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Treatment of Depression in Nursing Home Residents without Significant Cognitive Impairment: a Systematic Review

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Abstract

Background—Depression in nursing facilities is widespread and has been historically under-recognized and inadequately treated. Many interventions have targeted depression among residents with dementia in these settings. Less is known about depression treatment in residents without dementia who may be more likely to return to community living. Our study aimed to systematically evaluate randomized control trials (RCTs) in nursing facilities that targeted depression within samples largely comprised of residents without dementia.

Methods—The following databases were evaluated with searches covering January 1991 through December 2015 (PubMed, PsycINFO) and March 2016 (CINAHL). We also examined national and international clinical trial registries including ClinicalTrials.gov. RCTs were included if they were published in English, evaluated depression or depressive symptoms as primary or secondary outcomes, and included a sample with a mean age of 65 and older for which most had no or only mild cognitive impairment.

Results—A total of 32 RCTs met our criteria including those testing psychotherapeutic interventions (n=13), psychosocial and recreation interventions (n=9), and pharmacologic or other biologic interventions (n=10). Seven psychotherapeutic, six psychosocial and recreation, and four pharmacologic or other biologic interventions demonstrated a treatment benefit.

Conclusions—Many studies had small samples, were of poor methodological quality, and did not select for depressed residents. There is limited evidence suggesting that cognitive behavioral therapies, reminiscence, interventions to reduce social isolation, and exercise-based interventions have some promise for decreasing depression in cognitively intact nursing home residents; little can be concluded from the pharmacologic or other biologic RCTs.

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Conflicts of Interest

None.

Description of Authors' Roles

A. Simning and K.V. Simons designed the study, implemented the search strategy (with assistance from K. Liljequist), reviewed the articles, interpreted the findings, and wrote and approved of the article.

Keywords

Mental health; older adults; long-term care

Introduction

Compared to depression in community-dwelling older adults, depression in nursing home residents is more prevalent (Blazer, 2003) with estimates ranging widely from 11 to 78% (Gaboda *et al.*, 2011). In a rigorous study that utilized psychiatrists and standardized depression assessments, the prevalence of probable/definite major depressive disorder and minor depression in nursing home residents were 14.4% and 16.8%, respectively (Teresi *et al.*, 2001), which is consistent with other estimates of major depressive disorder in this setting (Boyce *et al.*, 2012). Late-life depression often has a chronic course and can have severe consequences such as increased disability, functional decline, heart disease, utilization of services, death-by-suicide, and non-suicide mortality (Alexopoulos, 2005; Beekman *et al.*, 2002; Blazer, 2003). In nursing facilities, depression historically has been under-recognized and inadequately treated (Blazer, 2003; Parker *et al.*, 2009; Teresi *et al.*, 2001). Evidence prior to the implementation of the Minimum Data Set 3.0 (which regularly monitors depressive symptoms) suggests that depression identification and treatment was increasing (Gaboda *et al.*, 2011). However, the adequacy or appropriateness of nursing facility antidepressant use remains uncertain (Oslin *et al.*, 2003).

Depression management in nursing homes can be broadly divided into non-pharmacological interventions (e.g., psychotherapeutic, psychosocial) and pharmacologic or other biologic interventions. Non-pharmacological approaches are highly varied and consist of interventions such as individual and group therapies, staff/provider training and implementation of depression care best practices, and physical activity, recreation, and rehabilitation activities. There is relatively little guiding the pharmacological management of depression in nursing home residents with much of the antidepressant evidence base arising from younger and healthier populations and because antidepressant trials in older adults often have excluded disabled and medically frail participants (Burrows *et al.*, 2002). Extrapolating antidepressant trial results based on younger and healthier samples may be suboptimal as older adults can be more susceptible to side effects and have different response profiles.

The breadth of this literature makes it challenging to comprehensively review approaches for depression treatment in nursing facility residents. Furthermore, review articles examining depression treatment in long-term care settings have been relatively heterogeneous and have included both lower-level dependency facilities (e.g., assisted living facilities) and higher-level dependency facilities (e.g., nursing facilities) (Cody and Drysdale, 2012), residents with dementia and cognitively intact residents (Cody and Drysdale, 2012; Boyce *et al.*, 2012), and open-label trials as well as randomized controlled trials (RCTs) (Boyce *et al.*, 2012). Distinguishing residents by cognitive impairment status is relevant because non-pharmacological and pharmacological approaches to depression management can differ accordingly. For example, reminiscence therapy is relatively well-studied for alleviating

depression in residents with dementia (Cody and Drysdale, 2012) and researchers have found differential responses to antidepressants based on cognitive impairment status (Streim *et al.*, 2000). Likewise, residents who are cognitively intact are more likely to transition from a nursing facility to the community (Gassoumis *et al.*, 2013; Thomas *et al.*, 2010), consistent with the goal of Money Follows the Person demonstrations (Irvin *et al.*, 2015); yet depression is a known risk factor for long-term placement (Yoo *et al.*, 2013). This review therefore aims to systematically assess RCTs in nursing facilities that evaluate depression as an outcome in residents without moderate or severe cognitive impairment because these residents may be more likely to transition back to the community as part of a short or long-stay placement and optimal depression management may differ by cognitive impairment status.

Methods

Inclusion and Exclusion Criteria

We searched for RCTs that: 1) evaluated depression or depressive symptoms as primary or secondary outcomes, 2) were conducted in nursing homes (i.e., health care facilities which provide around-the-clock nursing staff), 3) included participants with a mean age of 65 years or older, 4) had 50% or more of the sample with mild cognitive impairment or better, as indicated by mean scores on standardized measures of cognition within treatment arms (e.g., Mini-Mental Status Exam score of 21 or higher (Folstein *et al.*, 1975)), and 5) were published in English in peer-reviewed journals. We excluded RCTs not meeting our inclusion criteria as well as RCTs that were: 1) based in intensive post-acute care rehabilitation settings, assisted living facilities, or facilities that were determined to be unlikely to meet our definition of a nursing home and 2) based on dissertation or thesis research that was not subsequently published in a research journal. We included interventions that randomized at the individual, unit, or facility levels.

