Systematic overview of non-pharmacological interventions to treat behavioral disturbances in older patients with dementia. The SENATOR-OnTop series

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Systematic overview of non-pharmacological interventions to treat behavioral disturbances in older patients with dementia. The SENATOR-OnTop series

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Abstract

**Objective** The provide an overview of non-pharmacological interventions for behavioral and psychological symptoms in dementia (BPSD).

**Design** Systematic overview of reviews


**Eligibility criteria** Systematic reviews (SRs) that included at least one comparative study evaluating any non-pharmacological intervention, to treat BPSD.

**Data extraction** Eligible studies were selected and data extracted independently by 2 reviewers. The AMSTAR checklist was used to assess the quality of the SRs.

**Data analysis** Extracted data were synthesised using a narrative approach.

**Results** Forty-one systematic reviews and 142 primary studies were identified, comprising the following categories of non-pharmacological interventions: (a) Sensory Stimulation Interventions (12SR, 27 primary studies) that encompassed: acupressure, aromatherapy, massage/touch therapy, light therapy, sensory garden; (b) Cognitive/Emotion-oriented Interventions (33 SRs; 70 primary studies) that included cognitive stimulation, music/dance therapy, dance therapy, snoezelen, transcutaneous electrical nerve stimulation, cognitive stimulation, reminiscence therapy, validation therapy, simulated presence therapy; (c) Behavior Management Techniques (6 SRs; 32 primary studies); and (d) other therapies (5 SR, 12 primary studies) comprising exercise therapy, animal-assisted therapy, Special Care Unit and Dining Room Environment based interventions.

Music therapy was effective in reducing agitation (SMD, -0.49; 95% confidence interval (CI), -0.82 to -0.17; p=0.003), and anxiety [SMD, -0.64; 95% CI, -1.05 to -0.24; P=0.002]. Home based behavioral management techniques, caregiver-based interventions or staff training in
communication skills, person-centered care or dementia care mapping with supervision during implementation were found to be effective for symptomatic and severe agitation.

Conclusions

A large number of non-pharmacological interventions for BPSD were identified. The majority of the studies had great variation in how the same type of intervention was defined and applied, follow-up duration, type of outcome measured, usually with modest sample size. Overall, music therapy and behavioural management techniques were effective for reducing BPSD.

Strengths and limitations of this study

- Non-pharmacological interventions have gained increasing attention in recent years as an alternative first-line approach to treat Behavioural and Psychological Symptoms in Dementia (BPSD).

- The strength of this review is its extensive, comprehensive systematic search of studies that investigated non-pharmacological interventions for BPSD. It provides a compendium of the types of non-pharmacological interventions, including the component of each single intervention, the dosage (when available), and the duration of the treatment.

- Primary studies were generally of limited sample size; there was substantial variation in the characteristics of the intervention and the authors of primary studies reported different conceptual frameworks, and sometimes broad and quite generic descriptions, of the interventions.
Introduction

Dementia is a neuropsychiatric syndrome characterized by cognitive decline and progressive deterioration of daily function, often associated with behavioral disturbances.

The prevalence of dementia in older subjects is reported to be approximately 6% worldwide [1] and, with global population ageing, it is expected to rise although some recent studies have suggested declining trends in dementia frequency[2]. Dementia presents a considerable burden to families and caregivers and is becoming a major challenge for all healthcare systems as well as for society at large[3 4]. Alzheimer’s disease (AD) is the most common form of dementia in older people, accounting for 60 percent of cases.

Approximately 5 in every 6 patients with dementia, including those living at home, will develop behavioral and psychological symptoms during the course of the disease [5-8]. Behavioral and psychological symptoms of dementia (BPSD) are defined as signs and symptoms of disturbed behavior, mood, thought, or perception [9]. These disturbances, namely agitation, depression, elation, delusions and hallucinations are strongly correlated with each other[10 11]. Twenty percent of those initially without symptoms will manifest them within 2 years of dementia diagnosis [12], whereas 50 to 80% of those with clinically important symptoms remain agitated for several months [13]. In addition, at least 50% of patients with dementia present with significant BPSD on a monthly basis [14]. Agitation, together with depression, hinder activities and relationships, cause feelings of helplessness and distress in families and formal caregivers [15] and are strong predictors for poor quality of life [16] as well as nursing home admission [17].

Currently, options for treating BPSD include both pharmacological and non-pharmacological therapies[18 19]. Psychotropic medications are often used to reduce the frequency and severity of BPSD, but in the majority of patients, they provide only modest symptom control [20-22]. A recent trial reported that the addition of citalopram to psychosocial support significantly reduced agitation and caregiver distress[23]. However, their adverse effects are common and problematic, in
particular the increased risk of falls and fractures [24] stroke and even mortality [25]. In addition, there is some evidence that the use of benzodiazepines to treat agitation in patients with dementia may increase cognitive decline [24] and may expose patients to an immediate risk of injurious falls [26]. Finally, memantine and cholinesterase inhibitors are considered to be of very limited value for improving agitation in subjects with AD [27 28].

In general, non-pharmacological interventions are considered as preferable alternative to psychotropic pharmacotherapy for treating BPSD [29]. However, there is conflicting evidence concerning the efficacy and practicality of non-pharmacological interventions for improving BPSD, particularly agitation [9 30].

The purpose of the present overview is to assess the evidence supporting these non-pharmacological interventions with a view to providing a working compendium for the non-drug management of BPSD.

The present overview updates the evidence on the same theme gathered by a previous systematic overview published in 2011 [31].
**Methods**

This work is part of the ONTOP (Optimal Evidence-Based Non-drug Therapies in Older People) project, a workpackage of a European Union funded FP 7 research named SENATOR (Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older peRsons). The ONTOP aim is to undertake a literature search of systematic reviews and provide clinical recommendation concerning evidence-based non pharmacological treatments of several prevalent medical conditions affecting older people, including delirium[32 33], pressure ulcers [34-36], falls[37], stroke and heart failure. A protocol that describes the process of search strategy, screening, inclusion criteria has been previously published[38].

**Search Strategy and Inclusion Criteria for Systematic Reviews**

The search sources included the Cochrane Database of Systematic Reviews, PubMed, PsychINFO, and CINAHL (from 2009 to March 2015; Appendix 1). Two criteria were considered for further evaluation of an abstract: a) a paper defined as a review or meta-analysis, b) the use of any non-pharmacological intervention to treat behavioral disturbances in patients with dementia. The publication year ranged from 2009 to 2015.

Subsequently, full-texts of relevant abstracts were obtained and screened to identify systematic reviews (SR) of interest based on: a) the use of at least one medical literature database; b) the inclusion of at least one primary study; and c) the use of at least one non-pharmacological intervention to treat behavioral disturbances in people aged 60+ years.

We assessed the methodological quality of each SR using the AMSTAR (A Measurement Tool to Assess Reviews) instrument that contains 11-items [39]. Final grading of the methodological quality of each SR was based on the overall score and reported as either "high" (score ≥ 8), "medium" (score 4-7) or "low" (score ≤ 3). Two reviewers independently assessed the quality of the SRs and disagreements were resolved by consensus.
Data extraction and management

From each study the following data were collected: the publication year, the databases searched, the study population, the non-pharmacological interventions, the number of primary studies included, the outcome measures and the AMSTAR score. Pairs of reviewers independently screened titles, abstracts and full-texts of articles. Disagreements were resolved by discussion or, where necessary, by consulting another author.

Outcome measures

We focused on reviews that considered BPSD, as a primary outcome, measured by (a) multi-domain scales (e.g. Neuropsychiatric Inventory (NPI), Brief Psychiatric Rating Scale (BPRS)), (b) scales specific to agitation (e.g. Cohen-Mansfield Agitation Inventory (CMAI)), (c) scales specific to depression or anxiety (e.g. Cornell Scale for Depression in Dementia (CSDD)).
Results

Our search strategy identified 4,392 abstracts of which 2,549 were duplicates and were subsequently removed. After abstract screening, 67 records were identified for full-text assessment. Of these, 41 reviews were included in this overview. Figure 1 shows the study screening process.

The interventions in this overview were classified according to the following categories: (a) Sensory Stimulation Interventions that encompass acupuncture, aromatherapy, massage therapy, light therapy, sensory garden intervention, cognitive stimulation, music/singing and dance therapy, snoezelen and transcutaneous electrical nerve stimulation (TENS) therapy; (b) Cognitive/Emotion-oriented Interventions that include reminiscence therapy, validation therapy, simulated presence therapy; and (c) Behavioral management technique and (d) Other interventions, such as exercise therapy, pet-therapy or special care unit. Overall 142 primary studies were identified. Tables are reported in Appendix 2

Sensory Stimulation Interventions

Shiatsu and acupressure

Only one SR was identified. Robinson 2011[40] (AMSTAR=7) investigated the evidence available for shiatsu and acupressure in BPSD. Shiatsu is a form of complementary medicine primarily developed in Japan, which employs gentle manipulations, stretches and pressure with the fingers, elbows, knees and feet. Acupressure is similar, but exerts pressure for longer on specific meridian points according to traditional Chinese medicine. Acupressure is a non-pharmacological technique similar in principle to acupuncture and consists of promoting individual well-being with the use of constant pressure to stimulate meridians or acupoints of the human body in order to “balance energy fields”.

The authors identified 40 RCTs, 8 controlled clinical trials, 5 crossover trials, 6 within-subjects studies, 1 observational study, 10 uncontrolled studies and one prospective study. Only one randomized trial (n=133 participants) using acupressure in dementia subjects resulted relevant for
our assessment [41]. The authors reported that agitation, aggression and physically non-aggressive behavior all declined significantly in demented subjects.

**Aromatherapy**

Aromatherapy is proposed as a complementary intervention, to treat a wide range of health problems, including lack of sleep and behavioral symptoms for people with dementia [42].

Aromatherapy is based on the use of plant products or aromatic plant oils to produce essential oils and blends of aromatic compounds. Aromatherapy can be delivered through massage or topical application, inhalation and water immersion to obtain the desired outcome.

Our systematic search identified 3 SRs that considered aromatherapy as an intervention to treat agitated behaviors and other outcomes in patients with dementia. The AMSTAR scores ranged from 6 to 8 across the reviews. The range of included primary studies varied from 4 to 13 [29 43 44].

The most recent SR was a Cochrane review [44], which had the highest AMSTAR quality score (8). The review included only randomized trials and launched its last search strategy in January 2013. Seven studies with 428 participants were identified. The types of interventions included lavender-based (4 studies [45-48]), Melissa-based (two studies [49 50]) and lemon balm oil (1 study) aromatherapy. However, only two of these had usable data for pooling. The first study (n=71) reported a favorable treatment effect on measures of agitation (MD -1.1, 95% CI -1.9 to -2.2) and behavioral symptoms (MD -15.8, 95% CI -24.4 to -7.2), whereas the second trial (n=63) did not detect any difference in agitation (MD 0.00, 95% CI -1.36 to 1.36) or behavioral symptoms (n = 63, MD 2.80, 95% CI -5.84 to 11.44). The review authors remarked that the published studies used different scales to assess the behavioral symptoms and were limited both in sample size and methodological quality, particularly because of selective reporting bias.

The second review by Seitz [29] consisted of any non-pharmacological interventions, including aromatherapy, to treat outcomes relevant to patients with dementia. The review reported data in a
narrative way and cited only one study of aromatherapy [49], which was also included in the Cochrane review above [44]. The review received an AMSTAR score of 6.

The third study was a review by Fung et al [43], which considered only aromatherapy as a non-pharmacological intervention. The review was judged to have moderate methodological quality (AMSTAR score=6). After performing a comprehensive search in several electronic databases, 11 studies were identified, with a total of 405 patients in different settings, including long-term care homes, clinical centers and general and old age psychiatry. In addition to the trials included in the above cited Cochrane review, the review by Fung et al. [43] included one randomized trial [51] which was excluded in the Cochrane review because the route of administration was not reported and there was no mention of the type of the aromatherapy, - and 5 controlled clinical trials [52-56]. Moreover, the Fung et al review [43] did not include the two trials [45 57] [47] that were evaluated in the Cochrane review. The controlled clinical trials could not be included in a meta-analysis because of heterogeneity. The review highlighted the methodological limitations of the studies and reported promising results of aromatherapy. Table 1 describes the type of interventions, the outcomes and the results of the primary studies included in the Aromatherapy reviews.

**Massage Therapy**

Massage and touch therapy have been proposed as non-pharmacological interventions to be used in dementia to offset manifestations of cognitive decline and behavioral disturbances, including related psychological problems such as depression and anxiety and to improve quality of life [58 59]. Two reviews were identified. The first was a Cochrane review that was included in the review by O’Neil [59]. This review assessed the efficacy of Massage and Touch therapy for the treatment of BPSD. Its last search strategy was launched in 2006. The aim of the overview was to evaluate the effects of a range of massage and touch therapies on conditions associated with dementia, such as anxiety, agitated behavior and depression, to identify any adverse effects, and to provide recommendations for future trials. The review considered only randomized trials. The primary
outcome measures were changes in the frequency and severity of various types of agitated behavior, as observed by staff or investigators (short term and long term using any rating method), and the emotional well-being and the quality of life of the patients (rated by staff, investigators and/or patients themselves using any method).

Remington (2002) [60] assessed the effect of music and massage in 68 nursing home residents with dementia (Alzheimer's disease, multi-infarct dementia or senile dementia). The subjects were randomly allocated into 4 groups: calming music, hand massage, simultaneous calming music and hand massage, and no intervention. The intervention lasted 10 minutes, and was given to each patient once.

Efficacy of treatment on 'agitation level' was evaluated with a modified version of the Cohen-Mansfield Agitation Inventory (CMAI) administered by trained research assistants who were blinded to treatment allocation when possible. The method of randomization was unclear and to conceal allocation, sealed envelopes, without further explanation, were used. However, patients could have been excluded after allocation (if they had a CMAI score of 0 at baseline) and consequently the study was considered to have high risk of selection bias.

The trial found that agitated behavior decreased, more so in the group receiving hand massage than in the group receiving no treatment. This treatment effect was consistently found, compared to baseline, for measurements taken during treatment, immediately after treatment, and one hour after treatment, and it was practically identical among the three groups receiving treatment (hand massage, calming music or both). The mean agitation score was in favor of massage therapy immediately after treatment [MD 7.83 (4.30 to 11.36)] and 1 hour after treatment [MD 12.12 (6.58, 17.66)].

The second review by Moyle et al. [61] conducted a search in 10 databases in October 2011. The authors identified 13 studies that evaluated massage therapy for the treatment of behavioral disturbances in patients with dementia, but only one study with a high methodological score, using the Validity Rating Tool, was identified. The included study, performed by Hollyday-Walsh [62],
was a prospective before-after study in which 52 participants (39 women and 13 men; mean age 90 years) from two skilled nursing facilities in Northeastern Minnesota, USA, were enrolled. Patients were cognitively impaired and had a history of agitated behavior confirmed by facility staff. The intervention consisted of a 10- to 15-minute massage of the upper extremities (including the head, shoulders and hands), undertaken by a physical therapy assistant, during a 1-hour period identified by caregivers as the time the participant was usually most agitated (individualized for each participant). The outcomes of interest were assessed with a scale that used the five Behavioral Symptoms from the minimum data set; a) wandering; b) verbally abusive behavioral symptoms; c) physically abusive behavioral symptoms; d) socially inappropriate/disruptive behavior; and e) resistance to care.

Methodologically, the study was considered at high risk of selection and performance bias given the study design and nature of the intervention. In addition, it was unclear whether the outcome assessor was blinded. Massage therapy was significantly associated with improvement for 4 of the 5 outcomes examined, including wandering (0.38 vs. 0.16, P<0.001), verbally agitated behavioral symptoms (0.59 vs. 0.49, P=0.002), physically agitated behavioral symptoms (0.82 vs. 0.40, P<0.001), and resistance to care (0.10 vs. 0.09, P=0.022). Table 2 describes the type of interventions, the outcomes and the results of the primary studies included in the Massage therapy reviews.

