

Geriatric Social Work Initiative • Funded by The John A. Hartford Foundation



MENTAL HEALTH AND OLDER ADULTS

CHAPTER 5: DEPRESSION IN OLDER ADULTS WITH DEMENTIA

Literature Review

Zvi D. Gellis, Kim McClive-Reed, and Stanley G. McCracken*

This evidence-based review of the literature on depression disorders among older adults with dementia focuses on prevalence, clinical recognition, assessment, and treatment. A search of the empirical literature was undertaken to determine the extent of the problem and the effectiveness of various pharmacological and nonpharmacological treatments.

Dementia is a constellation of symptoms caused by diseases and disorders that affect the brain, including strokes, Alzheimer's disease (AD), Parkinson's disease (PD), and others. Dementia involves progressive loss of memory and other cognitive functions such as problem-solving and emotional control. The earliest diagnosable stage of dementia is referred to as mild cognitive impairment (MCI). As dementia progresses, abilities to independently perform instrumental and basic activities of daily living are generally impaired.

Worldwide, dementia is one of the most disabling health conditions. An estimated 24.3 million people had dementia in 2005, with 4.6 million new cases of dementia occurring annually. The number of people affected is expected to double every 20 years (Ferri et al., 2005). Alzheimer's and other dementias ranked as the fourth leading cause of disease burden in adults age 60 and older worldwide, outranked only by heart disease and chronic obstructive pulmonary disease (World Health Organization, 2003). Generally, AD is believed to be the most common type of dementia, followed by vascular dementia (VaD), frontotemporal dementia (FTD), dementia associated with PD, and dementia with Lewy bodies (DLB).

Behavioral and psychological symptoms of dementia (BPSD), also known as neuropsychiatric symptoms of dementia, affect up to 95% of those with dementia during the course of the illness (Steinberg et al., 2006) and are frequently the first manifestation of its progress. According to classifications developed during the International Psychogeriatric Association Consensus Conference on the Behavioral Disturbances of Dementia (2002), BPSD fall into two clusters: (1) behavioral and (2) psychological. Behavioral symptoms are usually identified through observation of the patient, and include physical aggression, screaming, restlessness, agitation, wandering, culturally inappropriate behaviors, sexual disinhibition, hoarding, cursing, and shadowing. Psychological symptoms, primarily assessed through interviews with patients and caregivers, include depressive mood, anxiety, hallucinations, and delusions.

BPSD have important implications for the prognosis of dementia in older adults. BPSD reduce patients' quality of life (Amore, Tagariello, Laterza & Savoia, 2007; Teng, Lu & Cummings, 2007), may accelerate cognitive and functional decline, and are associated with increased mortality (Fitzpatrick, Kuller, Lopez, Kawas, & Jagust, 2005; Potter & Steffens, 2007). Furthermore, these symptoms significantly increase caregiver burden and stress, and are associated with increased rates of depression in caregivers (Black & Almeida, 2004). They have also been found to increase the risk for institutionalization (Coehlo, Hooker & Bookman, 2007). Finally, management of BPSD has been estimated to account for approximately one-third of the total cost of dementia care (Beeri, Werner, Davidson & Noy, 2002).

The behavioral symptoms of dementia, which may be even more apparent and distressing to observers than the psychological symptoms, are generally more prevalent in moderate to severe dementia. However, psychological symptoms such as depression may cause greater distress to the patient, especially during the earlier stages of dementia, as sufferers develop insight regarding the impact of the diagnosis on their future.

Search Strategy

This evidence-based review consists of systematic reviews, meta-analyses, other reviews of the literature, experimental, quasi-experimental designs, and case studies with older adults (65+) as participants reported in English language peer-reviewed journals. Keyword search terms included aged, elderly, geri*, older adult, long-term care, dementia, Alzheimer* depress*, mood disorder, treatment, and randomized controlled trials. Searches were conducted on the following databases: PubMed (1997-2007/December); PsychINFO (1972-2007); Ageline (1978-2007), and EbscoHost Research—Academic Search Premier (through 2007). Google Scholar was also searched using November 2007-February 2008 as the time range to identify recent publications that would not have been cited. Unpublished literature was not included in the review.

Prevalence and Comorbidity of Depression in Dementia

Depressive symptoms are very common in mild cognitive impairment and across the various types of dementia. The reported prevalence of depression in older patients with dementia ranges from 30 to 96% (Amore et al., 2007; Starkstein, Jorge, Mizrahi, & Robinson, 2005), and moderate to high rates of depression or its symptoms are consistently reported for persons with MCI (i.e., 36% by Palmer, Berger, Monastero, Winblad, Backman, & Fraitiglioni, 2007; 63.3% by Solfrizzi et al., 2007; 39% by Hwang, Masterman, Ortiz, Fairbanks, & Cummings, 2004). The wide prevalence range for depression in dementia is due to several factors including differences in researchers' focus on symptoms versus specifically defined depressive disorders; diverse study samples varying in causes of dementia, stage of illness, country of residence, and placement of older patient; and instrument variation used to assess depressive symptoms and disorders.

Comorbidity of depression in older persons with MCI or probable AD has been associated with greater impairments in activities of daily living (Teri et al., 1999). Likewise, increasing cognitive impairment appears to interact with the presence of depressive symptoms to further impair functional performance, above and beyond the effects of cognitive impairment alone (Schultz, Hoth, & Buckwalter, 2004). The presence of depression in cognitively impaired persons also appears to increase the level of other BPSD. Comorbid depression and dementia are associated with higher rates of institutionalization of older adults, likely due to the negative impact on caregivers (Black & Almeida, 2004; Potter & Steffens, 2007). Untreated depression has also been related to higher treatment costs for persons with dementia (Hemels, Lanctot, Iskedjian, & Einarson, 2001).