Data Sources and Search Method

We searched the following databases to identify articles published between January 1991 to when the searches were performed: PubMed (search completed in 12/2015), PsycINFO (search completed in 12/2015), and CINAHL (search completed in 3/2016). We combined strings of search terms that included descriptors of the setting (e.g., “long-term care,” “residential care,” “nursing home*”), depression (e.g., “depress*,” “dysthym*,” “mood”), the population of interest (e.g., “older adult*,” “elder*,” “geriatric*”), and intervention approaches (e.g., “antidepress*,” “medication,” “psychother*”). January 1991 was selected as the start date for the review as it coincides with implementation of the Nursing Home Reform Act in the United States, which ushered in an era of reforms aimed at improving nursing home quality of care and quality of life (Hawes *et al.*, 1997). In December 2015 we screened ClinicalTrials.gov, the International Standard Randomized Controlled Trial Number (ISRCTN) Registry, and the World Health Organization International Clinical Trials Registry Platform (WHOICTRP) for relevant RCTs. Please see Appendix I published as supplementary material online attached to the electronic version of this paper at: <http://journals.cambridge.org/ipg>.

Literature Screening and Quality Appraisal

Both investigators screened all titles and abstracts as well as the clinical trial websites. Articles that appeared to meet our inclusion criteria were identified as falling within the following broad treatment categories: 1) psychotherapeutic interventions, 2) psychosocial and recreation interventions, and 3) pharmacologic or other biologic interventions. When there was uncertainty as to whether an article met our criteria, both investigators reviewed the full text of the article and a consensus was reached. For certain articles in which eligibility remained unclear, we attempted to contact the article's corresponding author for further clarification. Articles meeting our inclusion criteria were assessed for quality with the Jadad Scale, a validated 3-item scale scored from 0 (lowest quality) to 5 (highest quality) that evaluates randomization (scored 0–2), blinding (scored 0–2), and study dropout (scored 0–1) (Jadad *et al.*, 1996). Double blinding was not always feasible in some of the interventions (e.g., group therapy) and, for these situations, we scored blinding a 2 if the assessors were blinded to the intervention assignment.

Results

Search Results

Our search strategy yielded 510 articles in CINAHL, 1,535 articles in PubMed, and 1,222 articles in PsycINFO for screening (see Figure 1, which is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations (Moher *et al.*, 2009)). With regards to the clinical trial databases, our search of [ClinicalTrials.gov](https://clinicaltrials.gov), the ISRCTN Registry, and the WHOICTRP, produced 87, 34, and 15 studies, respectively. After removing 145 duplicates, we were left with 3,258 records for the initial review of which 3,151 were excluded, at the outset, for not meeting our criteria. We ultimately examined 107 full text articles of which 35 articles met our criteria. We excluded three articles that had duplicated results or probable issues with data integrity. A total of 32 articles were thereby included in our systematic review.

As the goal of an RCT is to directly compare interventions to one another or a control group, we presented p-values that tested between group differences in Table 1. Due to the heterogeneity across studies with regards to participant characteristics, inclusion criteria, intervention approaches and duration, and outcome measurements, we did not calculate overall effect sizes.

Quality Scores

The mean quality rating was 2.2 (95% confidence interval (CI): 1.40 to 3.07) among psychotherapeutic interventions, 2.8 (95% CI: 1.99 to 3.56) among psychosocial and recreation interventions, and 3.6 (95% CI: 2.82 to 4.38) among pharmacologic and other biologic interventions. These differences were not significant ($F [2,29]=2.84$, $p=0.075$). Many RCTs did not provide an adequate description of randomization, blinding procedures, and within group attrition.

Psychotherapeutic Interventions

Thirteen RCTs were included in this category, and the interventions were divided among those utilizing cognitive behavioral therapy (CBT) (Cook, 1998; Hyer *et al.*, 2008; Konnert *et al.*, 2009; Sood *et al.*, 2003; Zerhusen *et al.*, 1991), reminiscence therapy (Chiang *et al.*, 2010; Cook, 1991; Haight *et al.*, 1998; Wang, 2005), and other types of psychotherapies and therapeutic approaches (Alonso-Fernandez *et al.*, 2015; McCurren *et al.*, 1999; Reinhardt *et al.*, 2014; Tsai *et al.*, 2008). Most studies (n=7) were conducted in the United States (Cook, 1998; Haight *et al.*, 1998; Hyer *et al.*, 2008; McCurren *et al.*, 1999; Reinhardt *et al.*, 2014; Sood *et al.*, 2003; Zerhusen *et al.*, 1991), while the rest were conducted in Taiwan (Chiang *et al.*, 2010; Tsai *et al.*, 2008; Wang, 2005), Canada (Cook, 1998; Konnert *et al.*, 2009), and Spain (Alonso-Fernandez *et al.*, 2015).

Interventions involving CBT included a pain management group in which reduction of depressive symptoms was a secondary outcome (n=38) (Cook, 1998), a multi-component intervention that involved several modalities (group, individual, and staff therapy – “GIST”; n=25) (Hyer *et al.*, 2008), a group intervention targeting residents at risk for depression (“Coping with Stress in Seniors”; n=64) (Konnert *et al.*, 2009), a group-based cognitive therapy intervention for residents with moderate to severe depression (n=60) (Zerhusen *et al.*, 1991), and an enhanced occupational therapy intervention for individuals that took place within a short-term rehabilitation unit of a nursing facility (“Geriatric Wellness Program”; n=19) (Sood *et al.*, 2003). Evidence of CBT effectiveness was mixed. For example, compared to a minimally structured support group, the pain management group did not reduce depressive symptoms among nursing home residents with chronic pain (Cook, 1998). Likewise, those assigned to Geriatric Wellness did not experience a significant reduction in depressive symptoms when compared to standard occupational therapy treatment, after controlling for education. However, fewer participants in the experimental group had depression (two of six) compared to those within the control group (six of eight) post-treatment in this very small study (Sood *et al.*, 2003). The remaining three studies, which included tests of GIST (Hyer *et al.*, 2008), Coping with Stress in Seniors (Konnert *et al.*, 2009), and group-based cognitive therapy (Zerhusen *et al.*, 1991) demonstrated significant effects at posttest when compared to care as usual (CAU). GIST involved two individualized sessions related to goal setting and barrier reduction, a staff or peer coach, and 13 weekly group sessions of 75 to 90 minutes each involving behavioral activation as a key component. Coping with Stress in Seniors met twice a week for 60 minutes over seven weeks and covered topics that included a mood diary, coping with stress, and scheduling pleasant events. The group-based cognitive therapy relied on training nursing home staff to deliver the 10 week intervention and involved techniques such as using a dysfunctional thought record (Zerhusen *et al.*, 1991).