**Light therapy**

Rest-activity and sleep-wake cycles are controlled by the endogenous circadian rhythm generated by the suprachiasmatic nuclei of the hypothalamus. Degenerative changes in the SCN appear to be a biological cause of circadian rhythm disturbances in people with dementia. In addition to the internal regulatory loss, older people (especially those with dementia) experience a reduction in sensory input because they are visually less sensitive to light and have less exposure to bright environmental light. Evidence suggests that circadian rhythm disturbances may be reversed by stimulation of the suprachiasmatic nuclei with light [63].
Four reviews considered the use of bright light therapy to treat behavioral problems in patients with dementia.

The first was a Cochrane review [63] (AMSTAR=10) with the aim of evaluating the effectiveness of light therapy to improve cognition, ADLs, sleep, challenging behavior, and psychiatric disturbances associated with dementia. The search strategy was launched in January 2014. The included studies were randomized trials that compared any bright light therapy, including dim red light or dim, low-frequency blinking light less than 300 lux, to usual care. The primary outcome measures included cognition (global or single domain, e.g. memory), ADLs, sleep-wake disturbances, challenging behavior (e.g. agitation), psychiatric disturbances (e.g. depression), and adverse effects. Secondary outcomes were rates of institutionalization and overall cost of care. The authors identified eleven studies, but stated that three of the studies could not be included in the analyses either because the data were insufficient or could not be retrieved from the trial authors. Only four of the included studies considered challenging behavior as an outcome, but the sample sizes were limited and the outcome measures were not the same across the studies [64-67]. A meta-analysis of challenging behavior however was performed and no substantial heterogeneity was found, although the results were not statistically in favor of bright light therapy.

The second review aimed to identify which non-pharmacological interventions were most effective for BPSD in long term care [29]. Only two studies[64 65] were included in the review (which were already included in the Forbes review[63]) but were not assessed in detail. The review received 4 points in the AMSTAR rating system.

The third review [68] aimed to assess the role of physical environment in supporting person-centered dining in long-term care. Only one study that evaluated the effect of ambient bright light in activity and dining areas among institutionalized people with dementia was identified [69]. This study was not included in the previous two reviews.
The fourth review [70] that addressed the effectiveness of environment-based interventions for people with Alzheimer’s disease or dementia, identified a cluster-unit crossover trial [71]. The trial was conducted in two geriatric units in a state-operated psychiatric hospital and in a dementia-specific residential care facility in Oregon, USA and enrolled 66 older adults with dementia to evaluate the effectiveness of ambient bright light therapy delivered through a high-intensity, low-glare lighting system installed in the public areas of study units at both sites, at reducing depressive symptoms. Each lighting condition was provided for multiple 3-week periods in a predetermined sequence. The CSDD was used to assess depressive symptoms. Results did not support the use of ambient bright light therapy as a treatment for depressive symptoms in people with dementia[71]. Table 3 describes the type of interventions, the outcomes and the results of the primary studies included in the Light therapy reviews.
Sensory garden and horticultural activities

Whear 2014 [72](AMSTAR=7) investigated the impact of gardens and horticultural therapy on the mental and physical wellbeing of residents with dementia, in nursing homes and specialized dementia care facilities. This approach uses either “sensory” gardens to stimulate the 5 senses (sight, vision, hearing, smell and touch), or plants and plant-related activities to improve well-being (horticultural therapy or therapeutic horticulture). Eighteen studies were identified: ten were quantitative studies (two RCTs (n=34), six pre-post studies, one crossover study, one prospective cohort study), seven qualitative and one used mixed methods. In one of the RCTs[73] there was a non-statistically significant decline in verbal and physical aggression and non-verbal aggression, and total CMAI score (Table 4).

Gonzalez et al. [74](AMSTAR=3) examined the effects of sensory garden and horticultural activities in dementia care. Sixteen studies were identified, including 2 RCTs (n=149), one of which was cluster randomized, 11 pre-post studies, 2 case studies and one survey. In the smaller of the two RCTs[75], verbal agitation significantly decreased in the outdoor horticultural group compared to the indoor horticultural group, while in the larger trial, the effect of subjects in the horticultural group did not differ from the traditional activity group. (Connell et al. study [75]was included in both systematic reviews [72 74]reviews.)

Table 4 describes the type of interventions, the outcomes and the results of the primary studies included in the Sensory Garden and Horticultural activities reviews.

Music and dance therapy

Music therapy is the application of music and/or its elements (melody, rhythm, harmony, sound) by a qualified musical therapist, in order to support and stimulate various aspects of cognitive, emotional, social and physical needs, such as expression, communication, learning and forming relationships. Subjects can passively listen to music or actively participate by singing, playing an instrument or moving. Dance therapy is a psychotherapeutic intervention that uses movement to “further the emotional, cognitive, physical and social integration of the individual” [76].
Six SRs that evaluated music therapy [29 77-81], and one review that assessed live singing to people affected with dementia [76], were identified. The number of included primary studies in the reviews varied from 3 to 18 and the AMSTAR scores of the reviews ranged from 2 to 7.

The review by Ueda 2013 [78], searched the following databases in February 2011: MEDLINE, CINAHL, PsycINFO, and Ichushi (a Japanese database). The review received the highest score (AMSTAR=7). Randomized trials, controlled clinical trials, and cohort studies that evaluated one music-related experience or a combination of music-related experiences, such as singing, listening, performing, rhythmic exercising, and improvising were eligible for inclusion. Uncontrolled before-and-after studies and case studies were excluded.

Ten randomized trials and 10 controlled trials (651 participants; range 12 to 68) that investigated music therapy (mean of 36 min/day, 2-3 days/week for 10 weeks (range 1 day to 11 months)) for BPSD were included. The music therapy comprised listening ([82-91]), moving/dancing ([82 84 85 92-96]), singing/playing a musical instrument [82 84 85 90 91 93-95 97-100], exercise [101] and reminiscence [85 95 98].

Music therapy was effective in reducing behavioral symptoms (6 RCTs + 5 CTs; 397 participants) [SMD= −0.49 (95% CI −0.82 to −0.17)] despite a moderate and statistically significant heterogeneity [I²=58%, P=0.009]. The same intervention achieved a statistically significant reduction on depression (4 RCTs + 5 CTs; 250 participants) [SMD= -0.32 (95% CI -0.68 to -0.04); I² = 44%, P=0.08] and anxiety (SMD -0.64, 95% CI -1.05 to -0.24; I²=55%; eight studies; 258 participants).

Wheat et al [81] investigated the effectiveness of mealtime interventions, including music, on BPSD in people with dementia in residential nursing homes or care homes. Eleven studies were identified: one controlled trial, three before/after studies and seven repeated measure time series studies. The results of the studies were described narratively. One before/after study with 22
participants found that music played at mealtime improved physical and verbal, aggressive and non-aggressive behavior using the CMAI.

Seitz [29] (AMSTAR=6) identified 40 RCTs of non-pharmacological interventions, of which 3 studies with 133 participants [94 96 102] evaluated music therapy for BPSD of dementia in long-term care (LTC) facilities. Due to the heterogeneity of the studies (study design, patient populations, interventions, treatment duration and outcomes measured), the authors did not perform a meta-analysis. The behavioral outcome was measured either with a modified Cohen-Mansfield Agitation Inventory (CMAI), Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD) or the NPI. In one study, the music therapy was performed with movement, in a group, for 30 minutes, twice/week for 4 weeks [96]). In a second study, the music intervention lasted 30 minutes, 3 times/week for 6 weeks [102]). And in a third trial, the duration and frequency of individual sessions were not specified, but the therapy lasted 14 weeks [94]). Two of the three studies employing music found a statistically significant difference between treatment and control groups, but all three were at risk of randomizations bias and 2 had unclear bias of incomplete outcome data. All the studies were included in Ueda’s review [78].

The review by McDermott [77]AMSTAR=4) searched MEDLINE, EMBASE, PsycINFO, CINAHL, the Cochrane Library, Web of Science, Journal of Music Therapy, and Nordic Journal of Music Therapy and identified 18 studies of which 6 were RCTs (the remaining were non-randomized controlled studies (n=4), before-and-after studies (n=5) and qualitative and mixed-method studies (n=3)). Two trials [94 99] and the case-control study [102] were already included in the reviews described above [29 78]. Three RCTs (n=165), two of which were carried out by the same group, measured BPSD using either the NPI or BEHAVE-AD. In one trial, the music therapy (patients and music therapist play musical instruments to express emotions and interact) was performed for 30 minutes, 3 times/week for one month followed by a one month interruption, over 6 months (Raglio 2010). In another study by the same group, the music therapy (singing and body
movement with music to stimulate communication) was administered for 30 minutes, 30 times over
16 weeks [94]. In the third trial, the therapy was executed for 30 minutes, 3 times/week for 6 weeks
(Svansdottir 2006). McDermott et al concluded that evidence for reduction of behavioral
disturbance was consistent, but there were no high-quality longitudinal studies that demonstrated
long-term benefits of music therapy. Of note, five of the RCTs included in the review were not
included in the review by Ueda [78].

Unlike the previous review, Vasionyte [79] (AMSTAR=4) provided a meta-analysis of the effects
of music interventions (median=8 weeks; range 2-53 weeks) on patients with dementia,
differentiating between different types of interventions (listening, active music therapy, recorded
music, live music, selected music, individualized music, classical/relaxation music, popular/native
music and group and individual interventions). This SR included 18 studies comprised of 6 RCTs
[83 88 103-106], 6 CCTs [84 89 97 100 107] and 6 pre-post-test studies. The outcomes evaluated
were behaviour (measured with the CMAI, NPI-Q, Multidimensional Observation Scale For Elderly
Subjects (MOSES), an agitation checklist or a behavioral chart), affect, cognition and physiology.
There was no statistically significant effect on behavior (Effect Size (ES) 1.16, 95% CI -0.65 –
2.98; 8 studies, n=217) or affect (ES 0.38, 95% CI -0.56 – 1.32; 6 studies, n=109), while cognition
(ES 1.56, 95% CI 1.11 – 2.01; 4 studies, n=63) and physiology (ES 0.72, 95% CI 0.36 – 1.08; 4
studies, n=88) were influenced. Three of the RCTs and four of the controlled trials in this review,
were also included in Ueda [78].

The review by Wall [80] included 13 studies that were presented narratively. The review was of low
quality (AMSTAR score 2).

The review by Chatterton et al [76] evaluated the efficacy of “live” singing to people with
dementia for cognitive, behavioral, physiological, and social outcomes. The study received an
AMSTAR score of 1. Table 5a describes the type of interventions, the outcomes and the results of
the primary studies included in the Music therapy reviews.
**Dance therapy**

Two reviews evaluated dance therapy in patients with dementia [108 109]. The first review’s objective was to evaluate the evidence concerning dancing interventions in physical and mental illnesses compared to other types of interventions or non-specific interventions [109]. The review received 3 points in the AMSTAR scoring system and identified 13 small studies reporting results from 11 randomized trials of which only one considered patients with dementia. The trial that considered subjects with dementia included 29 participants (mean age 79 years, SD 7.7; 75% female) in a nursing home and evaluated the efficacy of dance and movement therapy delivered in nine sessions, lasting 30 to 45 minutes each, once-a-week [110]. The outcome measures included the word list savings score, the Clock drawing test (for visual spatial ability), the Cookie Theft picture description task from the Boston Diagnostic Aphasia test and the Nurses’ Observation Scale for Geriatric Patients (NOSGER). The results did not show any important differences in favor of dance therapy.

The second SR aimed to evaluate the effects of dance (movement) therapy and ballroom dancing, compared to usual care, for adults with physical and mental illnesses [111]. The review received only 1 point on the AMSTAR scale and identified only one study that investigated the intervention in a population affected by dementia [110] and which was also included in the review above.

**Snoezelen Multisensory Stimulation Therapy**

Snoezelen Multisensory Stimulation Therapy (SMST) comprises multiple stimuli and is aimed at stimulating the primary senses of sight, hearing, touch, taste and smell. The intervention is provided in specially designed rooms which provide diverse sensory-stimulating effects/material including music, aroma, bubble tubes, fiber optic sprays and moving shapes projected across walls. SMST was investigated by two reviews [29 31]).
The first was an overview of reviews [31] and its evidence for SMST was based on a Cochrane review that included three studies [112]. The inclusion criterion was any randomized trial that assessed the efficacy of SMST and/or multi-sensory stimulation to treat people over 60 years of age suffering from dementia. The outcomes of interest included behavior, mood, cognition, physiological indices, and client-carer communication, as well as short-term effects measured during the sessions or post-session, and longer-term benefits measured post-intervention and at follow-up.

The three included primary studies evaluated a total of 311 patients with dementia, aged 60 or older. The first was a randomized trial [113] that compared eight standardized multi-sensory programs with eight standardized activity sessions. Both programs were implemented on a one-to-one basis, twice a week, with each session lasting 30 minutes. Fifty subjects (25 female, mean age 78) with a diagnosis of Alzheimer's disease (N=33), vascular dementia (N=7) or a mixed diagnosis (N=10) were enrolled. The objectives of the trial were the immediate effects of SMST on the behaviors of older people with dementia, the carry-over effects of SMST on mood and behavior to day hospitals and home environments, and the maintenance effects of SMST on mood, behavior, and cognition over time. The effects of SMST on behavior were measured by INTERACT [114]). The generalizations effects were measured by three outcome measures: the carryover effect of day-hospitals was measured with the General Behavior and Community Skills sub-scales of REHAB (Baker 1988); the carryover effect to home, at mid- and post-intervention, was measured with the Behavior and Mood Disturbance Scale (BMD) and the Behavior Rating Scale (BRS) of the Clifton Assessment Procedures for the Elderly (CAPE). The maintenance effect (at the one-month post-intervention follow-up) on behaviors and cognition were measured by REHAB, BMD, the Cognitive Assessment Scale (CAS) of CAPE and MMSE. No significant effects on any scale of behavioral symptoms were found either immediately after intervention or at one-month post-follow-up.
The second study [115] was a quasi-experimental pre- and post-test design with randomization performed at a ward level, which compared a 15-month, 24-hour individualized care plan that was integrated with SMST, with 15-month usual care. The study included 136 subjects diagnosed with Alzheimer's, vascular or mixed dementia from 3 different countries (UK = 94 day patients, the Dutch sample = 26 in-patients. Swedish sample = 16 in-patients). There was a significant group difference in mean baseline MMSE scores (data from the UK and the Dutch only) between the SMST group (9.4) and the control group (6.7) (p=0.01). All subjects attended eight, 30-minute sessions on a one-to-one basis according to their group assignment. The sessions were conducted by the same key workers throughout the study period. The following outcomes measured the short-term effects of SMST on behaviors: (1) INTERACT (22-item) measured behaviors during the sessions; (2) INTERACT (12-item) measured behaviors 10 minutes before and 10 minutes after the sessions; and (3) Behavior Observation Scale for intra-mural psycho-geriatrics (GIP) measured behaviors that were videotaped during the sessions in the Netherlands sample.

The study showed significant effects on two behavioral items of INTERACT during sessions: enjoying oneself (MD = -0.74; 95% CI (-1.29, -0.19); z = 2.62, P = 0.01) and bored/inactive (MD = -0.56; 95% CI (-1.11, -0.01); z = 1.99, P = 0.05). There were no longer-term treatment effects of the integrated SMST-care program on behavior.

The third study [116 117] assessed the effects of SMST when integrated into 24-hour daily care on nursing home residents with dementia. One hundred twenty-five patients with moderate or severe dementia and care dependency were recruited from 6 old age psychiatry wards for pre-test. A cluster randomized design was used to assign the wards to either experimental (integrated SMST care program) or control (usual activity) conditions. Twelve old age psychiatry wards in six nursing homes (out of 19 homes) were recruited to the study. At baseline, 125 subjects (female 79%, mean age 84) were recruited and were assigned to experimental or control conditions according to the ward in which they stayed. For the experimental group, subjects were given a stimulus-preference screening in 10 weekly one-hour sessions to identify their preferred sensory stimuli. Subsequently,
individual SMST care plans were developed for each participant based on their life history, stimulus preference, and discussions from multidisciplinary conferences. Certified nursing assistants (CNAs) used multi-sensory stimuli in the 24-hour care of the experimental subjects. Subjects in the control group were provided with individual usual care. A minimum period of three months was used for both experimental and control conditions.