Assessment of Depression in Dementia

Detection and assessment of depression in older adults with dementia can be challenging for the clinician. Many long-term care residents with dementia present with signs and symptoms that overlap with depression (for example, anhedonia, irritability, flat affect) (Gauthier, 2003). Based on current evidence-based practice guidelines, screening for depression in this population should occur at least every 6 months (Brown, Raue, & Halpert, 2007) (Level C). The depression screening assessment consists of the (a) Mini Mental State Exam (MMSE; Folstein et al., 1975) used frequently to screen for dementia, and either the (b) Cornell Scale for Depression in Dementia (CSDD; Alexopolous, Abrams, Young, & Shamoian, 1988), or the (c) Short Geriatric Depression Scale (GDS-15 item; Sheik & Yesavage, 1986) depending on patient cognitive functioning (Brown et al., 2007). The guidelines suggest using the GDS for patients scoring 15 to 23 on the MMSE or the CSDD if the patient scores below 15 on the MMSE. The CSDD collects interview information from both the patient and an informant. If patients score 6 or greater on the GDS, or 11 or greater on the CSDD, the primary health care provider should be notified for further evaluation and/or treatment for clinically significant depression (Brown et al., 2007). If the older adult with dementia does not screen positive for depressive symptoms, the guidelines suggest that the individual be reevaluated in 1 month if clinically warranted, otherwise, 6 months later. It is also recommended to interview caregivers and other reliable informants on behalf of the

individual with moderate to severe dementia (American Geriatrics Society & American Association of Geriatric Psychiatry, 2003). Attention needs to be paid to the biopsychosocial factors during assessment to obtain a clear picture of the patient. Assertive outpatient and community-based treatment of depression may also improve the course of coexisting dementia and depression and lengthen the time the patient can remain at home before nursing home placement.

A recent study focused on specific factors that might contribute to nursing home placement by examining the detection and course of coexisting dementia and depression (CDD) in elderly patients compared with patients with either disorder alone (Kales, Chen, Blow, Welsh, & Mellow, 2005) (Level C). This was a 1-year prospective study comparing outcomes among 82 elderly male veterans receiving inpatient and outpatient treatment. Subjects were recruited and reassessed at 3, 6, and 12 months after baseline. This study found lower rates of depression detection by treating (i.e., non-study) physicians in CDD patients. Only 35% of the CDD group were correctly diagnosed and received adequate treatment. The CDD group had significantly higher levels of functional impairment when compared to the dementia-only group. The CDD subjects used nursing home care at significantly higher rates. The investigators concluded that undetected, untreated, or inadequately treated depression may result in higher rates of nursing home placement in patients with dementia due to an increase in functional disability.

Course and Presentation of Depression in Dementia

Studies have identified pre-existing depression as a predictor or risk factor for subsequent dementia and estimated that persons experiencing depression have approximately double the risk of developing dementia that those without a prior history of depression have (Palmer et al., 2007; Teng et al., 2007). Although several studies indicate that the risk of depression in older adults with dementia tends to increase as cognitive decline in dementia progresses (Riccio, Solinas, Astara, & Mantovani, 2007; Solfrizzi et al, 2007; Steinberg et al., 2007; Teri et al., 1999), other research indicates a curvilinear, rather than linear, relationship between the symptoms of depression and the worsening of dementia (Bierman, Comijs, Jonker, & Beekman, 2007; Starkstein, Mizrahi, & Garau, 2005; Lopez et al., 2003). Participants in these studies appear to exhibit higher prevalence rates of depression in the early stages of dementia, but these disorders seem to diminish in reported prevalence as cognitive function becomes severely impaired and insight is lost. Yet, this apparent drop in prevalence may be due to differences in the presentation of depression in the later stages of dementia.

Lopez and colleagues (2003) examined the relationship between major depression and other observed psychiatric symptoms across mild, moderate, and severe stages of cognitive impairment. They found that fewer observed symptoms were associated with diagnosed depression as dementia increased. For example, confirmed depression in those with mild dementia was associated with anhedonia, sleep disturbance, depressed mood, and hopelessness, whereas moderate dementia and depression were associated with these symptoms, minus anhedonia, and severe dementia with depression was associated only with hopelessness. Another explanation of the differences in findings on the prevalence rates of depression and over the course of dementia may be disagreement among clinicians and researchers on whether and how to distinguish apathy from depression.

To investigate this further, researchers administered a structured interview intended to measure apathy and depression separately to 150 AD patients (Starkstein, Ingram, Garau, & Mizrahi, 2005). They reported that 12% met distinct criteria for both apathy and depression, while 7% met criteria for apathy only, and 31% met criteria for depression only. Supporting their argument that the two constructs were different, apathy, but not depression, was significantly associated with more severe cognitive deficits. However, in a later study, Starkstein, Jorge, Mizrahi, and Robinson (2006) found that apathy was related to a higher frequency of both minor and major depression, with apathy at baseline significantly predicting depression at follow-up evaluations, findings that support a relationship between the two constructs.

Consequences of Depression in Older Adults with Dementia

The occurrence of depression in older adults with MCI or dementia can lead to a number of negative outcomes. Depression may be a risk factor for progression from MCI to dementia. The occurrence of depression in persons with MCI or dementia has also been linked with increased general severity of cognitive deficits (Nakaaki et al., 2007). Co-morbid cognitive impairment and depression have also been associated with several other negative consequences, including increased risk of death (Sutcliffe et al., 2007). Although suicide attempts have been observed in less than 1% of dementia patients, suicidal ideation, intent, passive death wishes, and feelings that life is not worth living have been reported in 1% to 42% of dementia patients, particularly in those suffering from depression (Thompson, Herrmann, Rapoport, & Lanctot, 2007; Tsai, Tsai, Yang, & Hwang, 2007). Depression has also been associated with reduced quality of life reports from dementia patients and their caregivers (Appleby, Roy, Valenti & Lee, 2007; Hancock, Woods, Challis, & Orrell, 2006; Selwood, Thorgrimsen, & Orrell, 2006; Shin, Carter, Masterman, Fairbanks, & Cummings, 2005; Vogel, Mortensen, Hasselbalch, Andersen, & Waldemar, 2006; Winzelberg, Williams, Preisser, Zimmerman, & Sloane, 2005).

Treatments

Both pharmacologic and nonpharmacologic treatment approaches have been found to be helpful in reducing depression associated with cognitive impairment and dementia among older adults. A wide variety of medications have been used, with varying degrees of success. Nonpharmacologic interventions, such as behavioral modification programs and structured activity programs, have also been found to reduce depression though with modest outcomes. Recently, newer treatments drawn from the field of complementary and alternative medicine, such as dosing with gingko biloba extract, have been used for persons with dementia with some success.