Studies involving reminiscence therapy were conducted in both group (Chiang *et al.*, 2010; Cook, 1991) and individual modalities (Haight *et al.*, 1998; Wang, 2005) with sample sizes ranging from 54 to 256 (Cook, 1991; Haight *et al.*, 1998). Interventions in this subgroup involved: 1) a series of group sessions organized by topics (e.g., identifying positive relationships, recalling family history and life stories) (Chiang *et al.*, 2010); 2) weekly group sessions designed to focus on each decade of life (Cook, 1991); 3) a structured life review

occurring during one to one visits (Haight *et al.*, 1998); and 4) one to one unstructured reminiscence (Wang, 2005). Three out of four of these studies demonstrated treatment effects favoring the reminiscence conditions when compared to either CAU (Wang, 2005) or to another control condition (i.e., wait list (Chiang *et al.*, 2010), friendly visiting (Haight *et al.*, 1998)).

There were four other RCTs included in this category, which included interventions based on: 1) Acceptance and Commitment Therapy enhanced with selective optimization with compensation training, delivered to residents with chronic pain (n=101) (Alonso-Fernandez *et al.*, 2015); 2) problem-solving treatment delivered to a sample of primarily short-stay residents (n=37) (Reinhardt *et al.*, 2014); 3) a novel intervention described as “self-worth therapy,” delivered on an individual basis (n=111) (Tsai *et al.*, 2008); and 4) use of older adult volunteers as trained para-professional mental health providers engaging in twice weekly visits (n=85) (McCurren *et al.*, 1999). Most of these studies did not achieve statistically significant effects between intervention arms immediately following treatment. The exception was the use of trained older adult volunteers as paraprofessional mental health providers that, when compared to CAU, demonstrated improvement in depressive symptoms at 24 weeks (McCurren *et al.*, 1999). Likewise, while self-worth therapy did not demonstrate a significant effect in reducing depression at post-test, those who had received this intervention had fewer depressive symptoms at a two month follow-up (Tsai *et al.*, 2008).

Psychosocial and Recreational Interventions

Nine RCTs were grouped in this broad category, which included studies from Taiwan (n=3) (Tsai and Tsai, 2011; Chen *et al.*, 2015; Huang *et al.*, 2016), the USA (Rosen *et al.*, 1997; Jessen *et al.*, 1996), the Czech Republic (n=1) (Vankova *et al.*, 2014), South Africa (n=1) (le Roux and Kemp, 2009), Thailand (n=1) (Elsegood and Wongpakaran, 2012), and Turkey (n=1) (Cakar *et al.*, 2010). The following types of interventions were tested: exercise programs (n=78–127 participants) (Cakar *et al.*, 2010; Chen *et al.*, 2015; Huang *et al.*, 2016), guided imagery sessions provided in a group setting (n=31) (Elsegood and Wongpakaran, 2012), individually provided avian therapy (n=40) (Jessen *et al.*, 1996), group visitations with a companion dog (n=16) (le Roux and Kemp, 2009), self-directed activity (n=22) (Rosen *et al.*, 1997), videoconferencing with family members (n=90) (Tsai and Tsai, 2011), and weekly dance sessions (n=162) (Vankova *et al.*, 2014). The evidence supporting the effect of these interventions was also mixed. For example, guided imagery (Elsegood and Wongpakaran, 2012) and self-directed activity (Rosen *et al.*, 1997) were not found to significantly reduce depression symptoms compared to control groups when evaluated with standardized measures of depression. However, a staff nurse was more likely to rate those taking part in the self-directed activity program as having positively responded to this intervention. Further highlighting the mixed results is that two Taiwanese exercise interventions showed a reduction in depression symptoms (Chen *et al.*, 2015; Huang *et al.*, 2016), while a Turkish exercise intervention did not (Cakar *et al.*, 2010). A short course of avian therapy, which involved 10 days of a caged bird placed in participants’ rooms, contributed to a decrease in depressive symptoms when compared to CAU (Jessen *et al.*, 1996), as did a year-long videoconferencing intervention when controlling for age and length of stay (Tsai and Tsai, 2011). Examining only within subjects effects, depressive

symptoms among those receiving visits from a companion dog decreased from pre- to post-intervention, but those assigned to CAU did not experience a significant decrease in symptoms (le Roux and Kemp, 2009). Lastly, a weekly dance intervention that included functionally impaired and wheelchair-bound residents reduced depression symptoms (Vankova *et al.*, 2014).

Pharmacologic and Other Biologic Interventions

Ten RCTs were included in this category, which spanned antidepressant (n=3) (Burrows *et al.*, 2002; Oslin *et al.*, 2003; Streim *et al.*, 2000), other pharmacological agents (n=2) (Lenze *et al.*, 2012; Yeh *et al.*, 2000), prescriber and staff education (n=1) (Avorn *et al.*, 1992), supplementation (n=3) (Badrasawi *et al.*, 2013; Rondanelli *et al.*, 2010; Rondanelli *et al.*, 2011), and bright light therapy (n=1) (Wu *et al.*, 2015) interventions. Six of these RCTs were based in the United States (Burrows *et al.*, 2002; Oslin *et al.*, 2003; Streim *et al.*, 2000; Lenze *et al.*, 2012; Yeh *et al.*, 2000; Avorn *et al.*, 1992).