The short-term effects of the integrated SMST care program on behaviors were measured using a modified version of INTERACT, in which six items were deleted and eight new items were added during morning care sessions. The long-term effects of integrated SMST care programs on behaviors, mood, and interaction were evaluated at the 18-month follow-up using the eight items of GIP for apathy, anxiety and disoriented behaviors, the Dutch version of CMAI for agitated behaviors, physically non-aggressive behavior and verbally agitated behaviors, and the Cornell Scale for Depression for depressive symptoms. In terms of behavioral disturbances, when compared to the control, the 24-hour integrated SMST-care program [118]) showed significant effect on two behavioral items of INTERACT during sessions: enjoying self (MD = -0.74; 95% CI (-1.29, -0.19); z = 2.62, P = 0.01) and bored/inactive (MD = -0.56; 95% CI (-1.11, -0.01); z = 1.99, P = 0.05).

There were no longer-term treatment effects of the integrated SMST-care programme on behavior. In terms of mood, there were significant improvements in one mood item of INTREACT during sessions: the SMST group was happier and more contented than the control group (MD = -0.84; 95% CI (-1.39, -0.29); z = 2.98, P = 0.003). There were no significant effects of the 24-hour integrated SMST at post-intervention. The fourth review scored 6 in the AMSTAR evaluation and investigated different non-pharmacological interventions including SMST for the treatment of BPSD [29]. The review identified only one study that was included in the above cited review [118].

**Table 6** describes SMST -based interventions, outcomes and results of the primary studies included in the reviews.
**Transcutaneous electrical nerve stimulation**

Transcutaneous electrical nerve stimulation (TENS) is a simple, noninvasive, non-pharmacological intervention commonly used for pain control [119] and occasionally for neurological and psychiatric conditions such as drug/alcohol dependency, headaches, and depression [31]. TENS consists of attaching electrodes to the skin and applying an electrical current, whose frequency can vary from low (< 10 Hz) to high (> 50 Hz).

Two reviews were identified.

One review that evaluated current treatment options for sleep disturbance in Alzheimer’s dementia scored 3 in the AMSTAR evaluation [120]. Different non-pharmacological interventions were considered, including bright light therapy, behavioral and multi-faceted interventions (combined increased daytime physical activity and exercise, decreased daytime in-bed time, daily sunlight exposure, structured bedtime routine, and decreased night-time noise and light) and TENS. For the latter intervention, only one randomized trial of 19 nursing home residents was identified. The study did not evaluate behavioral outcomes.

A Cochrane review that was included in O’Neil’s review[31] was also considered [121]. The review was focused only on RCTs that enrolled in-patients and outpatients of any age (with or without caregivers), with a diagnosis of dementia. The outcomes of interest included visual and verbal short- and long-term memory, semantic verbal fluency, circadian rest-activity rhythm, affect/depression, level of independent functioning, adverse effects, and drop outs due to inefficacy. The review identified and included 9 trials that were performed in Japan and the Netherlands. The Dutch studies were performed by the same group of authors [122-127]. These studies were randomized placebo-controlled trials and the participants were chosen from a group of 350 to 500 residents of a residential home for older people. The age range of the subjects was approximately 70 to mid-90 years and were mostly female (>80%). All subjects met NINCDS-ADRDA criteria for the clinical diagnosis of probable AD; most subjects had early AD, but some had moderate AD.
Subjects generally had scores of 17 or less on the Hamilton Depression Rating Scale. All included studies used a similar TENS protocol, except the most recent one published in 2002, which addressed cranial electrostimulation.

The remaining 3 publications were performed by a group of authors from Japan and describe the results of the same study [128]. The study design was a double-blind cross-over and, in contrast to the Dutch studies, subjects were thought to have multi-infarct dementia or Alzheimer’s disease and were selected on the basis of irregular sleep-wake patterns in conjunction with nocturnal behavior disorders and/or dementia. Twenty-seven subjects completed the study. The intervention used a HESS-10 stimulator with rectangular pulse waveforms at a frequency of 6 - 80 Hz, a pulse duration of 0.2 ms maximum, 256 µAmps and an amplitude of 6-8 V. The outcomes evaluated were sleep disorder, motivation, behavior disorder, intelligence, emotion, language, neurological signs, subjective complaints and activities of daily life. All of these were rated on a 5-point scale: absence of the related symptom, 0; mildly disturbed, 1; moderately disturbed, 2; markedly disturbed, 3; and severely disturbed, 4. Of the 9 studies, only 3 could be included in a meta-analyses for a combined total of 63 subjects. Two of these studies were conducted in the Netherlands, and one was conducted in Japan. Results, however, were inconclusive. It should be noted that none of the other studies mentioned adverse effects, although it is unclear if adverse events were monitored.

Table 7 describes TENS-based interventions, outcomes and results of the primary studies included in the reviews.
Cognitive/Emotion-oriented Interventions

Cognitive stimulation

Cognitive stimulation involves a variety of pleasurable activities, such as word games, puzzles, music, cooking, gardening and discussing past and present events and is usually carried out by trained personnel with small groups of 4-5 people. It lasts for 45 minutes, minimally 2 times per week. It is based on Reality Orientation, which was developed in the 1950s to counteract the confusion and disorientation of older people during hospitalizations.

Seven reviews were identified [129-135]

Woods 2012 [129] (AMSTAR score =10). A Cochrane review identified 15 RCTs that used cognitive stimulation for people with dementia. The authors stated that most of the studies were of low quality, but that generally, investigators had taken measures to protect against the risk of allocation concealment bias. In a meta-analysis of 3 trials [136-138](n= involving 190 participants), the intervention had no effect on problem behaviors (SMD -0.14, 95% CI -0.44 – 0.17; I²=0%, P=0.57).

The review by Aguirre et al. in 2013 [130] (AMSTAR score =5) evaluated the effectiveness of cognitive stimulation in patients with dementia and identified 9 RCTs. Three trials that considered behavior-related outcomes were identified. These trials were already included in Woods’s review [129] and reached the same conclusion.

Alves et al. in 2013 [131] (AMSTAR score =4) identified 4 RCTs of cognitive interventions for AD patients. Only one trial that measured BPSD as an outcome was identified. The study population was composed of 32 patients with a score between 10 and 24 on the Mini Mental State Examination, no history of antidepressant medication, and a total Neuropsychiatric Inventory score greater than 5 points arising from at least 2 domains of behavior. The cognitive stimulation intervention was administered individually and focused on a set of tasks requiring executive
functions and working memory. The study found a statistically significant reduction of BPSD (MD -2.06; 95% CI -2.91 to -1.21).

The study of Carrion et al. in 2013 [132] (AMSTAR score = 4) found 17 RCTs of cognition oriented interventions (reality orientation and skills training) for dementia sufferers. Challenging behavior was evaluated in only 2 trials (n=156 and n=44, respectively) that employed the two categories of cognitive interventions, using the Neuropsychiatric Inventory and the Revised Memory and Behavior Problems Checklist. In both RCTs, the intervention group had a smaller increase in change from baseline compared to the control group. Due to the heterogeneity among the studies, the authors decided a meta-analysis was inappropriate.

Yu 2009 [133] (AMSTAR=3) included 15 studies (9 RCTs, 5 CCTs and 1 before-after study), in addition to 5 case studies and 3 undefined studies, all of which investigated different types of cognitive interventions for AD and dementia. The only study, a CCT (n=32; with early stage AD) that evaluated the effect of cognitive stimulation on behavioral disturbances, showed larger improvement than the cognitive training group.

Olazarán et al. in 2010 [134] (AMSTAR = 4) identified 179 RCTs of diverse types of non-pharmacological interventions for Alzheimer’s Disease patients and examined problem behavior, mood, QoL, cognition, ADLs, mechanical restraint and institutionalization of patients and mood, psychological well-being and QoL of CGs. The authors performed a meta-analyses of three low quality RCTs to determine the effect of cognitive stimulation on problem behavior and mood. There was a non-statistically significant reduction in problem behavior (group session cognitive stimulation (ES=0.61; 95% CI 0.09-1.12). The primary study by Baines et al.[136] was included in the Woods [129] review above, while the study by Robichaud et al. [139] was included in the review by Kim [140] which examined Behavior Management Techniques described below.

Thirty-three RCTs, employing cognitive interventions for cognitively impaired individuals (dementia and mild cognitive impairment), were identified in Kurz et al.[141] (AMSTAR score = 2).
Twelve of these trials examined behavioral disturbances, but only 3 studies found a significant effect of the intervention.

Zientz et al. [135]; (AMSTAR score =2) identified 3 studies (2 RCTs and 1 RCT or CCT; n=124 participants) of caregiver-administered cognitive stimulation for individuals with AD. One of the randomized trials (n=16) found that individuals who received the intervention displayed fewer behavioral problems compared to those who had not been given the intervention.

Table 8 describes Cognitive stimulation-based interventions, outcomes and results of the primary studies included in the reviews.

**Reminiscence therapy**

Reminiscence therapy is a non-pharmacological intervention that involves the discussion of past experiences, events and activities with family members or other groups of people. The intervention uses materials such as photographs, books, old newspapers and familiar items from the past to inspire reminiscences and facilitate people to share and value their experiences. Three reviews assessed reminiscence therapy as a non-pharmacological intervention to treat agitated behavior in patients with dementia [29 142 143].

The first review [29] received the highest score (AMSTAR score 6) and considered all non-pharmacological interventions to treat relevant outcomes in patients with dementia. The review identified two small studies involving a total of 107 patients [144 145] performed in care facilities. The Neuropsychiatric Inventory (NPI) and the Clifton Assessment Procedures for the Elderly-Behavioral Rating Scale (CAPE-BRS) were used to measure BPSD of dementia. Seitz et al.[29] reported that this outcome was unaffected in one study [145], while the effect of the intervention was unclear in the other study [144].

The second review [143] was focused only on reminiscence therapy as a sole treatment of behavioral outcomes for patients with dementia. The review was of low methodological quality
(AMSTAR score = 3). The results were presented in a narrative synthesis. The review included 5 trials with a before-after approach, containing 258 patients affected by dementia. The studies considered different interventions. Two studies (one with 31 participants [Haight 2006][146] and the other with 17 participants [Morgan 2010 [147]]) assessed a life review or story approach and found significant improvements in depression, communication, positive mood and cognition. The third study (101 participants [Lai 2004 [148]]) evaluated specific reminiscence, which produced a life-story book using personalized triggers for each person's life history. No significant differences were observed between groups except for outcomes such as well-being and social engagement. The remaining two trials (involving 73 participants [Haslam 2010 [149]] and 36 participants [Politis 2004 [150]]) evaluated individual reminiscence approaches. One study used six weekly sessions, which focused on a particular life phase, such as childhood or family life, while the other study used a basket of visual and auditory activities, based on five themes, such as musical instruments, designed to stimulate reminiscence. No significant differences were observed between the groups in terms of behavioral outcomes.

The third review [142] focused on whether reminiscence therapy could alleviate depressive symptoms in adults with dementia, but its methodological quality was extremely low (AMSTAR score=1). Four primary studies with a pre-post test design, were included and were described individually, three of which were randomized trials and one of which comprised a single group.

Table 9 describes Reminiscence therapy interventions, outcomes and results of the primary studies included in the reviews.
Validation Therapy

Validation therapy is based on the general principle of the acceptance of the reality and personal truth of another person’s experience and incorporates a range of specific techniques. Validation therapy is intended to give the individual an opportunity to resolve unfinished conflicts by encouraging and validating the expression of feelings. The specific interventions and techniques are based on a synthesis of behavioral and psychotherapeutic methods. The approach can be used as a structured therapeutic activity in a group setting, usually lasting several weeks, or it can be conducted individually as part of an ongoing approach to facilitate communication as a supplement to group work. The validation therapy techniques comprised non-threatening, simple concrete words; speaking in a clear, low and empathic tone of voice; rephrasing and paraphrasing unclear verbal communication; responding to meanings through explicit and implicit verbal and non-verbal communication; and mirroring verbal and non-verbal communication.

One Cochrane review that evaluated the effectiveness of validation therapy to reduce the BPSD was identified (AMSTAR score =7)[151]. The review included only randomized trials of subjects over 65 years of age, diagnosed with Alzheimer's disease, dementia or other forms of cognitive impairment, according to ICD 10, DSM IV or comparable criteria. The outcomes of interest were cognition, behavior, emotional state and activities of daily living. The review, updated in 2005, included 3 randomized trials (n=155 participants) [152-154]. Another SR that evaluated the effective characteristics of residential long-term care settings for people with dementia identified one trial [154] that was included in the Cochrane review [151].

Another SR that evaluated the effective characteristics of residential long-term care settings for people with dementia identified one trial that was included in the Cochrane review.

Primary studies

The first study [152] ((n=31) was performed in a nursing home and used an intervention (30 minutes once per week for 6 weeks) that included activities such as discussion off a subject
previously agreed, singing and movement, followed by a closing ritual and refreshments. Behavior was measured with the Behavior Assessment Tool. The control groups consisted of reminiscence therapy, which followed the guidance of a reality orientation manual (cues such as flannel boards and calendars were used to promote orientation) and usual care. At 6 weeks, validation therapy was associated with a decrease of problem behaviors (MD=−5.97, 95% CI -9.43 - -2.51; P<0.001; based on an analysis of subjects who completed the study).

The second study [153] enrolled 36 patients with moderate to severe disorientation of which 25 had a diagnosis of dementia. The study was performed in a long-term care institution in the USA. The validation therapy was performed twice a week for nine months; details of the validation therapy were not given. Agitation was measured using the Minimal Social Behavior Scale (MSBS; Farina 1957) where a reduction in score indicated improvement. No effects on behavior were detected.

The last study [154] was carried out in "skilled-care nursing homes" in the USA. In this study, patients were included if they had at least a moderate level of dementia (assessed by the Short Portable Mental Status Questionnaire – SPMSQ – and the Validation Screening Instrument), and displayed problem behaviors such as physical aggression. Validation therapy (four meetings lasting 30 minutes per week for 52 weeks) was composed of groups divided into 4 sessions of 5-10 minutes each. The first session included introductions, salutations and singing. The second session involved conversation regarding a subject of interest; recalling past events was promoted. The third session comprised an activity program and singing or poetry. The fourth session involved refreshments and individual goodbyes. Agitation was measured with the Cohen Mansfield Agitation Inventory (CMAI; Cohen-Mansfield 1986), carried out as CMAI(N) nurse observed and CMAI(O) non-participant observed). The authors reported that depression (MOSES) decreased at 12 months (MD -4.01, 95% CI -7.74 - - 0.28; P=0.04, based on an analysis of participants (66 out of 88) who completed the study). Table 10 describes validation therapy interventions, outcomes and results of the primary studies included in the reviews.
Simulated Presence Therapy

Simulated presence therapy (SPT) involves the use of video-audiotapes made by family members containing scripted “telephone conversations” about cherished memories from earlier parts of a person’s life, in an effort to stir remote memory, improve behavioral symptoms, and enhance the quality of life among people with dementia. Two SRs were identified [30 155].

The first review was written by only one reviewer and scored 3 in the AMSTAR scale. The review was aimed at investigating the effectiveness of SPT for challenging behaviors in dementia. The review searched PubMed, PsycINFO and the Web of Science, conducted hand searches of relevant articles and considered for inclusion, studies that reported pre-test and post-test, or pre-test and during-test data for SPT for challenging behaviors. The SPT consisted of audio or videotapes prepared by a spouse, family members, the caregiver, a psychologist, a surrogate or researchers. Of the seven included primary studies, only the data from four could be pooled, showing an overall mean effect of 0.70, with a 95% confidence interval of 0.38–1.02, but with statistically significant heterogeneity ($I^2=71\%, P=0.02$).

