(9):1325–1332.
122. Carreira K, Miller M, Frank E, et al. A controlled evaluation of monthly maintenance interpersonal psychotherapy in late-life depression with varying levels of cognitive function. *Int J Geriatr Psychiatry*. 2008; 23(11):1110–1113.
123. Hinrichsen GA. Interpersonal psychotherapy: a treatment for late-life depression. *Psychiatr Ann*. 2009;39(9):838–843.
124. Kozel FA, Trivedi M, Wisniewski S, et al. Treatment outcomes for older depressed patients with earlier versus late onset of first depressive episode: a Sequenced Treatment Alternatives to Relieve Depression (STAR*D) report. *Am J Geriatr Psychiatry*. 2008;16(1):58–64.
125. Reynolds CF III, Dew MA, Frank E, et al. Effects of age at onset of first lifetime episode of recurrent major depression on treatment response and illness course in elderly patients. *Am J Psychiatry*. 1998; 155(6):795–799.
126. Miller M, Reynolds CF III. Expanding the usefulness of interpersonal psychotherapy (IPT) for depressed elders with co-morbid cognitive impairment. *Int J Geriatr Psychiatry*. 2007;22(2):101–105.
127. Miller M. Using interpersonal therapy (IPT) with older adults today and tomorrow: a review of the literature and new developments. *Curr Psychiatr Rep*. 2008;10(1):16–22.
128. Teri L, Gallagher-Thompson D. Cognitive-behavioral interventions for treatment of depression in Alzheimer's patients. *Gerontologist*. 1991;31(3):413–416.
129. Kiosses DN, Arean PA, Teri L, Alexopoulos GS. Home-delivered problem adaptation therapy (PATH) for depressed, cognitively impaired, disabled elders: a preliminary study. *Am J Geriatr Psychiatry*. In press 2010.
130. Kiosses DN, Teri L, Velligan DI, Alexopoulos GS. A home-delivered intervention for depressed, cognitively impaired, disabled elders. *Int J Geriatr Psychiatry*. In press 2010.
131. Teri L, Logsdon RG, Uomoto J, McCurry SM. Behavioral treatment of depression in dementia patients: a controlled clinical trial. *J Gerontol B Psychol Sci Soc Sci*. 1997;52(4):P159–P166.

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