An antidepressant RCT examining the effectiveness of paroxetine in treating non-major depression in older adults (n=24) (Burrows *et al.*, 2002) found that, compared to placebo, paroxetine was not more effective and may have been more likely to cause delirium and worsening mini-mental state examination (MMSE) scores (Burrows *et al.*, 2002). A trial comparing venlafaxine to sertraline among residents with a depressive disorder (n=52) examined tolerability and depression treatment efficacy (Oslin *et al.*, 2003). This trial found no evidence that venlafaxine had superior efficacy in treating depression than sertraline, and venlafaxine was more poorly tolerated with 12 of 27 venlafaxine participants not completing treatment due to either a side effect or serious adverse event (compared to 5 of 25 in the sertraline group) (Oslin *et al.*, 2003). A third antidepressant trial investigated nortriptyline in depressed residents (n=69) and showed a differential response to the antidepressant based on cognitive impairment status (Streim *et al.*, 2000). A “regular dose” of nortriptyline (60–80 mg/day) demonstrated a 42% mean improvement in depression in residents with a MMSE of 25 or higher compared to a 14% improvement in residents with a MMSE score less than 18. In the low-dose (10–13 mg/day) group, however, the mean improvement was 17% in the cognitively intact group and 42% in the cognitively impaired residents (Streim *et al.*, 2000). Another pharmacological trial evaluated whether an N-methyl-D-aspartate antagonist, memantine, was effective in reducing depression in those newly admitted to a nursing home for rehabilitation following a disabling medical condition (n=35) (Lenze *et al.*, 2012). While the effect sizes were not explicitly stated, the investigators reported no difference between memantine and placebo after 12 weeks. Another 12 week RCT was designed to examine megestrol acetate’s effect in improving weight gain in residents with weight loss or weighing less than 20% of their ideal body weight (n=64); there were no depression-specific inclusion criteria and residents with weight loss secondary to depression were excluded. Compared to placebo, megestrol acetate did not improve depression symptoms (Yeh *et al.*, 2000).

Our review identified a large trial (12 facilities, n=823) that employed a multidisciplinary geriatric psychopharmacology education intervention targeting the prescribing behaviors of nursing home physicians and included education sessions for nursing home staff and

physicians (Avorn *et al.*, 1992). While the intervention successfully reduced the use of antipsychotics, benzodiazepines, and hypnotics, residents in the experimental nursing homes who had received antipsychotics were at elevated risk of worsening depression compared to the non-intervention group. Depression was a secondary outcome, however, and only assessed in approximately one in three participants (Avorn *et al.*, 1992).

Three small (fewer than 50 participants each) nutrient supplementation trials were identified and occurred in either Malaysia (Badrasawi *et al.*, 2013) or Italy (Rondanelli *et al.*, 2010; Rondanelli *et al.*, 2011). These RCTs included essential amino acids (Rondanelli *et al.*, 2011), long chain omega 3 polyunsaturated fatty acids (Rondanelli *et al.*, 2010), and Talbinah (a carbohydrate-rich food reportedly used by Arabs to alleviate depression) (Badrasawi *et al.*, 2013) and, relative to the control group, they improved depression symptoms (Badrasawi *et al.*, 2013; Rondanelli *et al.*, 2010; Rondanelli *et al.*, 2011).

Lastly, a Taiwanese bright light therapy RCT (n=84) exposed residents to 30 minutes of light therapy administered in a group setting three times a week for four weeks and did not demonstrate a light therapy benefit; there were no depression-specific inclusion criteria (Wu *et al.*, 2015).

Discussion

To our knowledge, this is the first systematic review examining treatment of depression or depression symptoms in nursing facility residents with relatively intact cognition. Our systematic review uncovered a wide array of depression treatment approaches from which several conclusions can be drawn: 1) there is a paucity of high quality, large-scale RCTs from which to guide the management of depression in this population, 2) psychotherapeutic approaches have had mixed results with some CBT and reminiscence-based interventions decreasing depression symptoms, 3) a larger proportion of the psychosocial and recreation interventions (six of nine RCTs) decreased depression symptoms in nursing home residents, and 4) the evidence base guiding pharmacological management of depression within our population of interest is limited.

The psychotherapeutic interventions had considerable heterogeneity and included both manualized interventions as well as those that were less structured. Approximately half of these interventions had non-significant effects compared to control conditions. Likewise, only reminiscence (Chiang *et al.*, 2010; Haight *et al.*, 1998; Wang, 2005) and CBT (Hyer *et al.*, 2008; Konnert *et al.*, 2009; Zerhusen *et al.*, 1991) therapies demonstrated significant effects in more than one of the included studies in this category. The cumulative evidence for both of these treatments, however, is still limited given the small pool of studies and varying treatment approaches. This finding is congruent with a prior systematic review evaluating RCTs of psychotherapeutic interventions targeting depression in long-term care with a broader set of inclusion criteria than our review (e.g., other settings and participants with dementia were allowed) (Cody and Drysdale, 2012).

Compared to the other intervention categories, while many of the studies were of lesser methodological quality, psychosocial and recreational activities were more promising with

six of the nine interventions demonstrating favorable outcomes. In particular, exercise and interventions targeting social isolation (e.g., companion bird, videoconferencing with family members) reduced depression symptoms (these studies did not select residents based on depression status, however). Furthermore, a 2013 Cochrane Review found exercise interventions to be moderately effective for depression treatment and potentially comparable to psychological and pharmacological interventions (Cooney *et al.*, 2013).

The pharmacological interventions examined in this systematic review are too limited (e.g., small samples sizes, heterogeneous study populations, at times lacking a placebo control) to meaningfully guide clinical decision-making. However, there were some interesting findings that warrant further investigation. For example, venlafaxine had more significant adverse events requiring treatment discontinuation while being similarly efficacious as sertraline for treating depression; the authors suggested that there may be “a trend for decreased tolerability of venlafaxine with increasing age” (Oslin *et al.*, 2003). Also of interest is that the antidepressant effect of nortriptyline was greater at higher doses for residents with relatively intact cognition and was more effective at lower doses for residents with severe cognitive impairment (Streim *et al.*, 2000). This is suggestive that optimal depression management in cognitively intact depressed nursing home residents may differ from depressed residents with dementia (Streim *et al.*, 2000). While amino acid, omega 3 fatty acid, and Tablinah supplementation were associated with lower depression scores, there are some caveats with these findings. For example, the amino acid RCT was not specifically tested in residents with depression, thereby limiting its clinical utility (Rondanelli *et al.*, 2011); the omega 3 fatty acid RCT excluded participants with major depression or dysthymia who were on antidepressants (Rondanelli *et al.*, 2010); and the Tablinah supplementation RCT did not directly compare treatment arms, had higher depression scores in the Tablinah supplementation group, and excluded residents receiving antidepressants (Badrasawi *et al.*, 2013). Additionally, a recent systematic review and meta-analysis found little evidence indicating that omega 3 fatty acids are effective in treating depression, with much of the reported effect likely due to publication bias (Bloch and Hannestad, 2012). Lastly, paroxetine (Burrows *et al.*, 2002), memantine (Lenze *et al.*, 2012), and megestrol acetate (Yeh *et al.*, 2000) were not superior to placebo in treating depression.