The second review examined the efficacy of any non-pharmacological intervention (including SPT) to reduce BPSD in patients with dementia [155]. After searching the databases MEDLINE, CINAHL, PsycINFO, EMBASE, Dissertations International, and the Cochrane Database of Systematic Review, from 1974 to May 2008, the review identified only 2 studies that were included in the Zetteler review above [30]. Table 11 describes SPT, outcomes and results of the primary studies included in the reviews.
Behavioral management techniques

There is a multitude of behavioral interventions that constitute Behavioral Management Techniques, which include behavioral or cognitive-behavioral therapy, functional analysis of specific behavior, individualized behavioral reinforcement strategies, communication training, and other therapies such as habit training, progressive muscle relaxation, and token economies. These behavioral interventions can be realized either with the patient or by training caregivers to perform the intervention with the patient.

One overview of reviews and four SRs that considered behavioral interventions were identified. The overview of reviews by O’ Neil 2011[31] identified three SRs and after performing additional searches of primary studies, included nine randomized trials [156-164]. The overview authors’ conclusions were in support of behavioral management techniques as effective interventions for behavioral symptoms of dementia although they admitted there were mixed results. In addition, the authors highlighted some concerns regarding the variety of specific interventions and methodological limitations in many studies, and advocated additional research with carefully assessed outcomes.

A Health Technology Assessment (HTA) [165] report that aimed to assess the clinical and cost-effectiveness of sensory, psychological and behavioral interventions to manage agitation in older adults with dementia, systematically searched and identified 4 randomized trials [159 166-168]. The intervention in all 4 trials was caregiver-based. The HTA authors concluded that the evidence in favor of behavioral management techniques was limited.

A Cochrane review [169] aimed to assess the effects of functional analysis-based interventions for people with dementia (and their caregivers) living in their own home or other settings and identified 18 randomized trials. The development of the intervention was driven by various approaches and theories, including knowledge and/or training approaches, the stress-coping model, the Progressively Lowered Stress Threshold model and problem solving approaches. In addition, the
time frame in which the intervention was delivered varied from 9 days to 18 months and the number of sessions used to deliver the intervention varied widely, from 1-2 sessions to more than 10 sessions. Of the 18 studies included [157-161 166 167 170-180] the authors were able to meta-analyse data from 4 trials (Burgio 2003 [171]; Farran 2004 [173]; Gitlin 2003[175]; Gitlin 2010[181]), of which one contained unpublished data. There were no significant reductions in the incidence of challenging behaviors reported post-intervention in four family care studies (SMD 0.02, 95% CI -0.13 to 0.17, P = 0.80, N = 722).

Among 179 RCTs of diverse types of non-pharmacological interventions for Alzheimer’s Disease patients, identified by Olazarán 2010[134] (AMSTAR score =4), the authors performed a meta-analysis of three low quality RCTs of behavioral interventions (analysis and modification of antecedents and consequences of behavior) and found a statistically significant reduction in problem behavior (ES=0.57 (95% CI 0.21-0.92); 3 trials; n=167). The same authors carried out another meta-analysis of four low quality RCTs of care staff training in behavioral management and found a reduction in problem behavior (ES=0.22; 95% CI 0.02-0.43; 4 trials; n=370).

Two primary studies examined emotion-oriented care. The first study [182] was a RCT of NH residents (n=146 older residents with AD, mixed AD and vascular dementia and dementia syndrome; mean age 84). The intervention of emotion-oriented care was associated with less anxious behavior in the group of residents who needed less assistance/care compared to similar residents in the usual care group. The second study [183] was a cluster randomized study of residential care homes (n=16 homes; n=151 residents). The authors reported that there was no statistically significant effect of the intervention on any behavioral outcome, including behavioral problems. Teri 2000 [167] was included in the Health Technology Assessment [165]; Gormley 2001 [166] and Teri 2005 [159] were included in the Brodaty 2012 review [184], Gonyea 2006 [176] was included in reviews in Behavior Management Techniques, McCallion 1999 and Teri 2005 were included in Eggenberger 2013 [185].
Eggenberger 2013 [185] (AMSTAR score = 3) aimed to evaluate interventions that were designed to enhance communication or interaction in dementia care, in any setting. Review authors identified 12 studies (7 randomised trial, 2 controlled clinical trials and 3 before-after studies) that focused on communication training for staff in institutions and family caregivers at home. In institutional settings, the results on challenging behavior, of residents with dementia, were not consistent. Four studies reported a significant reduction of challenging behavior [164 186 187]. McCallion et al.[164], for instance, demonstrated a decrease of physically aggressive behavior (15.16 (SD 9.81) to 12.21 (SD 8.31, p<0.001)), and a reduced mean occurrence of verbally aggressive behavior in patients with dementia (16.22 (SD 10.31) to 12.88 (SD 8.39, p<0.001)). In addition, one trial demonstrated a significant decrease of residents’ agitation during care routines (F(1.7=5.12, p<0.05)[187].) Conversely, three studies reported no effect on challenging behavior of people with dementia[188-190].

Only one trial [160] was included in the Brodaty 2012 review [184].

Kim et al [140], conducted a review to assess the effectiveness of occupational therapy on behavioral problems and depression in patients with dementia. MEDLINE, CINAHL, ProQuest and The Cochrane Library were searched up to the end of March 2011. The AMSTAR score was 7. The authors defined occupational therapy as an application of “activity analysis, caregiver training, sensory stimulation, behavior control skill teaching, physical and social environmental modification, cognitive training, and purposeful activity”. The review identified nine randomized trials with a total of 751 participants. Based on the type of intervention, the authors categorized four studies [139 191-193] as sensory stimulation, three studies (Clare 2010[194]; Gitlin 2008 [195]; Lam 2010 behaviors [193] as functional task activities, and 2 studies (Gitlin 2001[196];[195] as environmental modification. The authors performed a meta-analysis of the trials with occupational therapy-based sensory stimulation and found an effect size of 0.32 (95% CI, 0.04 to 0.59; 250 participants; no significant heterogeneity). No significant effect was detected for OT-based
functional task activities [0.15 (95% CI, −0.17 to 0.47); 203 participants] or environmental modification [0.13 (95% CI, −0.09 to 0.36; 298 participants].

**Primary studies**

Overall 22 trials were evaluated in the 6 reviews that were included. Except for one study performed in Taiwan, all the studies were carried out in Europe, the US and Australia. Thirteen studies were performed in family care settings [157 160 161 166 171 173 175-180]. Three studies with a total of 740 residents were conducted in care homes [158 172 174]. Finally, one study was located in an assisted living setting [159] and the other in a hospital setting [170].

Characteristics of the interventions varied greatly across the trials. Fifteen trials were focused on enhancing communication skills in family and formal caregivers. Eighteen trials focused on functional activity of which four were described as a Behavioral Management intervention. The intervention in one trial involved caregiver training on verbal or non-verbal communication focused on activities of daily living. Another trial was dedicated to teaching participants the basic technique for progressive muscle relaxation[163]. Time delivery of the intervention also varied widely. However, as noted by Moniz-Cook the intervention delivery was determined by setting: the interventions in care homes were provided weekly and lasted for six months [169]. In one family care study, the intervention was provided in just 4 sessions over eight weeks [166]. Follow-up data varied from a few weeks to 24 months.

**Setting based description**

**Family care.** In this setting, family caregivers assisted people with dementia at home, with or without support from formal caregivers, healthcare workers and adult day care centers. Thirteen trials were conducted in a family care setting [157 159 161 166 167 169 171 173 175-178 180 195 196]
Six of these trials investigated an intervention that was focused on enhancing communication skills of the caregiver. The duration of the intervention ranged from 3 weeks [177] to 12 months [171]. The number of weekly sessions administered were, according to a classification proposed by Moniz-Cook 2012 [169], high (> 10 session) in three trials -[157 171 173 178], moderate-high (6-10 sessions) [178] in one trial, moderate (3 to 5 sessions) in one trial [175] and minimal (1 to 2 sessions) in one trial [177]. The subjects that delivered the interventions varied from trial to trial: occupational therapists [175]; trained nurses or social workers [173]; professionals specialised in the REACH program [171]; healthcare professionals supervised by a an old age psychologist [157]; psychologists [178] or trial investigator together with an experienced nurse [177].

Four of the 13 trials in the family care setting investigated a behavioral intervention that was focused on providing support to the caregiver. The interventions lasted from 5 weeks [176] to 18 months behavior [179], with the number of sessions that varied from 4 [179] to 8 sessions [180], with home visits [169 180] and associated with or followed by telephone contacts [159 161]. Overall, the intervention dosage was high for three trials [159 161 169], medium-high in one trial [180] and moderate in one trial [176]. The interventions were delivered by different healthcare experts: Community Mental Health Nurses [169]; therapists [180]; occupational therapists [161]; community consultants trained by an old age psychologist [159].

The remaining two trials evaluated behavioral management techniques. Teri 2000 [167] compared the intervention consisting of 8 weekly and 3 biweekly sessions (high intensity intervention) with pharmacological interventions or placebo. The intervention was provided by a therapist with a master’s degree and one-year clinical experience, but did not report the intervention in detail. The post-intervention evaluation started at 4 months and the follow-up lasted beyond 12 months. The second study [166] did not completely describe the intervention for behavioral management. The intervention was delivered in 4 sessions (moderate intensity) over 8 weeks by the trial investigator.
In terms of results, no statistically significant change in the incidence of challenging behaviors was observed in any of the studies. Moniz-Cook 2012 meta-analyzed data of four studies (N=722), but did not find any difference among the groups (SMD 0.02, 95% CI -0.13 to 0.17, P = 0.80; I² = 0%) [161 171 173 175]. At follow-up of six months, two studies did not show any significant effect of behavioral management techniques [161 173].

When the frequency of challenging behaviors was examined, none of the studies detected a significant difference even when a meta-analysis, using the data from 10 studies, was performed (SMD -0.05 [95% CI -0.17 to 0.07]).

**Assisted Living.** In this setting, people with dementia lived in a residence, did not require full time nursing care, but needed assistance with some ADLs such as bathing, dressing or eating. Family members could still act as intermittent caregivers during visits by providing different types of support for ADLs, Instrumental ADLs (e.g., laundry washing, room cleaning, transportation to a doctor’s office), socio-emotional support (e.g., talking, reminiscing, socializing), monitoring care provision or advocating [197]. One study evaluated a behavioral management intervention to improve caregiver training to manage residents with dementia [159]. The intervention intensity was medium-high, delivered by a clinical psychologist and graduate nursing students who performed 2 half-day group workshops and 4 individualized sessions with a follow-up 2 months after the termination of the intervention. Results for residents showed a statistically significant effect, in intent-to-treat analyses, in favor of the STAR-caregivers (STAR-C) intervention, general behavioral disturbance (measured by the Revised Memory and Behavior Problems Checklist (RMBPC), NPI and ABID) and depression.

**Residential care.** This setting referred to both assisted living residences and nursing homes. The latter included facilities for people with dementia who needed significant nursing care. Three cluster randomized trials were conducted in residential care with a total of 743 residents [158 172 174].
In 15 residential care sites across metropolitan areas in Sydney (Australia), Chenoweth et al. [172] examined the efficacy of person-centered care vs usual care. The intervention was a high intensity, person-centered care, based on the needs-driven model in which staff, selected by managers, administered training sessions to caregivers. The topics covered during the sessions were derived from Bradford University's training manual. The duration of the intervention was 4 months and the overall follow-up was 8 months. The total number of residents enrolled was 289. During follow-up, the mean agitation score (measured with CMAI) in the person-centred care group decreased significantly, from 47.5 (9.1) at baseline, to 37.2 (9.1) at six months (P = 0.01), compared to usual care in which agitation increased from 50.3 (6.8) at baseline to 57.7 (6.8) at six months (P value not reported).

In 12 residential homes, Fossey 2006 [174] allocated 346 residents to an intervention that consisted of training and support delivered to nursing home staff over 10 months, focusing on person-centred care and skill development for the management of agitated behavior in dementia. The comparison intervention was usual care. The high intensity intervention was delivered during the whole period of follow-up (12 months) by a psychologist, an occupational therapist or a nurse supervised weekly by the trial investigators. The study’s main outcome measure was mean levels of agitated and disruptive behavior measured with the CMAI, but no significant difference between the groups was detected.

In 10 residential homes, Proctor 1999 [158] allocated 120 patients to a staff-based intervention or usual care. The intervention, of high-medium intensity, consisting of training on “psychosocial management of residents’” behavioral problems, was delivered through seven, one hour seminars by members of the hospital outreach team and psychiatric nurse during the whole period of follow-up (6 months). The seminars covered topics that the staff had identified to improve their knowledge and skills (e.g., management of dementia, aggression, etc.). The Crichton Royal Behavioral Rating scale was used to assess behavioral characteristics of residents (0=no problems, 38=severe
problems). In addition, the geriatric mental state schedule and the diagnostic algorithm AGECAT (automatic geriatric examination for computer-assisted taxonomy) was used to assess the effect of the intervention on residents’ organic and depressive symptoms. Despite the control group having mean scores on the Crichton scale higher than the intervention group at follow-up, this difference was not statistically significant [mean score -0.7 (-3.0 to 1.6)].

Although the clustered trials reported different types of interventions, intensities, durations and follow-up times, Moniz-Cook et al. [169] attempted an analysis using two studies and found a significant reduction in behavioral disturbances [SMD, -0.21 (95% CI -0.39 to -0.03); P=0.02; $I^2 = 9\%$].

Table 12 describes Behavioral Management Techniques based interventions, outcomes and results of the primary studies included in the reviews.
Multicomponent intervention

Integrated interventions combining psychiatric and nursing home care

Collet 2010 [198] (AMSTAR score = 5) carried out a SR in Medline, PsychInfo and Pubmed to determine the efficacy of interventions that combine psychiatric and nursing home care in nursing home residents. The authors identified 4 RCTs (n = 371 participants), 1 retrospective cohort study and 3 prospective case studies. All the studies used tailored treatment plans that combined psychosocial, nursing, medical and pharmacological interventions. The results of the RCTs were described narratively. Three out of the four randomized trials reported an improvement in behavior and mood, while one trial found no difference among the groups (Table 13).

Combination of environmental sensory stimulation

A SR [199] that evaluated the effective characteristics of residential long-term care settings for people with dementia, identified one controlled clinical trial [200]. The intervention in this trial was provided in five nursing homes and consisted of 15 agitated participants with dementia taking showers, 15 agitated participants with dementia taking walks in an environment where natural elements such as large bright pictures coordinated with audio, including bird songs, bird pictures, the sound of water flowing gently, as well as food (such as banana, pudding or soda). The control group consisted of 15 other agitated participants with dementia that received only usual care. Agitation was measured with a modified version of CMAI. The analysis showed a significant decline in agitation in the treatment group compared to the comparison group.

Combination of music and hand massage

Another review [68] that aimed to assess the role of physical environment in supporting person-centered dining in long-term care, identified another trial [201] that was not included in the previous reviews. This trial applied an experimental 3x3 repeated measures design and included 41 residents with dementia living in three special care units. Participants were mostly female (78.0%), with a mean age 84.5 years (SD = 6.0). Residents in the treatment group received each of three treatments...
(hand massage, favorite music, and the combination of both)) with each treatment lasting 10 minutes; the control group did not receive any treatment. The CMAI was used to measure agitation.

The results showed that each single and combined treatment, individually and combined, were effective in significantly decreasing agitation immediately following the intervention and one hour post-intervention.

Table 13 describes Multicomponent Interventions based interventions, outcomes and results of the primary studies included in the reviews.
Other interventions

Exercise therapy

The systematic search identified 2 reviews [202 203] that evaluated the efficacy of only exercise as a therapeutic intervention.