Pharmacological Treatments for Depression in Dementia

Depression is more likely than other BPSD in older adults to respond to pharmacological interventions (Herrmann & Lanctot, 2007). The neurotransmitters/receptors that have been targeted by pharmacological therapies include catecholamine receptors (i.e., serotonin and dopamine receptors), amino acid receptors (i.e., gamma-amino-butyric acid [GABA] and glutamate receptors), and cholinergic receptors (Lanari, Amenta, Silvestrelli, Tomassoni, & Parnetti, 2006).

Pharmacological treatment of depression in patients with dementia presents some unusual difficulties for the clinician. Older patients with dementia have more comorbid illnesses than non-demented peers, with approximately 60% of those with AD having 3 or more. This heightened level of comorbidity results in the use of multiple medications. Therefore, drug interactions and polypharmacy may help provoke depressive and other symptoms in some patients with dementia (Daiello, 2007). Given their physical and cognitive frailty, older adults with dementia may also be particularly susceptible to adverse effects. Since dementia patients may be less able to communicate, clinicians and caretakers must carefully observe patient's behavior for evidence of adverse events when new medications are introduced. Prescription of new medications intended to treat depression in dementia patients should always be made using the familiar axiom for the elderly, "Start low and go slow" (Thompson et al., 2007).

Antidepressants

Antidepressants are frequently prescribed for treatment of depression in older adults with dementia. A recent meta-analysis (Thompson et al., 2007) reviewed treatment of depression with tricyclic antidepressants (TCA; imipramine and clomipramine), and selective serotonin reuptake inhibitors (SSRI; sertraline and fluoxetine) in patients with dementia. The findings indicated that patient treatment response and remission was superior to the placebo response in the combined sample from all studies, but cautioned that significant declines in cognitive scores occurred during the use of TCAs (Level B). Other reviews (Buhr & White, 2006; Sink, Holden & Yaffee, 2005) provide further support for positive effects of treatment with various antidepressants (including sertraline, fluoxetine, citalopram, trazodone, and moclobemide) on depression in dementia, with citalopram and sertraline being the most commonly prescribed (Caballero, Hitchcock, Beversdorf, Scharre, & Nahata, 2006; Starkstein & Mizrahi, 2006) (Level A). Case reports and small pilot studies indicate that other antidepressants, including trazadone and mirtazapine may decrease depression in patients with dementia, but no large trials have been performed in persons with dementia to date (Level D).

Antipsychotics

Different classes of antipsychotics have also been used to treat depression with varying degrees of success (Snowdon, Sato, & Roy-Byrne, 2003). However, older adults with dementia taking haloperidol and other "typical" antipsychotics have been found to be at significant risk of extrapyramidal symptoms including parkinsonism and tardive dyskinesia (Sink et al., 2005). Because of this, many clinicians have recently focused their attention on "atypical" antipsychotics such as risperidone and olanzapine (Herrmann & Lanctot, 2007; Sink et al., 2005), which have been shown to have significant, though modest, effects, and fewer adverse effects than typical antipsychotics at lower doses (Level D).

Caution should be noted as both risperidone and olanzapine have been associated with an increased risk of stroke and associated mortality, and subsequent safety warnings have somewhat limited their use in older patients with dementia. There is some disagreement over the actual risk involved, and it has been suggested that the increased cardiac risk may only occur at high doses (Liperoti et al., 2005). Other authors have pointed out that the patients experiencing stroke events in the original trial of Brodaty, Withall, Altendorf, and Sachdev (2007) had other risk factors for stroke besides the use of risperidone in dementia (Lee et al., 2004). A recent meta-analysis (Katz et al., 2007) concluded that although cerebrovascular events and mortality observations across trials were more frequent in risperidone-treated groups, the frequency did not differ significantly from placebo groups.

Decreased cholinergic activity, primarily resulting from decreased acetylcholine concentrations caused by dementia-related neurological changes, has been associated with decreased cognitive ability in dementia, as well as increases in BPSD, including depression (Garcia-Alloza et al., 2005). Cholinesterase inhibitors, including tacrine, donepezil, rivastigmine, and galantamine, have been used to target these problems by increasing levels of acetylcholine, with some success, particularly in patients with mild to moderate dementia (Birks, 2006). A recent review of the literature on the effects of rivastigmine on BPSD reports that positive effects have been found for patients with a wide range of dementia, and that apathy and anxiety are among the behavioral domains demonstrating the most consistent positive response (Figiel & Sadowsky, 2008) (Level E).

Anticonvulsants

Though inconclusive, some evidence exists that anticonvulsants, through their modulation of GABA, may be another class of agents for treating BPSD and depressive symptoms. GABA concentrations are often decreased in cortical regions of the brain of patients with dementia, and medications that increase GABA levels have been shown to improve mood disorders (Sink et al., 2005). Trials of the anticonvulsant carbamazepine to treat BPSD have yielded contradictory results (Franco & Messinger-Rapport , 2006) (Level B), or have not reported data on depression. At least one clinical trial of valproate resulted in significant improvement in melancholic and sorrowful behaviors (Sival, Haffmans, Jansen, Duursma, & Eikelenboom, 2002), but the results of other small trials are contradictory (Sink et al., 2005) (Level B). Preliminary studies of another anticonvulsant, lamotrigine, in elderly patients with dementia noted improvement in symptoms of agitation and depression (Sajatovic, Ramsay, Nanry, & Thompson, 2007) (Level B).

Memantine, a drug that reduces excessive glutamate receptor signaling, has also been studied in patients with dementia. Glutamate signaling is important for learning and memory, but in some patients with dementia it may increase to "oversignalling" levels that destroy neurons. A recent review and meta-analysis of the research on memantine for the treatment of psychological symptoms (e.g., depression) of dementia showed small but significant improvements with limited adverse effects (Maidment et al., 2008).