Our systematic review has several limitations. First, our examination of CINAHL, PubMed, and PsycINFO only included publications written in English, which may have excluded some relevant RCTs. Second, the RCTs we included were highly heterogeneous in their inclusion and exclusion criteria as well as their primary outcome measures, which makes direct comparison between studies difficult and conducting a meta-analysis not feasible. Third, given our focus on RCTs, other study methods and approaches to improving depression in nursing facilities were not reviewed. For example, we did not evaluate studies on nursing home culture change, which in a prior review demonstrated mixed results with regards to reducing depression symptoms (Shier *et al.*, 2014). Fourth, to maintain the focus of our review on a population often excluded from clinical trials - older adults with a high level of medical comorbidity, disability, and frailty residing in nursing homes - we did not examine non-pharmacologic and pharmacologic interventions that treated late-life depression in other settings. There were many studies that did not meet our inclusion criteria and some promising interventions were likely excluded from our review. Fifth, although we

systematically reviewed the results from the CINAHL, PubMed, and PsycINFO search engines, we did not similarly systematically examine the reference lists of the articles we reviewed, which increases the possibility that we may have overlooked some relevant RCTs. Lastly, we did not contact experts in the treatment of depression in nursing home residents as part of our systematic review process and it is possible that there are pertinent treatment approaches and guidelines that are not discussed in our review.

Conclusions and Implications

Our systematic review ultimately shows that the evidence base for treating depression in nursing facility residents who are cognitively intact or with only mild impairment has significant limitations: 1) there was a notable lack of high quality, large-scale RCTs, 2) participant characteristics varied widely with many lacking depression-specific inclusion criteria, 3) many RCTs included did not account for concurrent antidepressant treatment, which limits their clinical utility, 4) studies inconsistently presented their findings, with some presenting only within group differences, and 5) the majority of studies relied on p values as the primary basis for hypothesis testing, a practice that has recently gained additional scrutiny (Wasserstein and Lazar, 2016). Nonetheless, this review provides some evidence that CBT, reminiscence, interventions to reduce social isolation, and exercise-based interventions have some promise for alleviating depression. Given that residents without dementia are more likely to transition back to the community and that depression may increase the risk of institutionalization, developing interventions for these residents has the potential to both reduce the considerable morbidity associated with depression and the costs of their care. In particular, newly admitted residents may comprise a high yield group for interventions as depression can interfere with physical recovery and may increase their risk of long-term institutionalization.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Preferred reporting items for systematic reviews and meta-analyses-based flow diagram

Table 1

Randomized controlled trials of depression treatment in nursing home residents

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
Psychotherapeutic Interventions							
(Alonso-Fernandez <i>et al.</i> , 2015)	To assess the effectiveness of a group psychological treatment program, i.e., acceptance and commitment therapy and selective optimization with compensation training (ACT-SOC), on a range of pain-related and psychological outcomes among residents with chronic pain.	Person	Spain; 5 facilities	101 participants diagnosed with chronic pain, without serious psychiatric or psychological disorders; no depression-specific inclusion criteria (53 in ACT-SOC and 48 in minimal support)	9 weeks of 2 hour weekly ACT-SOC group sessions versus a minimal support condition (2 hour educational group session without psychological training).	5	GDS (30 item) pre to post intervention mean scores (SD) for ACT-SOC vs. minimal support: ACT-SOC: 10.8 (6.4) vs. 8.9 (5.6) Minimal support: 12.0 (6.9) vs. 11.9 (7.2), $p = NS$
(Chiang <i>et al.</i> , 2010)	To assess the effectiveness of reminiscence group therapy on well-being, depression, and loneliness.	Person	Taiwan; 1 facility	130 participants; no depression-specific inclusion criteria (65 reminiscence and 65 wait list)	8 weeks of reminiscence therapy delivered once a week for 90 minutes in a group format versus a wait list control.	1	CES-D pre to post intervention mean scores for the reminiscence group vs. wait list: Reminiscence: 19.1(2.1) vs. 16.2(2.1) Wait list: 18.9(3.0) vs. 18.7(2.7), $p < 0.001$
(Cook, 1991)	To assess the effects of a reminiscence group on measures of ego integrity and despair.	Person	USA; 3 facilities	54 participants with length of stay > 1 month, without diagnosed mental illnesses; no depression-specific inclusion criteria (9 subjects in each of 6 groups; two treatment groups and four control groups that included two current events groups and two CAU)	16 weeks of 1 hour per week group reminiscence versus current events group or CAU.	2	GDS (30-item) post intervention mean scores in reminiscence vs. current events and CAU: Reminiscence: 11.6 Current events: 11.8 CAU: 12.1, $p = NS$
(Cook, 1998)	To assess the effectiveness of a CBT pain management group intervention on pain related symptoms and depression among residents with chronic pain.	Person	Canada; 2 facilities	28 participants experiencing chronic pain for > 3 months; no depression-specific inclusion criteria (14 in CBT and 14 in attention/support control group)	10 weekly CBT group sessions of 60 to 75 minutes versus attention/support condition (minimally structured, support group)	1	GDS (30 item) pre to post intervention mean scores (SD) in CBT group vs. attention/support: CBT: 8.7 (3.9) vs. 8.1 (4.8) Attention/support: 12.2 (5.1) vs. 11.6 (6.3)