The review by Potter et al. [202] received 6 points in the AMSTAR assessment and identified 13 randomized trials that evaluated the effects of physical activity on physical functioning, quality of life and depression in older people with dementia. Only four of these trials investigated depression as an outcome using four different rating scales (Geriatric Depression Scale (GDS15); Montgomery-Asberg Depression Rating Scale; a Dutch Evaluation scale for older patients (subscale used); and the Cornell scale for Depression in Dementia) and two trials measured behavioral disturbances (Neuropsychiatric Inventory and Stockton Geriatric Rating Scale).

The review authors stated that the methods of randomization were clear and adequate in six of the trials with only three of these also providing methods of allocation concealment; eight of the trials reported information regarding losses to follow-up and six trials declared intention-to-treat analysis.

The first study, Burgener 2008 [204], was a small trial (n=43) carried out in community-dwelling older people with dementia. The intervention was multimodal comprising Tai Chi (sitting and standing; 60’, 3 times a week for 40 weeks) and cognitive behavioral therapies. Depressive symptoms were measured with the Geriatric Depression Scale (GDS15). The authors reported that at 20 weeks of observation, there were no statistical differences between the groups.

The second study, Rolland 2007 [205] was a larger trial (n=134) carried out in nursing homes. Participants performed exercises including stretching, walking, strength, flexibility and balance training, for 60’, 2 times/week for 40 weeks. Depression was evaluated using the MADRS (Montgomery-Asberg Depression Rating Scale). After 12 months of observation, the MADRS (13.4 +/- 8.0) score was higher in the in intervention group than in the control group (14.8 +/- 7.2) but without any statistical difference.
The third study, [101] was also a small study (n= 25) conducted in a psychiatric hospital. The invention was composed of strength, balance and flexibility exercises with music, 30’ daily for 12 weeks. Depression was measured in older patients with the sub-scale *Beoordelinschaal voor Oudere Patienten*. At 3 months’ follow-up, no significant difference in depressive behavior was observed.

The last study [157], was a larger trial (n=153) that enrolled community-dwelling patients and their caregivers. The exercise intervention, for patients, comprised aerobic, endurance, strength, balance and flexibility training, 30 minutes twice weekly, reducing to twice monthly, for 23 weeks. Caregivers were given training in behavioral management techniques. The Cornell scale for depression in dementia was used to assess depression. At 2 years of follow-up the mean difference was 2.14 (95% CI, 0.14 to 4.17) statistically significant in favor of the intervention. The four trials used different types of interventions, outcome measures and follow-up times that hindered the possibility of performing meta-analyses.

The two randomized trials [101 205] that considered behavioral disturbances used the Neuropsychiatric Inventory and Stockton Geriatric Rating Scale, respectively.

The second review by Thuné-Boyle [206] received an AMSTAR score of 2 and included 6 studies comprising 2 small randomized trials (n= 31), 2 prospective design and 2 repeated measures studies that examined the effect of exercise on BPSD. In the first trial (Hokkanen 2003), the exercise intervention consisted of 16 sessions of dance and rhythmic movement lasting 30–45 minutes, once a week. This trial was already discussed in the dance section. The second trial [207] aimed to assess the efficacy of a home-based exercise intervention program to improve the functional performance of patients with Alzheimer's Disease. The intervention consisted of a daily program of aerobic, balance and flexibility, and strength training, given to patients and caregivers. Depression and apathy were measured using NPI and the Cornell Scale for Depression in Dementia at 6 and 12 weeks. Table 14 describes Exercise therapy, outcomes and results of the primary studies included in the reviews.
Animal-assisted therapy

One review [208], performed a comprehensive literature search in PubMed, EMBASE, and PsycINFO to identify pertinent studies that evaluated the efficacy of Animal-Assisted Therapy (AAT) in older patients with dementia or other psychiatric disorders. The authors identified 23 eligible studies of which 18 recruited patients with dementia but only 10 studies investigated the effect of AAT on BPSD. The design of the studies was as follows: 3 case-control and 7 repeated measures (e.g., interrupted time series analysis) studies. Overall, the authors concluded that animal-assisted therapy may have positive influences on demented patients by reducing the degree of agitation and improving the amount and quality of social interaction. However, they advocated more research examining the issue of optimal AAI duration, frequency of sessions, and suitable target group.

Primary studies

Churchill et al. [209] included 28 residents of three special care units with dementia (25% women; mean age 83.8 years; dementia evaluated with Bourke Dementia Rating Scale). The authors administered pet-therapy visits during the difficult "sundown" time to examine the effect on residents with a history of agitated "sundowning" behavior. The active group was exposed to 30-minutes’ interaction with an investigator and a dog, which ameliorated agitated/aggressive behavior measured with the Agitated Behaviors Mapping Instrument scale. However, the study did not report the P-values. In addition, the variability in resident response over time after the departure of dog was not explored.

The effect of dog-based AAT was also evaluated in another special care unit. McCabe et al. [210] enrolled 22 subjects with dementia (women 68%; mean age 83.7, range 68 - 96 years). The study introduced a resident dog and agitated behavior was measured using the Nursing Home Behavior Problem Scale. Data were collected 1 week before and for the first 4 weeks after introduction of the
dog. The authors reported a significant reduction in daytime behavioral disturbances among residents but not during evening shift.

In a small pilot study Richeson et al [211] evaluated visiting therapy dogs in 15 residents with dementia (14 women; age range 63 - 99 years; dementia MMSE mean score: 3.9; 26% with depression). The session with visiting therapy dogs lasted 1 hour daily for 3 weeks. Agitated behavior, measured with the CMAI, decreased significantly after 3 weeks and increased significantly after 2 weeks washout subsequent to the end of AAT.

Libin and Cohen-Mansfield [212] assessed the efficacy of a robotic cat (NeCoRo) and a soft toy cat in reducing agitated behavior in 9 women with moderate dementia in nursing homes. The intervention consisted of two 10 minute interactive sessions on different days. The robotic cat produced a significant increase in pleasure and interest, but did not reduce agitation. Conversely the soft toy cat significantly reduced agitation.

Motomura et al. [213] included 8 women (mean age 84.8 years) residing in a nursing home and evaluated the efficacy of animal-assisted therapy, consisting of two dogs visiting for 1 hour, over 4 consecutive days, to reduce apathy or irritability. The outcomes were measured using the Geriatric Depression Scale, Physical Self-Maintenance Scale and MMSE. The intervention did not show any significant change on any of the outcomes evaluated.

Sellers et al. [214] included 4 residents with dementia to evaluate the efficacy of a visiting dog. Agitation was measured with the Agitated Behaviors Mapping Instrument and Social Behavior Observation Checklist. The authors reported that the intervention reduced agitated behavior during treatment and increased observed social behavior, but data and p-values were not reported.

**Dining Room Environment**

Two small (n=38) pre-post studies examined the effect of improved lighting and table-setting contrast in dining room environment [81] (AMSTAR score =7). One study (Brush 2002; n=25)
found a positive effect on problem behaviors using the Meal Assistance Screening Tool, while the other study (Koss 1998; n=13) found a statistically significant reduction in daily agitation.

**Special Care Units**

In a Cochrane review, Lai 2009 (AMSTAR=8) examined Special Care Units (SCUs) for dementia individuals with behavioral problems. SCUs are characterized by trained staff, special care programs, an altered physical environment, and involvement of families. This SR included one quasi-experimental study and seven observational studies (6 prospective cohort studies and 1 prospective case-controlled study). The absence of randomized trials is likely a consequence of important practical and ethical issues in applying this methodology in older subjects with dementia and behavioral problems. Only one case-controlled study evaluated agitation and used NPI and CMAI to measure the outcome in 65 participants with dementia [215]. The results showed no significant changes in outcomes at three months; however, there were small but significant improvements in the NPI score in favor of the SCU group at 6 months (WMD -4.30 (95% CI -7.22 to -1.38), 12 months (WMD -4.30 (95% CI -7.22 to -1.38)), and 18 months (WMD -5.40 (95% CI -9.16 to -1.65)). The same study also evaluated the effect of SCU on mood at three months and the results showed a small significant effect in favor of SCU [WMD -6.30 (95% CI -7.88 to -4.72)][215].
Discussion

Given the well-known negative side effects of commonly prescribed drugs to control behavioral disturbances (BPSD) in patients with dementia, non-pharmacological interventions have gained increasing attention in recent years as an alternative first-line approach to treat BPSD. This overview addresses the evidence supporting the efficacy of these interventions in community and residential care settings. We identified a number of SRs, which often focused on single interventions although, in several instances, multicomponent interventions were also examined. With the present overview, we have created a compendium of the types of non-pharmacological interventions, including the component of each single intervention, the dosage (when available), and the duration of the treatment.

In the absence of a validated taxonomy, we categorized the interventions according to the following classification: sensory stimulation interventions; cognitive/emotion-oriented interventions; behavior management techniques (further subdivided according to the recipient of the intervention, i.e. the person with dementia, the caregiver or the staff); Multicomponent interventions and other interventions, such as exercise and animal-assisted therapies.

Among sensory simulation interventions, the only convincingly effective intervention for reducing behavioral symptoms (specifically agitation, aggressive behavior) was music therapy. According to the most comprehensive review of music therapy, this treatment also reduced anxiety. However, the evidence supporting the effectiveness of music therapy was limited by moderate, but significant, heterogeneity, probably related to the variability of the intervention (e.g., type of music, active involvement such as singing/playing a musical instrument and dancing or passive involvement such as listening) and the heterogeneity of the patient population in terms of the severity of dementia and type of dementia. The efficacy of Aromatherapy and Massage therapy, both associated with conflicting results, remains unknown. Light therapy and SMST therapy did not show any noteworthy effect for clinical practice.
The body of evidence concerning cognitive/emotion-oriented interventions, which include Reminiscence Therapy, Simulated Presence Therapy and Validation Therapy, had important methodological limitations. The quality of the primary studies was low, as reported by the review authors, and the sample size of the studies was not powered to detect statistically significant effects. Even when it was possible to combine studies in a meta-analysis, for example, for Simulated Presence Therapy, the pooled estimated effect was not statistically significant. Added to these shortcomings was the variability in the length and type of the interventions and the multitude of outcomes measured. Overall, convincing evidence supporting the effectiveness of these psychological interventions is lacking.

The most frequently assessed intervention in several trials was behavioral management techniques. The elements included in this type of intervention include behavioral or cognitive-behavioral therapy, functional analysis of specific behavior, individualized behavioral reinforcement strategies, communication training, and other therapies such as habit training, progressive muscle relaxation, and token economies [31]. The body of evidence supporting the effectiveness of behavioral management techniques includes both positive studies and negative studies. Among the types of behavioral management techniques which aimed to enhance communication skills, formal caregiver training, and dementia mapping provided in residential care, were found to be effective at reducing agitation. The evidence was convincing when the intervention was supervised by healthcare professionals, with the effectiveness possibly persisting for 3 to 6 months.

There is some evidence that multicomponent interventions that use a comprehensive, integrated multidisciplinary approach combining medical, psychiatric and nursing interventions can reduce severe behavioral problems in nursing home patients.

Other interventions such as animal-assisted and exercise therapy did not show any convincing effect on any BPSD.
Strengths of this overview

The present overview represents a substantial update of the overview [31], using a search strategy launched in 2009, that provided a comprehensive synthesis of the evidence about non-pharmacological interventions on BPSD. We systematically searched reviews available in 4 electronic databases and systematically collected the evidence regarding non-pharmacological interventions for the treatment of behavioral disturbances in patients with dementia. To allow the identification of SRs of all potential non-pharmacological interventions, we used a highly sensitive search strategy by avoiding the inclusion of any specific name of non-pharmacological interventions. We also assessed the methodological quality of the reviews using the AMSTAR criteria. Another strength of the present overview was the adoption of a systematic and transparent method, and use of duplicate, independent reviewers who performed the phases of study selection, data abstraction and data interpretation separately [38].

Limitations of the interpretation of the results

Overall, the SRs had a number of methodological limitations that could have affected the confidence in the reported results. First, the heterogeneity of the types and characteristics of the interventions, even within the same class of non-pharmacological interventions, was the most significant problem that emerged from the present study. One implication is that there are serious methodological issues that question the correctness, in our opinion, of combining studies in a meta-analysis as some authors have done previously. Moreover, in some studies the description of the interventions is too vague to allow a complete understanding of what was actually done. In addition, even in cases in which the intervention is well characterized, the dosage of the intervention, and the means used for its delivery, varied considerably. For example, in the case of music therapy, music interventions such as listening to music via headphones, based on participants’ musical preferences [83], differed from listening, playing percussion instruments, singing, movement or dance [82] and was observed across all 9 trials combined in the meta-analysis. In the case of aromatherapy, there were several essential oils that were used in the primary studies, but in some instances, even when
similar components were used (e.g., Melissa essential oil), the mode of administration differed among trials. Similarly, there was great variation in the intensity (from 2,500 to 10,000 lux), duration (1 to 9 hours), frequency of exposure (10 days to 10 weeks), and type of device used (Dawn-Dusk Simulator [216]), when light therapy was investigated for behavioral problems in dementia.

The variation in the characteristics of the interventions was particularly pronounced in the trials ascribed to behavioral management techniques. The trials used different conceptual frameworks, and sometimes broad and quite generic descriptions, to illustrate the interventions that at times were difficult to interpret and which influenced the content and quality of evidence of the SRs. In this area, it is therefore difficult to produce a satisfactory classification, which implies that different SRs did not consider the same group of studies, even when they clearly investigated non-pharmacological interventions specifically designed to improve behavioral management.

Finally, the arbitrary age cut-off of the patients (more than 60 years of age) and the exclusion of reviews published before 2009, constitute other limitations of the present overview. We did not evaluate the methodological assessment of the primary studies included in the reviews, as this will be the scope of our next publication in which we will also apply the GRADE criteria [38].

**Conclusion**

This overview succeeded in providing a complete and up-to-date compendium of non-pharmacological interventions in older people with dementia using recently published SRs and meta-analyses. The most promising treatments appeared to be music therapy and some behavioral management techniques, particularly those involving caregiver-oriented and staff-oriented interventions. Despite the considerable number of published articles included in this overview, the evidence supporting the efficacy of non-pharmacological interventions is limited due to methodological quality and sample size and to the presence of important variations in the taxonomy
of the non-pharmacological interventions, the outcomes assessed and the tools used to evaluate the outcomes.

Footnotes

Contributors IA, JMR, AC, RS, ACJ and DO conceived and designed the study. The manuscript of this protocol was drafted by IA, JMR, AC, RS, ACJ, AdG, and BHM and revised by MP, AnG, FMT and GDA. IA and JMR designed the search strategies; IA, JMR, FMT, and GDA performed the search, screening and assessment independently. AC arbitrated disagreements during the review. All authors contributed to data analysis and critical revision of the paper; additionally every author approved the final version.

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Competing interests

No conflicts of interest.