The growth of complementary/alternative medicine may yield some helpful treatments for BPSD in the future. In particular, studies provide some support for the theory that Ginkgo biloba special extract EGb 761 enhances cognitive functioning and stabilizes mood in cognitively impaired elderly subjects (Woelk, Arnoldt, Kieser, & Hoerr, 2007). A review of the research (Birks & Grimely-Evans, 2007) concluded that the evidence that the extract has predictable and clinically significant benefit for older people with dementia or cognitive impairment is inconsistent and unconvincing. However, a recent trial of this extract involving patients with dementia found that compared to controls, those taking the extract experienced improvements in apathy and depression (Scripnikov, Khomenko, & Napryeyenko, 2007).

In summary, a wide variety of pharmacological treatments have efficacy (of varying degrees) in the treatment of depression in older adults with dementia, but care must be exercised in their use with generally frail older persons to avoid adverse effects. Alexopoulous, Jeste, Chung, Carpenter, Ross, and Docherty (2005) constructed an expert consensus response after surveying 50 experts in dementia from North America on preferred, alternate, and unacceptable pharmacological treatment choices for BPSD.

The general consensus was that SSRIs were preferred for treating depression in patients with dementia. Further research appears to be needed to establish the effects of both older and newer pharmacological options for depression in dementia patients.

Non-Pharmacological Treatments for Depression in Dementia

Clinical guidelines specify the use of non-pharmacological treatments for BPSD before pharmacological treatments are tried (Buhr & White, 2006; Woods, 2004) (Level C). As well as avoiding potential effects of polypharmacy, drug interactions, or exacerbation of comorbid conditions, non-pharmacological treatments may improve the quality of life for the patient with dementia above and beyond the reduction of depression (Cohen-Mansfield, 2005). Yet, the current state of the evidence on non-pharmacological treatments is weak because few randomized controlled studies have been conducted, and therefore, it is difficult to provide information on the therapeutic benefits that these interventions may hold for older adults with dementia in long-term care.

Non-pharmacological therapies that specifically include depression as a target outcome fall roughly into three categories: (a) emotion-oriented therapies including reality orientation, validation therapy, and reminiscence therapy; and (b) brief psychotherapies including cognitive and behavioral therapy.

Emotion-Oriented Therapies

Reality Orientation Groups. Commonly conducted in long-term care settings, the original aim of Reality Orientation, as first developed for older people with mild to moderate dementia, was to reduce confusion by giving repeated orientation clues, e.g., the time of day, date, and season, but this was only partially successful. Researchers suggested that the main benefits were the stimulation from the social group and the positive impact on staff, who acquired a better knowledge of the residents and their earlier lives and interests, through which they were able to provide more personoriented care (Moos & Bjorn, 2006). Livingston and colleagues (2005) reported the results of 11 studies consisting of randomized and quasi-experimental designs on reality orientation. The largest controlled trial (N=57 subjects) demonstrated no differences between reality orientation and an active ward orientation (Hanley, McGuire, & Boyd, 1981). The smaller sample nonrandomized studies mostly showed benefits of reality orientation in decreasing depressive symptoms or delaying institutionalization. The current research does not offer clear evidence of its benefits for older adults with dementia.

Reminiscence Therapy. Reminiscence therapy encourages persons with dementia to talk about their pasts, and may utilize audiovisual aids such as old family photos and objects to retrieve positive events and emotions. Reminiscence provides dementia sufferers a chance to interact positively with others; can enhance an individual's sense

of identity, sense of worth, or general well-being; and may also stimulate memory processes (Moos & Bjorn, 2006). Two reviews that included information on reminiscence therapy report potentially positive effects on depressed mood in patients with dementia, but caution that most trials were small or otherwise methodologically questionable and therefore the evidence is weak and inconclusive (Douglas, James & Ballard, 2004; Livingston et al., 2005).

Validation therapy. Validation therapy is a type of psychosocial intervention for elderly persons with dementia. Basically, a therapist accepts the disorientation of a person with dementia and validates his/her her feelings (Feil, 2002). This self-affirming intervention is based on the assumption that individuals return to unfinished conflicts in their past, providing a background for meaningful conversations addressing their feelings. Neal and Briggs (2003) reviewed trials of this therapy and reported that only one study (Toseland et al., 1997) showed a trend towards improvement of depression a year after completing validation therapy, but the finding was not statistically significant. Another recent study using validation therapy in a group format found similar results (Deponte & Missan, 2007). The empirical evidence for the usefulness of this therapy for depression in dementia is weak and unconvincing.

Brief Psychotherapies

Cognitive and Behavioral Therapy. Behavioral therapy requires a period of detailed assessment in which the personal triggers, behaviors, and reinforcers (also known as the ABCs: antecedents, behaviors, and consequences) are identified and their relationships made clear to the patient. The therapist will often use some kind of chart or diary to gather information about the manifestations of a behavior and the sequence of actions leading up to it. Interventions are then based on an analysis of these findings. The efficacy of behavioral therapy has been demonstrated in the context of dementia in a few earlier studies (Burgio & Fisher, 2000) (Level B). For example, there is evidence of successful reductions in wandering, incontinence, and other forms of stereotypical behaviors (Woods & Bird, 1999). Meares and Draper (1999) (Level F) presented case studies confirming the efficacy of behavioral therapy, but they noted that the behaviors had diverse causes and maintaining factors, and cautioned that behavioral interventions must be tailored to individual cases.

A recent systematic review examined 20 studies using behavioral management techniques for outcomes of depressive (3 studies) and neuropsychiatric symptoms (17 studies) in older adults with dementia (Livingston et al., 2005). Of the 3 on depression outcomes, one large randomized controlled trial showed significant improvement in depressive symptoms immediately post-treatment and at 6-month follow-up examination in two treatment conditions: (1) one emphasizing patient pleasant events and one emphasizing caregiver problem solving, as compared to treatment as usual and waitlist control conditions (Teri, Logdson, Uomoto, & McCurry., 1997) (Level A). The

two smaller randomized trials also demonstrated significant reductions in behavioral symptoms compared to usual primary care (Benedict et al., 2000; Suhr, Anderson, & Tranel, 1999). However, no significant effects were found on depression (Benedict et al., 2000). The results of the larger randomized trial studies were consistent and showed benefits as compared to the control condition, and these beneficial effects were maintained over time.