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Haight <i>et al.</i> , 1998)	To assess the effects of a life review intervention on prevention of despair among people newly relocated to nursing homes.	Person	USA; 12 facilities	256 participants without clinical depression newly admitted to nursing homes (2 experimental groups and 2 control groups of roughly 64 participants each)	6 weeks of life review (form of reminiscence therapy) individually delivered during 1 hour weekly visits versus friendly visits.	3	p = NS when adjusting for pre-test GDS score BDI pre to post intervention group scores in life review group vs. friendly visits: Life review group: 2.0 (4.2) Friendly visiting: 0.4 (5.5) p=0.05.
(Hyer <i>et al.</i> , 2008)	To assess the effectiveness of a CBT intervention, GIST (Group, Individual, and Staff Therapy), on depression symptoms.	Person	USA; 1 facility	Trial 1: 25 participants diagnosed with depression (13 in GIST and 12 in CAU).	Multi-component intervention involving 1 to 2 individual sessions, staff/ peer coaching, and 13 weeks of 75 to 90 minute group sessions versus CAU.	4	GDS (15 item) pre to post intervention mean changes (SD) in GIST vs. CAU: GIST: 10.4 (3.8) vs. 5.0 (3.5) CAU: 9.0 (1.7) vs. 10.5 (1.6) p<0.001.
(Konnert <i>et al.</i> , 2009)	To assess the effectiveness of preventative CBT on reduction in depression.	Person	Canada; 7 facilities	64 participants at risk for depression who did not meet criteria for major depression (35 in CBT groups of four to six members and 29 in CAU)	7 weeks of 13 group sessions of CBT delivered twice weekly for 60 minutes versus CAU.	1	GDS (30 item) pre to post intervention mean scores (SD) in CBT vs. CAU: CBT: 14.0 (3.3) vs. 10.1 (3.0) CAU: 13.4 (3.2) vs. 12.5 (2.6) p<0.01 Group by time interaction with GDS across six months p<0.05
(McCurren <i>et al.</i> , 1999)	To assess the effectiveness of paraprofessional mental health support provided by trained older adult volunteers.	Person	USA; 3 facilities	85 participants: no depression-specific inclusion criteria (44 in mental health support and 41 in CAU).	24 weeks of an individualized plan of care involving paraprofessional mental health support visits delivered twice weekly and a once weekly visit by a geropsychiatric nurse versus CAU.	1	GDS (30 item) mean score changes indicated greater improvement within treatment group vs. CAU at a mid-point of 12 weeks (-5.0 vs. -0.2, p<0.05) and at 24 weeks (-6.9 vs. 0.2, p<0.05).
(Reinhardt <i>et al.</i> , 2014)	To assess the effectiveness of problem solving treatment (PST) to address depressive symptoms and subthreshold depression.	Person	USA; 1 facility	37 participants with significant depressive symptoms (21 in PST and 16 in social contact)	6 one hour weekly sessions of individually provided PST versus 6 friendly visits. Short-stay residents (n = 32) were given an option for twice a week sessions and completing sessions from home.	2	HAM-D and PROMIS depression scale net mean differences (adjusted) for PST vs. friendly visits from baseline to 4 months after baseline: PST: 6.5 (HAM-D) and 6.8 (PROMIS depression scale)

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Sood <i>et al.</i> , 2003)	To assess the effects of a behavioral intervention (i.e., Geriatric Wellness Program-GWP) on depressive symptoms among residents of a nursing home rehabilitation unit.	Person	USA; 1 facility	19 participants meeting criteria for depression were randomized but only 14 completed the study (6 in GWP and 8 in standard occupational therapy).	Individually provided enhanced occupational therapy, which draws on pleasant events and CBT, delivered, on average, over 7.5 weeks, 4 days per week in 50 – 80 minute sessions versus standard occupational therapy (CAU).	1	Friendly visits: 3.6 (HAM-D) and 1.5 (PROMIS depression scale) vs. NS GDS (30 item) mean scores (SD) at baseline and discharge in the CBT group vs. standard occupational therapy: 18.0 (6.3) vs. 9.3 (5.9) CAU: 19.3 (5.0) vs. 13.4 (7.4) p = NS when controlling for education
(Tsai <i>et al.</i> , 2008)	To assess the effects of self-worth therapy on depressive symptoms.	Person	Taiwan; 1 facility	111 participants meeting criteria for depression (56 in self-worth therapy and 55 in friendly visiting control group)	4 weeks of weekly half hour sessions of individual self-worth therapy, administered by a mental health nurse versus friendly visiting.	5	GDS (30 item) pre to post intervention scores (SD) in self-worth therapy group vs. friendly visiting: Self-worth: 16.1 (3.0) vs. 12.8 (2.9) Friendly visit: 14.3 (3.4) vs. 11.3 (4.8). p = NS when controlling for baseline GDS.
(Wang, 2005)	To assess the effect of reminiscence on depressive symptoms and mood.	Person	Taiwan; 5 facilities	55 participants were randomized; no depression-specific inclusion criteria (baseline group sizes not presented). 48 completed the study (25 in reminiscence and 23 in CAU).	4 months of weekly 30 to 45 minute sessions of one to one unstructured reminiscence versus CAU.	1	GDS (15 item) pre to post intervention mean scores (SD) in the reminiscence and CAU groups: Reminiscence: 8.3 (4.8) vs. 6.2 (4.1) CAU: 9.2 (4.0) vs 8.8 (4.5) p<0.05
(Zerhusen <i>et al.</i> , 1991)	To assess the effects of cognitive therapy on depressive symptoms.	Person	USA; 1 facility	60 participants with elevated depressive symptoms were randomized (20 in cognitive therapy, 20 in music therapy, and 20 in CAU)	10 weeks of cognitive therapy group sessions, music therapy group sessions, or CAU	2	BDI net mean differences in cognitive therapy, music therapy, and CAU groups: Cognitive Therapy: 12.4 Music Therapy: 1.5 CAU: -2.6 p<0.001
Psychosocial and Recreation Interventions							
(Cakar <i>et al.</i> , 2010)	To assess whether an exercise program, with and without a jumping component, improves balance, fall risk, quality of life, and depression.	Person	Turkey; 1 facility	78 participants: no depression-specific inclusion criteria (38 in intervention group without jumping and 40 in intervention group with jumping)	6 weeks of an exercise program occurring 3 times weekly for less than 45 minutes each time.	3	GDS (30 item) mean pre- and post-intervention scores (SD): Exercise without jumping: 8.7 (7.1) vs. 9.3 (7.6) Exercise with jumping: 6.8 (5.6) vs. 6.4 (5.5)