Data Sharing

There are no additional data.
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Figure 1. Study screening process

Potentially relevant reviews identified: 4392
Medline (PubMed): 1905
Embase: 3511
The Cochrane Library: 160
ISI Web of Knowledge: 646
CINAHL (EBSCO): 719
PsycINFO: 703

Reviews excluded based on abstract evaluation: 4328

Reviews identified for full-text evaluation: 64

Reviews excluded with reason: 23
- Behavioral outcomes not considered: 12
- Caregiver related outcomes: 8
- Non-pharmacological interventions not considered: 2
- Participants did not have dementia: 1

Systematic review/meta-analysis included: 41

Primary studies included for evaluation: 142

Figure 1. Study screening process

210x297mm (200 x 200 DPI)
Appendix 1

1. **Medline (via Pubmed)**
   (*dementia*[MeSH Terms] OR *dementia*[All Fields] OR dement*[tiab] OR "Alzheimer*[All Fields] OR "cognitive impairment" [tiab])
   MEDLINE[Title/Abstract] OR (systematic AND review[Title/Abstract] OR meta-analysis[Publication Type])

2. **EMBASE**
   #1 'dementia'/exp OR 'dementia'
   #2 'alzheimers disease'
   #3 cognitive AND impairment
   #4 'systematic review'
   #5 'meta analysis'
   #6 #1 OR #2 OR #3
   #7 #4 OR #5
   #8 #6 AND #7
   #9 #6 AND #7

3. **CINAHL**
   S1 (MH Dementia OR Alzheimer OR dementia)
   S2 (systematic review OR meta-analysis OR AB medline)
   S3 S1 AND S2

4. **Cochrane Library**
   #1 MeSH descriptor: [Dementia] explode all trees
   #2 dementia
   #3 alzheimer
   #4 cognitive impairment
   #5 MeSH descriptor: [Mild Cognitive Impairment] explode all trees
   #6 #1 or #2 or #3 or #4 or #5

5. **PsychInfo (via Ovid)**
   #1. (exp dementia/) OR (dementia.mp.) OR (alzheimer*.mp.) OR (exp alzheimer's disease/)
   #2. (systematic review.mp.) OR (exp Meta Analysis/) OR (MEDLINE.ab.)
   #3. #1 AND 2
Table 1. Aromatherapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akhondzadeh 2003 (1)</td>
<td>Placebo controlled, randomized trial</td>
<td>N=42; female 18; mean age 73; Diagnosis of AD, ADAS &lt;=2, CDR &gt;= 2 satisfied the NINCDS/ADRD A criteria</td>
<td>Intake of 60 drops of Melissa officinalis extract, daily for 4 months</td>
<td>Alzheimer’s disease assessment scale- cognitive subscale</td>
<td>Proportion of participants with agitation was significantly less in the treatment arm</td>
</tr>
<tr>
<td>Ballard 2002 (2)</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>N=72, female 43, mean age 78; agitation as defined on CMAI or NPI</td>
<td>10% blended Melissa oil in lotion; application on face and arms; 2 times/day for 4 weeks</td>
<td>CMAI, NPI BI, DCM, CDR</td>
<td>Significant improvement in CMAI score</td>
</tr>
<tr>
<td>Burns 2011 (3)</td>
<td>3-arm, double-blind parallel-group placebo-controlled randomized trial</td>
<td>N=114; female 48; mean age 85; agitation for 4 weeks minimally, CMAI &gt;39, satisfied the NINCDS/ADRD A criteria for possible Alzheimer disease</td>
<td>Arm 1: 10%Melissa oil in base lotion massage into the hands and upper arms, 1–2 min 2 times/day by carer of participants for 12 weeks. Arm 2: 5 mg donepezil daily for 1 month and increased to 10 mg afterwards, plus10% of placebo oil (sunflower) massage</td>
<td>NPI, PAS, BI</td>
<td>No significant improvement.</td>
</tr>
<tr>
<td>Cameron 2011 (4)</td>
<td>Cross-over, double-blind placebo-controlled randomized trial</td>
<td>N=18; sex not reported; mean age not reported; inclusion criteria not clearly reported (moderate to severe dementia) (setting not reported)</td>
<td>&lt;2% lemon balm oil</td>
<td>CMAI, PAS, NPI</td>
<td>gradual, but not statistically significant, reduction in scores in all outcome measures</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Population</td>
<td>Intervention</td>
<td>Outcome</td>
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<tr>
<td>Fu 2013 (5)</td>
<td>Single-blind parallel-group placebo-controlled randomized trial</td>
<td>N=67; female 40; mean age 84; MMSE &lt;=24/30; AD according to American Psychiatric Association DSM-IV-TR; a documented history of a minimum of two weeks of agitation or aggression in total (consecutively or 14 single days), within the past three months</td>
<td>Arm 1: 3% lavender mist (75 drops); Am 2: 3% lavender mist (75 drops) plus and massage twice a day for 10 days; each hand massaged for 2.5 minutes</td>
<td>CMAI-SF, MMSE</td>
<td>Significant less aggressive behavior in the arms that used active treatment</td>
</tr>
<tr>
<td>Gray 2002 (6)</td>
<td>Placebo controlled clinical trial</td>
<td>N=13; females 6; subjects that have “difficult-to-manage behaviors”</td>
<td>A mix of lavender, sweet orange, tea tree oil soaked into a cotton ball and taped to the lapel of each subject by caregiving staff; Total application: 16 times</td>
<td>Subjects were videotaped and rated by trained observers for frequency of resistive behaviors</td>
<td>No significant difference found</td>
</tr>
<tr>
<td>Holmes 2002 (7)</td>
<td>Placebo controlled clinical trial</td>
<td>N=15; females 7; diagnostic criteria based on ICD-10 for severe dementia and on a minimum score of 3 points on the PAS; NINCDS/ADRDA criteria for possible AD</td>
<td>Diffusion of 2% lavender oil for 10 sessions; each session lasted 2 h (16.00–18.00 hours) and was followed by placebo (water) for another 2 h; aroma-streams were used for diffusion</td>
<td>PAS</td>
<td>Nine patients (60%) showed an improvement, five (33%) showed no change and one patient (7%) showed a worsening of agitated behavior during aromatherapy</td>
</tr>
<tr>
<td>Lin 2007(8)</td>
<td>Placebo-controlled crossover randomized trial</td>
<td>N=70; female 41; mean age 78; Participants with dementia diagnosed with DSM-IV, with clinically significant agitation identified using Chinese version CAMI</td>
<td>Inhalation of essential oils in cosmetic cotton containing lavender diffused by aroma diffuser. Diffusers were placed at each side of the pillow during sleep at night for at least 1 h.</td>
<td>Chinese version CMAI, CNPI, Chinese version MMSE</td>
<td>Significant improvement in CNPI and CCMAI</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcome</td>
<td>Findings/Comments</td>
</tr>
<tr>
<td>-------------------------------</td>
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</tr>
<tr>
<td>O'Connor 2011 (9)</td>
<td>Cross-over, single-blind placebo-controlled randomized trial</td>
<td>N=66; female 39; mean age 78; Clinical Dementia Rating scale; physically agitated behavior;</td>
<td>30% lavender (<em>Lavandula angustifolia</em>) in jojoba oil</td>
<td>Observation of behavior, MMSE, CMAI, Philadelphia Geriatric Center Affect Rating Scale</td>
<td>No statistical difference between the groups</td>
</tr>
<tr>
<td>Smallwood 2001 (10)</td>
<td>3-arm, single-blinded randomized, controlled trial</td>
<td>N=21; Participants with dementia diagnosed by a psychiatrist</td>
<td>Arm 1: lavender oil massage; Arm 2: plain oil massage; Arm 3: conversation and lavender oil diffusion; All 3 arms received treatment twice in a specific period of the day and twice a week</td>
<td>Video-tapes recording behavior for 15 min in each specified 4 periods during the day, at baseline, and after treatment. Video recordings were rated by 2 blinded raters.</td>
<td>Only in 1 period (between 15.00–17.00 hours) a consistent reduction in agitation was observed in the lavender oil massage arm than in the other two arms.</td>
</tr>
<tr>
<td>Snow 2004 (11)</td>
<td>Placebo controlled clinical trial</td>
<td>N=28; females 26; mean age 86; Probable AD with “marked agitation”; CMAI applied by nursing staff</td>
<td>2 drops of undiluted oil containing lavender, thyme, and unscented grape-seed oil was placed every 3 h on an absorbent fabric sachet pinned near the clavicular part of each subject’s shirt. 3 applications/day</td>
<td>CMAI (rated every 2 days); Severe Impairment Rating Scale; MMSE</td>
<td>No evidence of reduction of agitation</td>
</tr>
</tbody>
</table>
Table 2 describes the type of interventions, the outcomes and the results of the primary studies included in the Message therapy reviews.

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hollyday-Walsh</td>
<td>Before-after study</td>
<td>52 participants (39 women and 13 men; mean age 90 years)</td>
<td>Intervention group: 10- to 15-minute massage of the upper extremities; Control group:</td>
<td>Behavioral Symptoms from the MDS; a) wandering; b) verbally abusive behavioral symptoms; c) physically abusive behavioral symptoms; d) socially inappropriate/disruptive behavior; and e) resistance to care</td>
<td>Massage therapy was significantly associated with improvement for 4 of the 5 outcomes</td>
</tr>
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<tr>
<td>Remington 2002</td>
<td>Randomized trial</td>
<td>42 nursing home residents with a diagnosis of &quot;Chronic organic brain syndrome&quot;</td>
<td>Intervention group: hand massage Frequency: One treatment of 10 min.) Control group: no touch</td>
<td>a) agitation (CMAI) b) Agitation reduced: MD 7.83 (4.30, 11.36)]</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Characteristics of Bright light therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancoi-Israel 2003</td>
<td>3-arm, single-blind, randomized controlled trial</td>
<td>92 nursing home residents; female; mean age 82; MMSE mean=5.7 (SD 5.6, range 0-22)</td>
<td>Active group: Bright light &gt; 2500 Lux: time of day 9.30-11.30 or 17.30-19.30 daily; Control group: Dim, red light (control)&lt; 300 Lux: time of day 9.30-11.30 daily; Device used: Apollo “Brite-Lite” box placed 1 m from resident Duration of treatment: 10 days</td>
<td>Agitation: ABRS and CMAI; Sleep: sleep duration, sleep efficiency, night-time activity measured after 10 days of treatment</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Findings</td>
</tr>
<tr>
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<tr>
<td>Barrick (15)</td>
<td>Cluster-unit crossover design</td>
<td>66 participants in two residential care settings</td>
<td>Active group: AM bright light (7–11 AM); PM bright light (4–8 PM); All Day bright light (7 AM – 8 PM); Control group: Standard light (i.e. the baseline condition).</td>
<td>CMAI</td>
<td>Ambient bright light resulted in not effective in reducing agitation and may exacerbate behavioral symptoms</td>
</tr>
<tr>
<td>Burns 2009 (16)</td>
<td>Single-blinded randomized trial</td>
<td>48 nursing home residents, female 32; mean age 83; any type of dementia</td>
<td>Active group: Bright light 10,000 lux from 10.00 hrs - noon (Brite-Lite box placed in front of resident); Control group: Standard florescent tube light at 100 lux from 1000 hrs - noon. Received treatment daily for two weeks. Duration of treatment: 14 days (weeks 2 and 3)</td>
<td>CMAI (agitation) MMSE (cognition) CSDD (depression)</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Dowling 2005 (17)</td>
<td>Randomized controlled trial</td>
<td>70 nursing home residents; female 57; mean age 84; MMSE 0-23 (mean=7, SD 7)</td>
<td>Active group 1: Bright light exposure &gt;2500 lux morning (9:30-10:30 am); Active group 2: Bright light exposure &gt;2500 lux afternoon (3:30-4:30pm) or supplemented using Apollo Brite Lite IV box placed at least 4 feet from resident. Control group: The control group received usual indoor light (150-200 lux) and participated in their regular activities. Frequency: Daily, Monday through Friday. Duration: 10 weeks.</td>
<td>NPI-NH (agitation, depression)</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Hickman (18)</td>
<td>Cluster-unit crossover trial</td>
<td>66 older adults with dementia</td>
<td>Active group: Morning bright light, evening bright light, all-day bright light (2,000 to 2,500 lux). Control group and 500 to 600 lux</td>
<td>Depression was assessed using the CSDD</td>
<td>No significant effect</td>
</tr>
</tbody>
</table>
### Table 4. Characteristics of Sensory Garden and Horticultural activities for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riemersma 2008 (19)</td>
<td></td>
<td>199 nursing home patients; mean age 85; any type of dementia</td>
<td>Active group 1: light exposure (using Plexiglas diffusers mounted in ceiling) 1000 lux Active group 2: light exposure (using Plexiglas diffusers mounted in ceiling) 400 lux + melatonin Active group 3: melatonin only Light exposure frequency: from 9:00 - 18:00 Control group: inactive light</td>
<td>Agitation (CMAI), Cognition (MMSE), Sleep latency and sleep latency ADLs (NI-ADL), Psychiatric symptoms (NPI-NH), Depression (Cornell Scale)</td>
<td>No significant different between the groups</td>
</tr>
</tbody>
</table>