Hyer and colleagues (1990) compared the effectiveness of a12-week group psychotherapy, in a cognitive behavioral format, to usual care in a small sample of 22 residents. At post-treatment, depression scores decreased in the treatment group but not in the control group. Koder (1998) discussed two case reports in which cognitive behavioral therapy was offered using techniques such as relaxation, distraction, and cognitive restructuring. Over the past decade, there has been an increasing interest in applying some of the brief therapeutic frameworks such as cognitive behavioral therapy (CBT) to dementia. For example, Teri, Curtis, Gallagher-Thompson, and Gallagher-Thompson (1994) reported positive findings from a clinical trial of CBT with people in the early stages of AD. Individual and group CBT has also been used by other researchers with some favorable results (Kipling, Bailey, & Charlesworth, 1999).

Both cognitive and behavioral therapies have obvious limitations, particularly for persons with severe dementia. Nevertheless, owing to the fact that these therapies have relatively simple conceptual models underpinning them, they have been shown to be helpful, even for severe cognitive impairment (Logsdon, McCurry, & Teri, 2007; Yuhas, McGowan, Fontaine, Czech, & Gambrell-Jones, 2006). For example, Douglas, James, and Ballard (2004) believes that a CBT perspective is very suitable for people with dementia, since many of the behavioral difficulties encountered emerge through one or more of the following cognitive features: cognitive misinterpretations, biases, distortions, erroneous problem-solving strategies, and communication difficulties. Hence, CBT offers a framework within which to understand the individual's distressing experiences, and this understanding allows the clinician to target interventions more appropriately.

Overall, the evidence on non-pharmacological interventions as effective treatments for depression in older adults with dementia residing in long-term care is sparse and deficient. There are several limitations to the literature. First, most research studies have focused on behavioral and not depressive symptom outcomes. Second, the diversity of sample elderly populations makes it difficult to compare results across studies. Third, the majority of studies lack a description of intervention protocols or manuals making it difficult to understand, analyze, or replicate the treatment components. Finally, the inconsistency of follow-up protocols across studies provides further barriers to determine long-term effects of the interventions. A few psychosocial interventions such as group and individual behavioral therapies show some potential but require further investigation, improved study design, and clear intervention protocols for duplication and treatment component analysis.

Summary Take Home Points

- Depression is a common problem in older adults with dementia in long-term care settings.
- Behavioral and psychological symptoms of dementia (**BPSD**), also known as neuropsychiatric symptoms of dementia, affect up to 95% of those with dementia.
- Reported prevalence of depression in elderly with dementia ranges from 30% to 96%.
- The depression screening protocol consists of the Mini Mental State Exam (MMSE) and either the Cornell Scale for Depression in Dementia (CSDD) or the Short Geriatric Depression Scale (SGSD) depending on MMSE score.
 - The GDS should be used for patient scores of 15 to 23 on the MMSE.
 - The CSDD should be used if the patient scores below 15 on the MMSE.
 - If GDS is 6 or greater or CSDD is 11 or greater the primary health care provider should be notified for further evaluation and/or treatment for clinically significant depression.
- Apathy has been found to be related to a higher frequency of both minor and major depression.
- Depression may be a risk factor for progression from MCI to dementia.
- Expert consensus recommends SSRIs as the preferred pharmacological treatment for depression in patients with dementia.
- Due to physical and cognitive frailty, drug interactions, and polypharmacy may trigger depressive and other symptoms in some patients with dementia and patients may be susceptible to adverse effects.
- Clinical guidelines specify the use of non-pharmacological treatments for BPSD before pharmacological treatments.
- Scientific evidence for emotion-oriented therapies (Reality Orientation, Validation Therapy, and Reminiscence Therapy) is weak.
- Scientific evidence for cognitive and behavioral therapies is somewhat stronger. Results of a few large randomized trial studies were consistent

and showed benefits as compared to control groups, and outcome effects on depression reductions were maintained over time.

Bibliography

- Agronin, M.E. (2008). Alzheimer's disease and other dementias. 2nd edition. Philadelphia, PA: Lippincott, Williams, & Wilkins.
- Alexopoulos, G. S., Abrams, R., Young, R., & Shamoian, C. (1988). Cornell Scale for Depression in Dementia. *Biological Psychiatry*, 23, 271-284.
- Alexopoulos, G. S., Jeste, D. V., Chung, H., Carpenter, D., Ross, R., & Docherty, J. P. (2005). The expert consensus guideline series. Treatment of dementia and its behavioral disturbances. Introduction: methods, commentary, and summary. *Postgraduate Medical Journal, Spec No*, 6-22.
- American Geriatrics Society and The American Association for Geriatric Psychiatry. (2003). Consensus statement on improving the quality of mental health in U. S. nursing homes: Management of depression and behavioral symptoms associated with dementia. *Journal of the American Geriatric Society*, *51*(1287-1298).
- Amore, M., Tagariello, P., Laterza, C., & Savoia, E. M. (2007). Subtypes of depression in dementia. *Archives of Gerontology and Geriatrics*, 44(*Suppl 1*), 23-33.
- Appleby, B. S., Roy, P., Valenti, A., & Lee, H. B. (2007). Diagnosis and treatment of depression in Alzheimer's disease: impact on mood and cognition. *Panminerva Medica*, 49(3), 139-149.
- Beeri, M., Werner, P., Davidson, M., & Noy, S. (2002). The cost of behavioral and psychological symptoms of dementia (BPSD) in community dwelling Alzheimer's disease patients. *International Journal of Geriatric Psychiatry*, 17(5), 403-408.
- Benedict, R., Shapiro, A., Priore, R., Miller, C., Munschauer, F., & Jacobs, L. (2000). Neuropsychological counseling improves social behavior in cognitively-impaired multiple sclerosis patients. *Multiple Sclerosis*, *6*, 391-396.
- Bierman, E. J., Comijs, H. C., Jonker, C., & Beekman, A. T. (2007). Symptoms of anxiety and depression in the course of cognitive decline. *Dementia and Geriatric Cognitive Disorders*, 24(3), 213-219.
- Birks, J. (2006). Cholinesterase inhibitors for Alzheimer's disease. *Cochrane Database of Systematic Reviews*, 1, CD005593.
- Birks, J., & Grimley Evans, J. (2007). Ginkgo biloba for cognitive impairment and dementia. *Cochrane Database of Systematic Reviews*, 2, CD003120.
- Black, W., & Almeida, O. P. (2004). A systematic review of the association between the Behavioral and Psychological Symptoms of Dementia and burden of care. *International Psychogeriatrics*, *16*, 295-315.