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Chen <i>et al.</i> , 2015)	To assess the effectiveness of elastic band exercises on sleep quality and depression on wheelchair bound older adults.	Facility	Taiwan; 10 facilities	127 participants; no depression-specific inclusion criteria (64 in intervention and 63 in control group)	40 minute elastic band exercise 3 times per week for 6 months versus regular daily activities.	3	p=0.14 Taiwanese Depression Questionnaire (18 item) adjusted mean intervention vs. control group scores at 6 months: 5.5 vs. 11.4, p<0.001
(Elsegood and Wongpakaran, 2012)	To assess the effects of guided imagery on affect, cognition, and pain among Thai older adults living in a nursing home.	Person	Thailand; 1 facility	31 participants; no depression-specific inclusion criteria (16 in guided imagery and 15 in CAU)	16 days of once or twice daily guided imagery group sessions with residents attending as desired versus CAU.	1	GDS (30 item; Thai version) mean change scores (SD) in guided imagery and CAU: Guided imagery: -0.1 (3.3) CAU: 1.1 (2.8) p = NS
(Huang <i>et al.</i> , 2016)	To assess the effectiveness of cognitive-behavioral strategies, with and without exercise, in reducing the fear of falling.	Person	Taiwan; 6 facilities	80 participants; no depression-specific inclusion criteria (27 in cognitive-behavioral and exercise group, 27 in cognitive-behavioral group, and 26 in comparison group)	The cognitive-behavioral intervention consisted of 8 weekly group sessions lasting 20-25 minutes. The exercise intervention consisted of twice weekly 30 minute exercise sessions for 8 weeks. The comparison group received CAU.	5	Taiwanese Depression Questionnaire (18 item) pre and post intervention mean scores (SD): Cognitive behavioral and exercise: 17.6 (8.2) to 3.6 (4.0) Cognitive behavioral: 19.6 (12.8) to 17.2 (11.2) Control: 17.3 (12.0) to 16.5 (10.8) p<0.001
(Jessen <i>et al.</i> , 1996)	To assess the effects of a companion bird on depression, morale, and loneliness.	Person	USA; 2 facilities	40 participants; no depression-specific inclusion criteria (20 in avian therapy and 20 in CAU)	10 days of a caged bird placed in rooms of those in the avian therapy group versus CAU.	2	GDS (30 item) pre to post intervention mean scores (SD) for avian therapy and CAU: Avian: 8.9 (4.9) vs. 5.9 (4.4) CAU: 8.8 (6.5) vs. 8.6 (5.8) p=0.01
(le Roux and Kemp, 2009)	To assess the effect of a companion dog on depression and anxiety.	Person	South Africa; 1 facility	16 participants; no depression-specific inclusion criteria (8 in animal therapy and 8 in CAU)	6 weeks of weekly half hour group visitations with a dog versus CAU.	2	BDI pre to post intervention mean (SD) scores for within animal therapy and CAU: Animal therapy: 19.9 (8.9) vs. 11.9 (8.8) CAU: 13.9 (8.0) vs. 15.9 (10.2). Depression outcomes were not tested across treatment arms.
(Rosen <i>et al.</i> , 1997)	To assess the effects of a self-directed activity program on depression.	Person	USA; 1 facility	31 participants with minor or major depressive episode, with mild or moderate	8 weeks of self-directed, recreation therapy (i.e., program of planned activities) with typically 1	3	HAM-D pre and post intervention mean scores not reported for those randomized (p = NS)

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Tsai and Tsai, 2011)	To assess the effectiveness of a videoconference intervention on nursing home residents' social support, loneliness, and depressive status.	Facility	Taiwan; 16 facilities	90 participants; no depression-specific inclusion criteria (40 in the videoconferencing intervention program and 50 in CAU)	A 1 year videoconferencing program comprised of 3 months of no less than once weekly videoconferencing with family members, assisted by research assistants, followed by 9 months of nursing home staff assisted videoconferencing provided at residents' request, versus CAU.	2	4 of 11 of those who were randomized to the self-directed activity group were categorically rated by a staff nurse as having responded to the intervention versus none of the controls (p=0.045). GDS (30 item) mean scores (SD) at baseline, 3, 6, and 12 months in videoconferencing vs. CAU: Videoconferencing: 12.8 (5.5), 11.6 (5.3), 12.9 (5.4), 13.0 (4.5) CAU: 10.5 (4.1), 10.6 (3.9), 14.4 (4.9), 15.0 (4.6), p<0.001 at 3, 6, and 12 months after accounting for age and length of stay. With greater improvement noted among those in videoconferencing.
(Vankova <i>et al.</i> , 2014)	To assess the effect of a weekly dance intervention on depression.	Person	Czech Republic; 7 facilities	162 participants; no depression-specific inclusion criteria (79 in intervention group and 83 in control group)	Weekly 60 minute dance session over 3 months versus CAU.	4	GDS (15 item) pre- and post-intervention mean scores (SD): Intervention: 5.7 (3.8) vs. 5.0 (3.3) Control: 4.9 (3.2) vs. 5.3 (3.3) p=0.001
Pharmacologic and Other Biologic Interventions							
(Avorn <i>et al.</i> , 1992)	To assess the effectiveness of a psychopharmacology educational program in reducing the use of psychoactive medications.	Facility	USA; 12 facilities (6 experimental and 6 control)	823 residents; no depression-specific inclusion criteria (431 in experimental facilities and 392 in control facilities)	5 month multidisciplinary geriatric psychopharmacology education program.	3	Risk of depression (based on HSCL) worsening in the experimental vs. control group facilities, rate ratio (95% CI): Residents who received antipsychotics: 2.0 (1.1–3.9) Residents who received benzodiazepines or hypnotics: 1.1 (0.5–2.3)
(Badrasawi <i>et al.</i> , 2013)	To assess the effect of Talbinah dietary supplementation on depression, anxiety, and mood.	Person	Malaysia; 1 facility	36 participants with depression symptoms participated in a cross-over randomized clinical trial (2 groups of 18)	7 weeks total (3 weeks of either Talbinah supplementation or diet as usual followed by 1 week washout period and another 3 week course of treatment or control).	3	Mean scores (SD) pre- and post-intervention, Talbinah vs. control. GDS-R: 6.6 (3.1), 3.7 (2.7) vs. 4.4 (2.5), 4.8 (2.6)