CSDD = Cornell Scale for Depression in Dementia
### Table 5a. Music therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi 2009(27)</td>
<td>CT</td>
<td>N=20, mean age 75, dementia (Alzheimer’s, vascular, other)</td>
<td>Singing song, analysis of libretto, making musical instruments, playing piano and hand bells, song drawing and writing; 50 min/3x per week for 5 weeks;</td>
<td>MMSE, GDS, Gqol, NPI-Q</td>
<td>reduced behavioral symptoms and depression</td>
</tr>
<tr>
<td>Clark 1998(28)</td>
<td>RCT</td>
<td>N=18, all types of dementia</td>
<td>Listening to music individually, 2 weeks duration,</td>
<td>Agitation checklist</td>
<td></td>
</tr>
<tr>
<td>Cooke 2010 (29)</td>
<td>RCT</td>
<td>N=24, early to mid stage dementia</td>
<td>Singing, playing music, listening to music in a group, 8 weeks,</td>
<td>GDS</td>
<td></td>
</tr>
<tr>
<td>Goka 2005 (30)</td>
<td>CT</td>
<td>N=22, mean age 78, mild to moderate Alzheimer’s dementia</td>
<td>Combined music and reminiscence therapy. Singing songs associated with memories of the participants; 60 min/1x per week for 10 weeks;</td>
<td>MMSE, HDS-R, DAD, NPI, TORS</td>
<td>non statistically significant reduction of behavioral symptoms</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N</td>
<td>Age</td>
<td>Diagnosis</td>
<td>Intervention</td>
</tr>
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</tr>
<tr>
<td>Groene 1993 (31)</td>
<td>RCT</td>
<td>30</td>
<td>Mean age 78, Alzheimer's dementia</td>
<td>Listening, playing percussion instruments, singing, movement or dance. Music based on personal references; 7 sessions, 15 min each</td>
<td>Wandering behavior, seating/proximity behavior, MMSE</td>
</tr>
<tr>
<td>Guétin 2009 (32)</td>
<td>RCT</td>
<td>30</td>
<td>Mean age 86, mild to moderate Alzheimer's dementia</td>
<td>Listened to music based on participants' music preferences via headphones; 20 min/1x per week for 24 weeks; control group: rest and reading</td>
<td>Hamilton Scale, GDS</td>
</tr>
<tr>
<td>Ikeda 2006 (33)</td>
<td>RCT</td>
<td>12</td>
<td>Mean age 86, severe senile dementia</td>
<td>One on one rhythm exercise. Shake hands and clap in rhythm to music based on participant's music preferences with a familiar song; 15 min/5x per week for 7 weeks;</td>
<td>MMSE, GBS, ROM-T, D-EMS</td>
</tr>
<tr>
<td>Irish 2006 (34)</td>
<td>CT, repeated measures</td>
<td>10</td>
<td>Mean age 86, Alzheimer's dementia</td>
<td>Listening to classical music individually, 2 weeks</td>
<td>State-Trait Anxiety Inventory</td>
</tr>
<tr>
<td>Ledger 2007 (35)</td>
<td>CT</td>
<td>45</td>
<td>Mean age 85, mild to moderate senile Alzheimer's dementia</td>
<td>Listening to music played by the therapist, singing, playing instruments, moving to music and discussing feelings and memories; 30-45 min/1x per week for at least 42 weeks to 1 year;</td>
<td>CMAI-long</td>
</tr>
<tr>
<td>Mihara 2004 (36)</td>
<td>CT</td>
<td>19</td>
<td>Mean age 86, dementia</td>
<td>Greeting, gentle stretching exercise and breath control, singing familiar music, playing a musical instrument and rhythm activity; 30-45 min/1x per week</td>
<td>AR-MCL, TORS, JSS-D, JSS-E, VI</td>
</tr>
<tr>
<td>Reference</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Findings</td>
</tr>
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</tr>
<tr>
<td>Miura 2005 (37)</td>
<td>CT</td>
<td>N=31, mean age 78, mild Alzheimer's, vascular, frontotemporal and Lewy body and other dementia</td>
<td>Opening song, rhythm exercise, singing, music appreciation and reminiscence; &lt;60 min/1x per week for 8-10 weeks;</td>
<td>BI, GDS, MMSE, SKT, ZBI, SPECT, D-EMS</td>
<td>Non statistically significant increase of depression</td>
</tr>
<tr>
<td>Nair 2010 (38)</td>
<td>Randomized, cross-over</td>
<td>N=37</td>
<td>Listening to classical music in a group, 12 weeks duration,</td>
<td>Behavior chart</td>
<td></td>
</tr>
<tr>
<td>Hokkanen 2008 (39)</td>
<td>RCT</td>
<td>29 nursing home residents, female 22, mean age 82, dementia (Alzheimer's, vascular, other)</td>
<td>Dance movement therapy; 30-45 min/1x per week for 9 weeks; control group: regular nursing home activities</td>
<td>The word list savings score; Clock drawing test; Cookie Theft; NOSGER</td>
<td>No change in behaviors</td>
</tr>
<tr>
<td>Raglio 2008 (40)</td>
<td>RCT</td>
<td>N=59, mean age 85, Alzheimer's, mixed and vascular dementia</td>
<td>Singing and body movement with music to promote communication; 30 sessions of 30 min/session for 16 weeks; control group: educational and entertainment activities</td>
<td>MMSE, BI, NPI, MTCS</td>
<td>Reduction of behavioral symptoms; non statistically significant reduction of depression</td>
</tr>
<tr>
<td>Raglio 2010 (41)</td>
<td>RCT</td>
<td>N=20, female 15, mean age 86</td>
<td>Improvisation-based music therapy: two 30-min/session/week for 15 weeks; control group: educational and occupational activities</td>
<td>NPI</td>
<td>NPI no change; NPI sub-score depression improved</td>
</tr>
<tr>
<td>Raglio 2010 (42)</td>
<td>RCT</td>
<td>N=60, female 55, mean age 85, Alzheimer's, mixed and vascular dementia</td>
<td>Patients and music therapist express their emotions playing musical instruments and interacting; 30 min/3x per week for 12 weeks; control group: educational support and entertainment activities</td>
<td>MMSE, BI, NPI</td>
<td>Non statistically significant reduction of behavioral symptoms and depression</td>
</tr>
<tr>
<td>Remington 2002 (43)</td>
<td>RCT</td>
<td>N=34, mean age 82, mild</td>
<td>Listening to music with a</td>
<td>CMAI</td>
<td>Reduced behavioral</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N</td>
<td>Population Description</td>
<td>Treatment</td>
<td>Outcomes</td>
</tr>
<tr>
<td>------------------</td>
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</tr>
<tr>
<td>Silber 1999(44)</td>
<td>RCT</td>
<td>18</td>
<td>N=18, mean age 78, senile Alzheimer's dementia</td>
<td>Slow tempo via a portable CD player; 1 session for 10 min;</td>
<td>MMSE</td>
</tr>
<tr>
<td>Smith 1986(45)</td>
<td>CT</td>
<td>12</td>
<td>N=12, mean age 84, Alzheimer's dementia</td>
<td>James Last's “violins in love” playing as background music; 1 session/month for 2 months;</td>
<td>MMSQ</td>
</tr>
<tr>
<td>Sung 2006a(46)</td>
<td>RCT</td>
<td>36</td>
<td>N=36, mean age 78, dementia</td>
<td>Body and limb movement to participant’s familiar music with moderate tempo via a CD player; 30 min/2x per week for &gt;4 weeks; control group: usual care</td>
<td>CMAI</td>
</tr>
<tr>
<td>Sung 2006b(47)</td>
<td>RCT</td>
<td>57</td>
<td>N=57, mean age reported, dementia</td>
<td>Listened to music based on personal references; 30 min/2x per week for 6 weeks;</td>
<td>CMAI</td>
</tr>
<tr>
<td>Sung 2010(48)</td>
<td>CT</td>
<td>52</td>
<td>N=52, mean age 80, moderate and severe senile dementia</td>
<td>Listened to music based on participant’s music preferences via CD players; 30 min/2x week for &gt;6 weeks;</td>
<td>RAID</td>
</tr>
</tbody>
</table>
| Suzuki 2004(49)  | CT     | 23   | N=23, mean age 84, Alzheimer’s and vascular dementia                                  | Opening song, singing songs based on personal references, playing hand-held drums; 60 min/2x per week | MMSE, NM scale, N-ADL, MOSES, CgA MMSE language subscale: improved (d=0.60, p=0.012); MOSES: ‘irritability’ sub-

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Table 5b. Dance therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hokkanen 2008</td>
<td>RCT</td>
<td>29 nursing home residents, female 22, mean age 82, dementia (Alzheimer’s,</td>
<td>Dance movement therapy; 30-45 min/1x per week for 9 weeks; control group: regular nursing home activities</td>
<td>The word list savings score; Clock drawing test; Cookie Theft; NOSGER</td>
<td>No change in behaviors.</td>
</tr>
</tbody>
</table>
NOSGER (Nurses’ Observation Scale for Geriatric Patients)

Table 6. Snoezelen Multisensory Stimulation Therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker 2001 (53)</td>
<td>Randomized trial</td>
<td>50 subjects with Alzheimer’s disease, vascular dementia or mixed diagnosis; mean age 78; female 25</td>
<td>Eight standardized multi-sensory programs.</td>
<td>INTERACT (22-item); INTERACT (12-item); Carry-over and long-term effect Behavioral: REHAB (general behavior subscale and deviant behavior subscale) Behavior Rating Scale (BRS) of CAPE</td>
<td>No significant effects on any scale of behavioral symptoms were found either immediately after intervention or at one-month post-follow-up</td>
</tr>
<tr>
<td>Baker 2003 (54)</td>
<td>Randomized trial</td>
<td>136 subjects diagnosed with Alzheimer’s, vascular or mixed dementia; mean MMSE scores snoezelen group (9.4) and the control group (6.7) (p=0.01)</td>
<td>Eight multi-sensory programs</td>
<td>INTERACT (22-item); INTERACT (12-item); Carry-over and long-term effect Behavioral: REHAB (general behavior subscale and deviant behavior subscale) Behavior Rating Scale of CAPE</td>
<td>There were no longer-term treatment effects of the integrated snoezelen-care program on behavior.</td>
</tr>
<tr>
<td>van Weert 2005 (55)</td>
<td>CT</td>
<td>N=125, female 101, mean age 84, dementia (DSM-III-R)</td>
<td>Snoezelen; 18 months, control group non specified</td>
<td>CMAI (Cohen-Mansfield Agitation Inventory);</td>
<td>Improvement in intervention group for short term period but not for long follow-up</td>
</tr>
<tr>
<td>Primary study</td>
<td>Study design</td>
<td>Population</td>
<td>Type of intervention, dose, route of administration in active group</td>
<td>Outcome measures</td>
<td>Results</td>
</tr>
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</tr>
<tr>
<td>Hozumi 1996 (56)øé</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>27 subjects With multi-infarct dementia with irregular sleep-wake patterns and nocturnal behavior disorders and/or delirium; 15 female; age 58 - 86 Inpatients</td>
<td>Stimulator type: HESS-10 Waveform: rectangular pulses Frequency: 6 - 80 Hz Pulse duration: 0.2 ms maximum, rms of 256 microA Amplitude: 6 - 8 V Electrode location: transcranial with electrodes attached to the &quot;forehead and inion with a head-band&quot; Treatment duration: 20 minutes daily for 2 weeks Placebo treatment: same as experimental but electrodes disconnected from the device.</td>
<td>Behavior disorder improved p &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Scherder 1998 (57)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>18 subjects in a residential home. mean age 82 (70 – 91); Shortened MMSE mean 4.4/12. 7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances, NINCDS-ADRDA criteria</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental except no current delivered.</td>
<td>Beoordelingsschaal vor Oudere Patienten</td>
<td>Behavioral disorder not improved</td>
</tr>
<tr>
<td>Scherder 1999 (58)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>18 subjects, 9 expt, 9 control Lived in a residential home for elderly people. Age: 70 - 91yrs, mean 81.7 Shortened MMSE mean 4.4/12. 7 or less/12 on this</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz</td>
<td>Beoordelingsschaal vor Oudere Patienten</td>
<td>Behavioral disorder not improved</td>
</tr>
<tr>
<td>Scherder 1999 (59)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Holland</td>
<td>15 subjects, 8 experimental, 7 control (16 initially, one from the control group did not tolerate the actigraphic assessment and was therefore excluded from the study) Lived in a residential home for elderly people. Shortened MMSE mean 4.4/12, 7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances. Met NINCDS-ADRDA criteria for clinical diagnosis of Alzheimers type, GDS stage 6 (mid-stage) with symptoms present at least 6 months, all scored 17 or less on Hamilton Rating Scale for Depression. Exclusion: history of psychiatric disorder, alcoholism, cerebral trauma, cerebrovascular disease, hydrocephalus, neoplasm, infection, epilepsy, disturbances of consciousness, focal brain abnormalities, pacemaker.</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Poles switched daily. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental except no current delivered.</td>
<td></td>
</tr>
<tr>
<td>Scherder 1999 (60)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Holland</td>
<td>Lived in a residential home for elderly people. Meeting NINCDS-ADRDA criteria for clinical diagnosis of dementia of Alzheimer's type, GDS stage 6 (midstage) with symptoms. Stimulation not described except that Premier 10s stimulator used. Study 1: TENS for 6 hours/day, therapist present throughout</td>
<td>Beoordelingsschaal voor Oudere Patiënten No improvement in behavioral disturbances Behavioral disorder not improved</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Country: Holland</td>
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<tr>
<td>Scherder 2000 (61)</td>
<td>20 subjects, 10 experimental, 10 control Institutionalized elderly persons 17 F, 3 M Age: 62-91 yrs, mean 86.9 Inclusion criterion for shortened MMSE 8 - 12/12, BUT a range of 7 - 11, mean of 9.4 described for the experimental group, range 8 - 12, mean 9.7 for controls.</td>
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<tr>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Poles switched daily. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental except no current delivered.</td>
<td>Beoordelingsschaal voor Oudere Patienten</td>
<td>Need of help subscale only: ns Behavior inventory: ns</td>
<td></td>
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<tr>
<td>Scherder 2002 (62)</td>
<td>18 subjects, 9 experimental, 9 control Institutionalized elderly persons. Mean age: experimental group 87.1, control group 87.67. Mean education: experimental group 3.11, control group 2.88. MMSE experimental group 18.33, control group 19.67. All met NINCDS-ADRDA criteria for the clinical diagnosis of probably AD and stage 5 of the GDS.</td>
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<tr>
<td>Stimulator: Alphastim 100 Waveform: Bipolar asymmetric rectangular waves, Frequency: 0.5 Hz Pulse duration: not given Amplitude: 10 - 600 microA, to just below reported sensation of tingling and/or dizziness or to maximum if no sensation experienced. Electrode Placement: clipped to the earlobes. Treatment duration and frequency: 30 minutes/day between 1500 and 1900 h, 5 days/week, 6 weeks Placebo</td>
<td>Beoordelingsschaal voor Oudere Patienten</td>
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</tr>
<tr>
<td>Study</td>
<td>Intervention</td>
<td>Subjects</td>
<td>Stimulator Type</td>
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<tr>
<td>Scherder 2003 (63)</td>
<td>Same as for the experimental group except no current administered.</td>
<td>16 subjects, 8 expt, 8 control lived in a residential home for elderly people. Age: 70 - 91yrs, mean 81.7 Shortened MMSE mean 4.4/12. 7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances. Met NINCDS-ADRDA criteria for clinical diagnosis of dementia of Alzheimer's type, GDS stage 5 (midstage) with symptoms present at least 6 months</td>
<td>Stimulator type: Premier 10s 1. Stimulator: Alphastim 100 Waveform: Bipolar asymmetric rectangular waves, Frequency: 0.5 Hz 30 mins/day, 5 days a week 2. Control appeared the same with electrodes but no current</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Someren 1998 (64)</td>
<td>Randomized, double-blind, placebo-controlled Country: Holland</td>
<td>14 subjects (initial sample of 19, 14 completed), 6 treated, 8 placebo. 13 F, 1 M Nursing home patients. Diagnosed with early stage probable AD NINCDS-ADRDA Age mean 84 +/- 1.5 Dutch cognitive screening test (CST): mean 10.2 +/- 0.4 (approx 18 on MMSE)</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between shoulder blades. Treatment duration: 30 min/day, 5 days/week, 6 weeks</td>
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<tr>
<td>Placebo intervention: Same as experimental except no current delivered.</td>
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</tbody>
</table>
Table 8. Characteristics of cognitive stimulation-based interventions for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baines 1987 (65)</td>
<td>Cross-over, randomized trial</td>
<td>UK 15 residents living in care home, female 14; Mean age=81.5. ‘Moderate to severe Impairment of cognitive functioning’</td>
<td>Reality orientation (board and discussion of current orientating information through newspapers, photographs, calendars and clocks etc., with materials selected to stimulate all five senses) Reminiscence therapy</td>
<td>Cognitive: Information/Orientation &amp; Mental Ability (CAPE) Behavior: Behavioral Rating Scale (CAPE) Wellbeing: Life Satisfaction Index; Problem Behavior Rating Scale Communication: Holden Communication Scale</td>
<td>No significant difference between the groups in terms of the behavioral disturbances</td>
</tr>
<tr>
<td>Chapman 2004 (66)</td>
<td>Randomized controlled trial</td>
<td>donepezil-plus-stimulation group; n = 26; donepezil-only group; n = 28. mild to moderate Alzheimer’s disease (AD; Mini-Mental Status Examination score of 12-28); 54 to 91 years</td>
<td>Cognitive-communicational stimulation in combination with donepezil</td>
<td>Texas Functional Living Scale, NPI, QoL, the Clinician Interview-Based Impression of A group x time interaction for the stimulation plus donepezil-group on irritability compared with the donepezil-only group.</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Setting</td>
<td>Participants</td>
<td>Outcome Measures</td>
<td>Results</td>
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<tr>
<td>Ferrario 1991</td>
<td>Randomized controlled trial</td>
<td>19 elderly residents; female 8; mean age 82 Subjects with cognitive disturbances - MMSE range 18-25</td>
<td>Reality orientation</td>
<td>Cognition: CAPE I/O, Self-care: MOSES Behavior problems: MOSES - irritable, withdrawn Mood: MOSES</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Onder 2005</td>
<td>3-arm, randomized controlled trial</td>
<td>USA 156 home residents; female 113; mean Age 75.8 Subjects with probable Alzheimer's Disease, on Donepezil treatment for at least 3 months; MMSE 20.1 (sd 3.1)</td>
<td>Current information, topics of general interest, historical events and famous people, attention, memory and visuo-spatial</td>
<td>Cognition: MMSE; ADAS-Cog ADL: Barthel; IADL Behavior problems: NPI Family caregiver outcomes: Hamilton anxiety and depression scales; Caregiver Burden Inventory; SF-36</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Niu 2010</td>
<td>randomized, controlled, rater-blind clinical trial</td>
<td>China 32 patients with mild to moderate Alzheimer's disease showing marked BPSD</td>
<td>Cognitive stimulation focused on tasks requiring executive functions and working memory</td>
<td>BPSD</td>
<td>Change in Neuropsychiatric Inventory total score (MD -2.06 (95% CI -2.91 to -1.21, P&lt;0.001)</td>
</tr>
<tr>
<td>Spector 2001</td>
<td>Randomized controlled trial</td>
<td>UK 35 patients in day centers and residential homes Moderate dementia (MMSE: 11.5±4.4 for intervention group; 15.5±4.4 for control group) mean age: 85.7±6.7</td>
<td>Intervention: mixture of reality orientation and other Cognitive learning exercises (15 sessions twice weekly, 45 min/session) Control: usual care</td>
<td>BRS</td>
<td>No statistical difference between the two groups</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design</td>
<td>Country</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcome Measures</td>
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<tr>
<td>Spector 2003 (71)</td>
<td>Randomized controlled trial</td>
<td>UK</td>
<td>201 patients in residential homes or day centers (Moderate dementia, MMSE: 14.4±3.8, Mean age: 85.3±7.0)</td>
<td>Intervention: mixture of reality orientation and other cognitive stimulation exercises (14 sessions twice weekly, 45 min/session) Control: normal activities</td>
<td>CAPE-BRS</td>
</tr>
<tr>
<td>Tadaka 2004 (72)</td>
<td>Randomized controlled trial</td>
<td>60 community-dwelling older adults with dementia; mean age 83</td>
<td>Intervention: reminiscence and reality orientation (1.5h once a-week, for 10 weeks)</td>
<td>MMSE, MOSES</td>
<td></td>
</tr>
<tr>
<td>Wallis 1983(73)</td>
<td>Randomized controlled trial</td>
<td>UK</td>
<td>38 long-stay residential patients: mean age: 71.8±16.6 for intervention group; 68.0±15.4 for control group (Severe dementia, RCP mental scale: 34.5±29.9 for intervention group; 37.6±28.9 for control group)</td>
<td>Intervention: reorientation therapy (5 times a week, 30 min/session for 3 months) Control: occupational therapy, both individual and group activities</td>
<td>Crichton Behavior Rating Scale</td>
</tr>
<tr>
<td>Primary study</td>
<td>Study design</td>
<td>Population</td>
<td>Type of intervention, dose, route of administration in active group</td>
<td>Outcome measures</td>
<td>Results</td>
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<tr>
<td>Deponte 2007</td>
<td>Randomized trial</td>
<td>N=30, mean age 86.8; dementia diagnosis (unspecified)</td>
<td>Sensorial reminiscence, 3 months</td>
<td>NPI</td>
<td>Unclear</td>
</tr>
<tr>
<td>Haight 2006</td>
<td>Pre/post design, randomized controlled trial</td>
<td>N=31, age range 60-99, dementia</td>
<td>Life review/life story book sessions; 1 hr/1x per week for 8 weeks</td>
<td>MMSE; Cornell scale for depression in dementia; Alzheimer's mood scale; functional independence scale; communication observation scale; memory and behavior problems checklist</td>
<td>Significant change in depression, communication, positive mood and cognition</td>
</tr>
<tr>
<td>Haslam 2010</td>
<td>Pre/post design, randomized controlled trial</td>
<td>N=73, age range (dementia) 62-93, dementia and non-dementia</td>
<td>Discussion and conversation; 30 min/1x per week for 4 weeks</td>
<td>Addenbrooke's cognitive examination - revised; hospital anxiety and depression scale; OoL-AD</td>
<td>Group reminiscence enhanced memory performance.</td>
</tr>
<tr>
<td>Lai 2004</td>
<td>Pre/post design, randomized controlled trial</td>
<td>N=101, age 86, dementia</td>
<td>Stimulate recall during conversation with life story book; 30 min/1x per week for 6 weeks</td>
<td>Social engagement scale, well-being/ill-being scale</td>
<td>Psychosocial well-being improved significantly in the intervention group.</td>
</tr>
<tr>
<td>Morgan 2010</td>
<td>Pre/post design, randomized controlled trial</td>
<td>N=17, age 83, dementia</td>
<td>Life review/life story book sessions; 30 min-1 hr/1x per week for 8-12 weeks</td>
<td>Geriatric depression scale; autobiographical memory interview</td>
<td>Improved autobiographical memory and reduced depression</td>
</tr>
<tr>
<td>Politis 2004</td>
<td>Pre/post design, randomized controlled trial</td>
<td>N=36, age 84, dementia</td>
<td>Generating questions from a geriatrics network kit and using the responses of participants to initiate conversations; 30 min/3x per week for 4 weeks</td>
<td>NPI, NPI-apathy, Alzheimer's disease-related quality-of-life scale; Copper Ridge activity index</td>
<td>No difference between intervention and control groups on NPI and NPI-apathy</td>
</tr>
<tr>
<td>Wang 2009</td>
<td>Randomized trial</td>
<td>N=77, age 79; mild-moderate dementia (clinical dementia)</td>
<td>Structured group reminiscence therapy; 1x per week for 8 weeks</td>
<td>CAPE-BRS</td>
<td>No difference between intervention and control groups</td>
</tr>
</tbody>
</table>
CAPE-BRS (Clifton Assessment Procedures for the Elderly–Behavioral Rating Scale); NPI (Neuropsychiatric Inventory)