- Borson, S., Scanlan, J.M., Brush, M., Vitallano, P., & Dokmak, A. (2000). The Mini-Cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, 15(11), 1021-1027.
- Brodaty, H., Withall, A., Altendorf, A., & Sachdev, P. S. (2007). Rates of depression at 3 and 15 months poststroke and their relationship with cognitive decline: the Sydney Stroke Study. *American Journal of Geriatric Psychiatry*, 15(6), 477-486.
- Brown, E., Raue, P., & Halpert, K. (2007). Detection of depression in older adults with dementia Evidence-Based Guideline. In M. Titler (Series Ed.), Series on Evidence-Based Practice for Older Adults. Iowa City, IA: The University of Iowa College of Nursing Gerontological Nursing Interventions Research Center, Research Translation and Dissemination Core.
- Buhr, G., & White, H. (2006). Difficult behaviors in long-term care patients with dementia. *Journal of the American Medical Director's Association*, 7(3), 180-92.
- Burgio, L., & Fisher, S. (2000). Application of psychosocial interventions for treating behavioral and psychological symptoms of dementia. *International Psychogeriatrics*, 12, 351-358.
- Caballero, J., Hitchcock, M., Beversdorf, D., Scharre, D., & Nahata, M. (2006). Long-term effects of antidepressants on cognition in patients with Alzheimer's disease. *Journal of Clinical Pharmacy and Therapeutics*, *31*(6), 593-598.
- Coehlo, D. P., Hooker, K., & Bowman, S. (2007). Institutional Placement of Persons With Dementia. *Journal of Family Nursing*, 13(2), 253-277.
- Cohen-Mansfield, J. (2005). Nonpharmacological interventions for persons with dementia. *Alzheimer's Care Quarterly*, 6(2), 129-145.
- Daiello, L. A. (2007). Current issues in dementia pharmacotherapy. *The American Journal* of Managed Care, 13(Suppl 8), S198-202.
- Deponte, A., & Missan, R. (2007). Effectiveness of validation therapy (VT) in group: Preliminary results. *Archives of Gerontology and Geriatrics*, 44(2), 113-117.
- Douglas, S., James, I., & Ballard, C. (2004). Non-pharmacological interventions in dementia. *Advances in Psychiatric Treatment*, *10*(3), 171-177.
- Feil, N. (2002). *The validation breakthrough revised*. Baltimore, MD: Health Professions Press.
- Ferri, C. P., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli, M., et al. (2005). Global prevalence of dementia: a Delphi consensus study. *Lancet*, 366(9503), 2112-2117.

- Figiel, G., & Sadowsky, C. (2008). A systematic review of the effectiveness of rivastigmine for the treatment of behavioral disturbances in dementia and other neurological disorders. *Current Medical Research and Opinion*, 24(1), 157-166.
- Fitzpatrick, A. L., Kuller, L. H., Lopez, O. L., Kawas, C. H., & Jagust, W. (2005). Survival following dementia onset: Alzheimer's disease and vascular dementia. *Journal of the Neurological Sciences*, 229-230, 43-49.
- Folstein, M., Folstein, S., & McHugh, P. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189-198.
- Franco, K. N., & Messinger-Rapport, B. (2006). Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. *Journal of the American Medical Directors Association*, 7(3), 201-202.
- Garcia-Alloza, M., Gil-Bea, F. J., Diez-Ariza, M., Chen, C. P., Francis, P. T., Lasheras, B., et al. (2005). Cholinergic-serotonergic imbalance contributes to cognitive and behavioral symptoms in Alzheimer's disease. *Neuropsychologia*, 43(3), 442-449.
- Gauthier, S. (2003). Clinical aspects. In A. C. Juillerat, M. Van Der Linden, & R. Mulligan (Eds.), *The Clinical Management of Early Alzheimer's Disease: A Handbook* (pp. 21-34). Mahwah, NJ: Lawrence Erlbaum.
- Hancock, G. A., Woods, B., Challis, D., & Orrell, M. (2006). The needs of older people with dementia in residential care. *International Journal of Geriatric Psychiatry*, 21(1), 43-49.
- Hanley, I., McGuire, R., & Boyd, W. (1981). Reality orientation and dementia: a controlled trial of two approaches. *British Journal of Psychiatry*, 138, 10-14.
- Hemels, M. E., Lanctot, K. L., Iskedjian, M., & Einarson, T. R. (2001). Clinical and economic factors in the treatment of behavioural and psychological symptoms of dementia. *Drugs Aging*, 18(7), 527-550.
- Herrmann, N., & Lanctot, K. L. (2007). Pharmacologic Management of Neuropsychiatric Symptoms of Alzheimer Disease. *Canadian Journal of Psychiatry*, 52(10), 630-646.
- Hwang, T. J., Masterman, D. L., Ortiz, F., Fairbanks, L. A., & Cummings, J. L. (2004). Mild cognitive impairment is associated with characteristic neuropsychiatric symptoms. *Alzheimer Disease and Associated Disorders*, 18(1), 17-21.
- Hyer, L., Swanson, G., Lefkowitz, R., Hillesland, D., Davis, H., & Woods, M. G. (1990). The application of the cognitive behavioral model to two older stressor groups. *Clinical Gerontologist*, 9(3/4), 145-190.