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Burrows <i>et al.</i> , 2002)	To assess the effectiveness of paroxetine compared to placebo for treating residents with non-major depression.	Person	USA; 1 facility	24 participants with non-major depression (12 in intervention group and 12 in control group)	8 weeks of either paroxetine or placebo following 1 week placebo run-in.	4	DASS-Depression: 17.1 (10.5), 7.9 (7.2) vs. 11.1 (5.9), 8.6 (7.4) Depression outcomes not tested across treatment arms. Mean scores pre- and post-intervention paroxetine vs. placebo. HAM-D (nurse administered): 13.8, 8.9 vs. 15.4, 10.2 HAM-D (subject administered): 11.2, 8.1 vs. 14.5, 10.7 CS (nurse administered): 12.2, 7.8 vs. 12.9, 10.1 CS (subject administered): 10.9, 7.3 vs. 13.1, 9.7 GDS (15 item): 8.3, 6.9 vs. 8.3, 7.6 There were no significant differences between paroxetine and placebo.
(Lenze <i>et al.</i> , 2012)	To assess the effectiveness of memantine in reducing depression and anotation in older adults after a disabling medical event.	Person	USA; 2 facilities	35 participants with depression and/or apathy symptoms (17 in intervention group and 18 in placebo group)	12 weeks of either memantine or placebo.	3	HAM-D scores graphed but not explicitly stated in article. No significant difference between intervention and control group.
(Oslin <i>et al.</i> , 2003)	To assess the efficacy and tolerability of sertraline and venlafaxine for depression treatment.	Person	USA; 13 facilities	52 participants with a depressive disorder (25 in sertraline group and 27 in venlafaxine group)	1 week of placebo followed by 10 weeks of sertraline or venlafaxine.	3	Baseline and follow-up mean scores (SD), sertraline vs. venlafaxine: HAM-D: 20.2 (3.4), 12.2 (5.1) vs. 20.3 (3.7), 15.7 (6.2), $p=0.069$ GDS (30 item): 16.9 (6.2), 13.4 (7.6) vs 17.1 (5.8), 16.3 (7.4), $p=0.151$ CS: 20.9 (4.4), 12.4 (6.3) vs. 20.2 (4.1), 16.2 (6.8), $p=0.008$
(Rondanelli <i>et al.</i> , 2011)	To assess the effect of amino acid supplementation on depression, nutrition, muscle function, daily physical activity, and	Person	Italy; 1 facility	41 participants; no depression-specific inclusion criteria (20 in intervention group and 21 in placebo group)	8 weeks of either essential amino acid supplementation or placebo.	5	GDS (30 item) scores graphed. Compared to the placebo group, the intervention group had a reduction in baseline to post-intervention depression scores, $p<0.001$

Citation (by first author name)	Purpose of Study	Unit of Randomization	Setting	Subjects at Baseline Following Randomization	Intervention	Quality Rating	Depression Differences across Treatment Arms
(Rondanelli <i>et al.</i> , 2010)	health-related quality of life. To assess whether omega 3 fatty acid supplementation improves depression and health-related quality of life in depressed residents.	Person	Italy; 1 facility	46 participants with major depression or dysthymia (22 in intervention group and 24 in placebo group)	8 weeks of either fatty acid supplementation or placebo.	5	GDS (30 item) post-intervention mean scores in intervention group minus placebo group (95% CI): -3.2 (-6.2, -0.3), $p=0.032$
(Streim <i>et al.</i> , 2000)	To assess the effect of low and regular dose nortriptyline on depression in residents	Person	USA; 8 facilities	69 participants with elevated depression symptoms (47 in regular dose group and 22 in low dose group)	1 week of placebo followed by 10 weeks of either regular or low dose nortriptyline.	4	HAM-D mean % improvement (MMSE<18, MMSE 18-24, MMSE 25-30). Regular dose: 14%, 30%, and 42% Low dose: 42%, 18%, and 17% Greater improvements noted among those patients who were cognitively intact and on the higher dose of nortriptyline, $p=0.008$.
(Wu <i>et al.</i> , 2015)	To assess the effect of light therapy on depression and sleep disruption.	Facility units	Taiwan; 1 facility, 4 units	84 participants; no depression-specific inclusion criteria (42 in intervention group and 42 in control group)	Light therapy in a group setting for 30 minutes, 3 times a week, for 4 weeks.	1	GDS (15 item) baseline to post-intervention mean score change (SD) by intervention vs. control groups: -1.3 (3.5) vs. -0.2 (3.2), $p=0.19$
(Yeh <i>et al.</i> , 2000)	To assess the effect of megesterol acetate on weight.	Person	USA; 1 facility	64 participants; no depression-specific inclusion criteria (33 in intervention group and 31 in placebo group)	12 weeks of either megesterol acetate or placebo with 13 additional weeks of follow-up.	5	GDS (15 item) baseline to 12 weeks mean score change (SE) by intervention vs placebo groups: -1.2 (0.6) vs. 0.2 (0.9), $p=NS$

Note: CAU, Care-As-Usual; CI, Confidence Interval; BDI, Beck Depression Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; CS, Cornell Scale for Depression; *Notes:* DASS-D, Depression, Anxiety, and Stress Scale-Depression; GDS, Geriatric Depression Scale; GDS-R, Geriatric Depression Scale Residential; HAM-D, Hamilton Depression Rating Scale; HSCL, Hopkins Symptom Checklist; MMSE, Mini-Mental State Exam; NH, Nursing Home; NS, Not Significant; PROMIS, Patient Reported Outcomes Measurement Information System; RCT, Randomized Controlled Trial.