- Kales, H., Chen, P., Blow, F., Welsh, D., & Mellow, A. (2005). Rates of clinical depression diagnosis, functional impairment, and nursing home placement in coexisting dementia and depression. *American Journal of Geriatric Psychiatry*, 13(6), 441-449.
- Katz, I., de Deyn, P. P., Mintzer, J., Greenspan, A., Zhu, Y., & Brodaty, H. (2007). The efficacy and safety of risperidone in the treatment of psychosis of Alzheimer's disease and mixed dementia: a meta-analysis of 4 placebo-controlled clinical trials. *International Journal of Geriatric Psychiatry*, 22(5), 475-484.
- Kipling, T., Bailey, M., & Charlesworth. G. (1999). The feasibility of a cognitivebehavioral therapy group for men with mild/moderate cognitive impairment. *Behavioural and Cognitive Psychotherapy*, 27(2), 189-193.
- Koder, D. A. (1998). Treatment of anxiety in the cognitively impaired elderly: can cognitive-behavior therapy help? *International Psychogeriatrics/IPA*, *10*(2), 173-182.
- Lanari, A., Amenta, F., Silvestrelli, G., Tomassoni, D., & Parnetti, L. (2006). Neurotransmitter deficits in behavioural and psychological symptoms of Alzheimer's disease. *Mechanisms of Ageing and Development*, 127(2), 158-165.
- Lee, P. E., Gill, S. S., Freedman, M., Bronskill, S. E., Hillmer, M. P., & Rochon, P. A. (2004). Atypical antipsychotic drugs in the treatment of behavioural and psychological symptoms of dementia: systematic review. *British Medical Journal*, 329(7457), 75-79.
- Liperoti, R., Gambassi, G., Lapane, K. L., Chiang, C., Pedone, C., Mor, V., et al. (2005). Conventional and Atypical Antipsychotics and the Risk of Hospitalization for Ventricular Arrhythmias or Cardiac Arrest. *Archives of Internal Medicine*, 165(6), 696-701.
- Livingston, G., Johnston, K., Katona, C., Paton, J., Lyketsos, C. G., & Old Age Task Force of the World Federation of Biological Psychiatry. (2005). Systematic Review of Psychological Approaches to the Management of Neuropsychiatric Symptoms of Dementia. *American Journal of Psychiatry*, 162(11), 1996-2021.
- Logsdon, R., McCurry, S., & Teri, L. (2007). Evidence-based psychological treatments for disruptive behaviors in individuals with dementia. *Psychology of Aging*, 22(1), 28-36.
- Lopez, O. L., Becker, J. T., Sweet, R. A., Klunk, W., Kaufer, D. I., Saxton, J., et al. (2003). Psychiatric Symptoms Vary With the Severity of Dementia in Probable Alzheimer's Disease. *Journal of Neuropsychiatry and Clinical Neurosciences*, 15(3), 346-353.
- Maidment, I. D., Fox, C. G., Boustani, M., Rodriguez, J., Brown, R. C., & Katona, C. L. (2008). Efficacy of memantine on behavioral and psychological symptoms related to dementia: a systematic meta-analysis. *Annals of Pharmacotherapy*, 42(1), 32-38.

- Meares, S., & Draper, B. (1999). Treatment of vocally disruptive behaviors of multifactorial aetiology. *International Journal of Geriatric Psychiatry*, 14(4), 285-290.
- Moos, I., & Bjorn, A. (2006). Use of the life story in the institutional care of people with dementia: A review of intervention studies. *Ageing and Society*, *26*(3), 431-454.
- Nakaaki, S., Murata, Y., Sato, J., Shinagawa, Y., Tatsumi, H., Hirono, N., et al. (2007). Greater impairment of ability in the divided attention task is seen in Alzheimer's disease patients with depression than in those without depression. *Dementia and Geriatric Cognitive Disorders*, 23(4), 231-240.
- Neal, M., & Briggs, M. (2003). Validation therapy for dementia. *Cochrane Database of Systematic Reviews*, *3*, CD001394.
- Palmer, K., Berger, A., Monastero, R., Winblad, B., Backman, L., & Fratiglioni, L. (2007). Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology*, 68(10), 1588-1602.
- Potter, G. G., & Steffens, D. C. (2007). Contribution of depression to cognitive impairment and dementia in older adults. *Neurologist*, *13*(3), 105-117.
- Reisberg, B., Ferris, S.H., de Leon, M.J. & Crook, T. (1982). The Global Deterioration Scale for assessment of primary degenerative dementia. *American Journal of Psychiatry*, 139, 1136-1139.
- Riccio, D., Solinas, A., Astara, G., & Mantovani, G. (2007). Comprehensive geriatric assessment in female elderly patients with Alzheimer disease and other types of dementia. *Archives of Gerontology and Geriatrics*, 44(Suppl 1), 343-353.
- Sajatovic, M., Ramsay, E., Nanry, K., & Thompson, T. (2007). Lamotrigine therapy in elderly patients with epilepsy, bipolar disorder or dementia. *International Journal of Geriatric Psychiatry*, 22(10), 945-950.
- Schultz, S. K., Hoth, A., & Buckwalter, K. (2004). Anxiety and Impaired Social Function in the Elderly. *Annals of Clinical Psychiatry*, *16*(1), 47-51.
- Scripnikov, A., Khomenko, A., & Napryeyenko, O. (2007). Effects of Ginkgo biloba extract EGb 761 on neuropsychiatric symptoms of dementia: findings from a randomised controlled trial. *Wiener Medizinische Wochenschrift*, 157(13-14), 295-300.
- Selwood, A., Thorgrimsen, L., & Orrell, M. (2005). Quality of life in dementia: A oneyear follow-up study. *International Journal of Geriatric Psychiatry*, 20(3), 232-237.
- Sheikh, J., & Yesavage, J. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. *Clinical Gerontology: A Guide to Assessment and Intervention* (pp. 165-173). New York, NY: The Haworth Press.

- Shin, I. S., Carter, M., Masterman, D., Fairbanks, L., & Cummings, J. L. (2005). Neuropsychiatric symptoms and quality of life in Alzheimer disease. *American Journal of Geriatric Psychiatry*, 13(6), 469-474.
- Sink, K. M., Holden, K. F., & Yaffe, K. (2005). Pharmacological Treatment of Neuropsychiatric Symptoms of Dementia: A Review of the Evidence. *Journal of the American Medical Association*, 293(5), 596-608.
- Sival, R. C., Haffmans, P. M., Jansen, P. A., Duursma, S. A., & Eikelenboom, P. (2002). Sodium valproate in the treatment of aggressive behavior in patients with dementia--a randomized placebo controlled clinical trial. *International Journal of Geriatric Psychiatry*, 17(6), 579-585.
- Snowden, M., Sato, K., & Roy-Byrne, P. (2003). Assessment and treatment of nursing home residents with depression or behavioral symptoms associated with dementia: a review of the literature. *Journal of the American Geriatrics Society*, *51*(9), 1305-1317.
- Solfrizzi, V., D'Introno, A., Colacicco, A. M., Capurso, C., Del Parigi, A., Caselli, R. J., et al. (2007). Incident occurrence of depressive symptoms among patients with mild cognitive impairment the Italian longitudinal study on aging. *Dementia and Geriatric Cognitive Disorders*, 24(1), 55-64.
- Starkstein, S. E., Ingram, L., Garau, M. L., & Mizrahi, R. (2005). On the overlap between apathy and depression in dementia. *Journal of Neurology, Neurosurgery, and Psychiatry*, *76*(8), 1070-1074.
- Starkstein, S. E., Jorge, R., Mizrahi, R., & Robinson, R. G. (2005). The construct of minor and major depression in Alzheimer's disease. *American Journal of Psychiatry*, 162(11), 2086-2093.
- Starkstein, S. E., Jorge, R., Mizrahi, R., & Robinson, R. G. (2006). A prospective longitudinal study of apathy in Alzheimer's disease. *Journal of Neurology*, *Neurosurgery & Psychiatry*, 77(1), 8-11.
- Starkstein, S. E., & Mizrahi, R. (2006). Depression in Alzheimer's disease. *Expert Review* of Neurotherapeutics, 6(6), 887-895.
- Starkstein, S. E., Mizrahi, R., & Garau, L. (2005). Specificity of symptoms of depression in Alzheimer disease: a longitudinal analysis. *American Journal of Geriatric Psychiatry*, 13(9), 802-807.
- Steinberg, M., Corcoran, C., Tschanz, J. T., Huber, C., Welsh-Bohmer, K., Norton, M. C., et al. (2006). Risk factors for neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry*, 21(9), 824-830.

- Steinberg, M., Shao, H., Zandi, P., Lyketsos, C. G., Welsh-Bohmer, K. A., Norton, M. C., et al. (2007). Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry*, 23(2),170-177.
- Suhr, J., Anderson, S., & Tranel, D. (1999). Progressive muscle relaxation in the management of behavioral disturbance in Alzheimer's disease. *Neuropsychological Rehabilitation*, 9, 31-44.
- Sutcliffe, C., Burns, A., Challis, D., Mozley, C. G., Cordingley, L., Bagley, H., et al. (2007). Depressed mood, cognitive impairment, and survival in older people admitted to care homes in England. *American Journal of Geriatric Psychiatry*, 15(8), 708-715.
- Teng, E., Lu, P. H., & Cummings, J. L. (2007). Neuropsychiatric symptoms are associated with progression from mild cognitive impairment to Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*, 24(4), 253-259.
- Teri, L., Logsdon R.G., Uomoto, J., & McCurry, S. (1997). Behavioral treatment of depression in dementia patients: a controlled clinical trial. *Journal of Gerontology: Psychol Sciences, Social Sciences*, 52(4), P159-66.
- Teri, L., Curtis, J., Gallagher-Thompson, D., & Thompson, L. (1994). In B. Lebowitz, A/ Friedhoff, L. Schneider, & C. Reynolds. (Eds.), *Diagnosis and treatment of depression in late life: Results from the NIH Consensus Development Conference* (pp. 279-291).
 Washington DC: American Psychiatric Association.
- Teri, L., Ferretti, I., Gibbons, L., Logsdon, R., McCurry, S., Kukull, W., et al. (1999). *Journals of Gerontology: Biological Sciences and Medical Sciences*, *54A*(70), M348-M352.
- Teri, L., & Logsdon R. G. (2000). Assessment and Management of Behavioral Disturbances in Alzheimer Disease. *Comprehensive Therapy*, *26*, 169-175.
- Thompson, S., Herrmann, N., Rapoport, M. J., & Lanctot, K. L. (2007). Efficacy and safety of antidepressants for treatment of depression in Alzheimer's disease: a metaanalysis. *Canadian Journal of Psychiatry*, 52(4), 248-255.
- Toseland, R., Diehl, M., Freeman, K., Manzanares, T., Naleppa, M., & McCallion, P. (1997). *Journal of Applied Gerontology*, *16*(1), 31-50.
- Tsai, C. F., Tsai, S. J., Yang, C. H., & Hwang, J. P. (2007). Chinese demented inpatients admitted following a suicide attempt: a case series. *International Journal of Geriatric Psychiatry*, 22(11), 1106-1109.
- Vogel, A., Mortensen, E. L., Hasselbalch, S. G., Andersen, B. B., & Waldemar, G. (2006). Patient versus informant reported quality of life in the earliest phases of Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 21(12), 1132-1138.

- Winzelberg, G. S., Williams, C. S., Preisser, J. S., Zimmerman, S., & Sloane, P. D. (2005).
 Factors Associated With Nursing Assistant Quality-of-Life Ratings for Residents
 With Dementia in Long-Term Care Facilities. *Gerontologist*, 45(suppl 1), 106-114.
- Woelk, H., Arnoldt, K. H., Kieser, M., & Hoerr, R. (2007). Ginkgo biloba special extract EGb 761 in generalized anxiety disorder and adjustment disorder with anxious mood: a randomized, double-blind, placebo-controlled trial. *Journal of Psychiatric Research*, 41(6), 472-480.
- Woods, B. (2004). Non-pharmacological interventions in dementia. *Advances in Psychiatric Treatment*, *10*(3), 178-179.
- Woods, B., & Bird, M. (1999). Non-pharmacological approaches to treatment. In K. Rockwood, G. Wilcock & R. Bucks (Eds), *Diagnosis and management of dementia: A manual for memory disorders teams* (pp. 311-331). New York, NY: Oxford University Press.
- World Health Organization. (2003). *World Health Report 2003—Shaping the future*. Geneva: WHO.
- Yuhas, N., McGowan, B., Fontaine, T., Czech, J., & Gambrell, J. (2006). Psychosocial interventions for disruptive symptoms of dementia. *Psychosocial Nursing in Mental Health Services*, 44(11), 34-42.