Table 10. Validation therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peoples 1982 (74)</td>
<td>RCT</td>
<td>N=31, female 23, mean age 88</td>
<td>A group leader, song leader or hostess was identified. Activities included discussion on a previously agreed topic, singing and movement activity, and a closing ritual followed by refreshments.; 30 min/1x per week for 6 weeks; control groups: reminiscence therapy and usual care</td>
<td>BAT TADCE</td>
<td>Behavior improved at 6 weeks.</td>
</tr>
<tr>
<td>Robb 1986 (75)</td>
<td>RCT</td>
<td>N=36 (N=25 with dementia), female?, mean age 80.5</td>
<td>Details of the Validation therapy were not reported; 2x per week for 9 months; control group: usual treatment (e.g. medication)</td>
<td>MSQ PGCMS MSBS</td>
<td>No effects detected.</td>
</tr>
<tr>
<td>Toseland 1997 (76)</td>
<td>RCT</td>
<td>N=88, female 66, mean age 87.6; moderate level of dementia (SPMSQ and VSI)</td>
<td>Four sessions, 5-10 minutes each. Session 1. Introductions, greetings and singing. Session 2. Interaction about a topic of interest, reminiscing encouraged. Session 3. Program activity, singing or poetry. Session 4. Refreshments and individual good byes.; 30 min/4x per week for 52 weeks; control groups: social contact group and usual care</td>
<td>CMAI MOSES GIPB</td>
<td>Depression decreased in validation therapy group.</td>
</tr>
</tbody>
</table>

Behavior assessment tool (BAT); Cohen Mansfield Agitation Inventory (CMAI); Geriatric Indices of Positive Behavior (GIPB); Minimum data set - Resident Assessment Protocol (MDS RAP); Multi-dimensional Observational Scale for Elderly Subjects (MOSES); Minimal Social Behavior Scale (MSBS); Mental Status Questionnaire (MSQ); Philadelphia Geriatric Center Morale Scale (PGCMS); Short Portable Mental Status Questionnaire (SPMSQ); Tool for Assessing the Degree of Confusion in the Elderly (TADCE); Validation Screening Instrument (VSI)

Table 11. Simulated presence therapy for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camberg 1999 (77)</td>
<td>Latin-square, double-blind</td>
<td>N=54, , mean age 83,</td>
<td>Audiotape prepared by a family member or a surrogate</td>
<td>SOAPD, visual analog scales, positive affect scales, facial diagrams of mood,</td>
<td>No significant difference for agitation and mood.</td>
</tr>
<tr>
<td>Cheston 2007(78)</td>
<td>within-subjects</td>
<td>N=6, , age range 75-91,</td>
<td>Audiotape prepared by participant’s spouse</td>
<td>PRS</td>
<td></td>
</tr>
<tr>
<td>Cohen-Mansfield 1997(79)</td>
<td>CT</td>
<td>N=32, , mean age 87,</td>
<td>Videotape prepared by family members or researchers</td>
<td>CMAI, tape recordings and standardized observations for verbally disruptive behaviors</td>
<td>Verbally disruptive behaviors decreased by 46% during the videotape, and 16% during the no-intervention.</td>
</tr>
<tr>
<td>Study</td>
<td>Design Type</td>
<td>N-value</td>
<td>Age Range</td>
<td>Source of Audiotape</td>
<td>Behavioral Symptoms Measure</td>
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<tr>
<td>Garland 2007</td>
<td>RCT (single-blind)</td>
<td>30</td>
<td>66-93</td>
<td>Audiotape prepared by a family member and a psychologist</td>
<td>CMAI</td>
</tr>
<tr>
<td>Miller 2001</td>
<td>quasi-experimental</td>
<td>7</td>
<td>68-89</td>
<td>Audiotape prepared by a family member</td>
<td>HRS (first 4 items)</td>
</tr>
<tr>
<td>Peak 2002</td>
<td>within-subjects</td>
<td>4</td>
<td>64-84</td>
<td>Audiotape prepared by participant’s spouse</td>
<td>modified PRS</td>
</tr>
<tr>
<td>Woods 1995</td>
<td>quasi-experimental</td>
<td>8</td>
<td>71-97</td>
<td>Audiotape prepared by caregiver</td>
<td>DBRS</td>
</tr>
</tbody>
</table>

CMAI (Cohen-Mansfield Agitation Inventory); DBRS (Disruptive Behavior Rating Scale); PRS (Positive Response Schedule for Severe Dementia)
Table 12. Characteristics of Primary studies that assessed Behavioral Management Techniques for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burgio 2003 (84)</td>
<td>Randomized controlled</td>
<td>Participants with dementia: mean MMSE score 14.53 for white participants and 10.98 for African American participants, with a mean age of 78.83; 70 white + 48 African American primary caregivers</td>
<td>Caregiver Skill Training Intervention based on a manual</td>
<td>Revised Memory and Behavior Problem Checklist (RMBPC)</td>
<td>No statistical difference between the groups.</td>
</tr>
<tr>
<td>(care giver based)</td>
<td>trial</td>
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<tr>
<td>Burns 2003 (85)</td>
<td>Randomized controlled</td>
<td>167 Dyads; 66 care givers</td>
<td>Active group: REACH intervention: behavior care (individualized educational program on BMT) + individualized care giver stress–coping management training in 8 face-to-face sessions and 30 telephone calls over 24 months Control group: behavior care only.</td>
<td>Change in care giver bother associated with CARE RECIPIENT problem behavior: RMBPC.</td>
<td>Significant improvement in care giver bother associated with care recipient behaviors;</td>
</tr>
<tr>
<td>(care giver based)</td>
<td>trial</td>
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<tr>
<td>Chenoweth 2009 (86)</td>
<td>(care giver based)</td>
<td>289 residents (15 residential homes) with need-driven behaviors, mean age: 85 years.</td>
<td>Caregiver training and support intervention in either: Person Centered Care or Dementia Care Mapping</td>
<td>Cohen Mansfield Agitation Inventory (CMAI) Neuropsychiatric Inventory (NPI) Quality of life in late stage dementia (QUALID) Quality interactions schedule (QUIS)</td>
<td>Significant reduction in agitation</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>Interventions</td>
<td>Outcomes</td>
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<tr>
<td>Farran 2004 (caregiver based)</td>
<td>Randomized controlled trial</td>
<td>295 participants with AD or dementia; MMSE &lt; 24, mean MMSE score: 12.6</td>
<td>Intervention: Caregiver skill. Control: Information and Support Orientated Group Intervention</td>
<td>Behavior Management Skill Revised (BMS-R); Revised Memory and Problem Behavior Checklist (RMPBC) No statistical differences between the two groups</td>
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</tr>
<tr>
<td>Fossey 2006 (87)</td>
<td>Cluster randomized controlled trial</td>
<td>346 residents with dementia (12 residential homes); mean age: 82 years.</td>
<td>Active group: Training and Support Intervention for nursing home staff. Control group: treatment as usual</td>
<td>Cohen Mansfield Agitation Inventory (CMAI) No statistical difference (mean difference 0.3, −8.3 to 8.9; P = 0.94).</td>
<td></td>
</tr>
<tr>
<td>Gitlin 2001 (88)</td>
<td>Randomized clinical trial</td>
<td></td>
<td>Active group: Education about dementia and impact of home environment on behavioral problems and activities of daily living deficits; instruction in problem solving and developing strategies, to manage caregiving concerns: Control group: usual care</td>
<td>-Frequency of behavioral problems: MBPC + 4 other behaviors; -care giver distress associated with behavioral problems - care-giving self-efficacy assessed by care givers No effects on frequency of care recipient behavioral problems (intervention 20.25-17.2; control 18.74-14.43);</td>
<td></td>
</tr>
<tr>
<td>Gitlin 2003 (89) (caregiver based)</td>
<td>Randomized clinical trial</td>
<td>255 ITT care givers; 190 IA at 6mth;</td>
<td>Active group: Home environmental skill building program over 5, 90-min home visits and 1, 30-min telephone contact: education, and physical and social environment modifications; similar to (44) (Philadelphia REACH) Control group: usual care(information only)</td>
<td>- Number of disruption-related behaviors: modified RMBPC presence or absence of behaviors rather than frequency; - care giver upset with disruptive behaviors: RMBPC No change in disruptive behaviors for care recipients (intervention 2.14-1.88; control 2.16-1.96);</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
<td>Findings</td>
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<tr>
<td>Gonyea 2006 (90) (caregiver based)</td>
<td>Randomized controlled trial</td>
<td>80 participants with Alzheimer's disease; mean age: 77; 80 caregivers, mean age 64 years,</td>
<td>Active group: Caregiver group based training intervention (Project CARE); Control group: Psychoeducational control group using similar structure to the intervention group.</td>
<td>Neuropsychiatric inventory (NPI) - Severity &amp; Distress</td>
<td>No statistical difference for severity of problem behaviors (-0.24 [-0.68 to 0.20]).</td>
</tr>
<tr>
<td>Gormley 2001 (91) (caregiver based)</td>
<td>Controlled clinical trial</td>
<td>62 participants with dementia; mean age 76 years, average MMSE score 13.3; 62 caregivers mean age was 68; predominantly female.</td>
<td>Active group: Education and aggressive behavior management training program for caregiver in 4 in-home sessions over 8 weeks Control group: discussions with caregiver and care recipient on a variety of non-specific care-related issues and advice on services.</td>
<td>a) Overall symptomatology and severity of behavioral problems: BEHAVEAD; b) care recipient aggressive behavior: Rating Scale for Aggressive Behavior in the Elderly</td>
<td>- no difference in overall behavioral problems (intervention 8-6.5; control 8-7.8); - no diff in patient's aggressive behavior(intervention 9.4-6.9; control 8.8-8.6);</td>
</tr>
<tr>
<td>Graff 2007 (92)</td>
<td>Randomized clinical trial</td>
<td>135 ITT dyads; 132 IA</td>
<td>Active group: Occupational therapy in 10 sessions over 5 weeks: therapist taught care recipient to use compensatory and environmental strategies to improve their performance of daily activities and caregiver trained by means of cognitive behavioral treatment. Control group: waitlist</td>
<td>care recipient mood (CSDD)</td>
<td>Significantly improved care recipients' mood (intervention 8.3 - 6.2; control 8.1-9.2).</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Setting</td>
<td>Participants</td>
<td>Intervention</td>
<td>Control Interventions</td>
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<tr>
<td><strong>Huang 2003 (93)</strong>&lt;br&gt;(care giver based)</td>
<td>Randomized clinical trial</td>
<td>Northern Taiwan.</td>
<td>48 participants with dementia (and their family caregiver); predominantly female; mean age of 76 years; mean MMSE score 13.1. (care givers predominantly female, mean age 56)</td>
<td>Active group: a home-based Caregiver Training Program; Control group: written materials only</td>
<td>Chinese version of Cohen Mansfield Agitation Inventory (CMAI) (care recipient Frequency of problem behaviors &amp; care giver Self efficacy).</td>
</tr>
<tr>
<td><strong>Losada-Baltar 2004 (94)</strong>&lt;br&gt;(care giver based)</td>
<td>Randomized clinical trial</td>
<td>Spain</td>
<td>31 participants with dementia; mean age 80</td>
<td>Active group: Caregiver Problem-Solving Skills Training Intervention Control group: usual care</td>
<td>Memory and Behavior Check List (MBCL) - Frequency &amp; Reaction</td>
</tr>
<tr>
<td><strong>Marriott 2000 (95)</strong>&lt;br&gt;(care giver based)</td>
<td>3-arm, controlled clinical trial</td>
<td></td>
<td>42 dyads</td>
<td>Care giver education, stress management and skills training to manage behavior of care recipient and coping with change; 1 session every 2 weeks, for a total of 14 sessions. Control groups: one group received one type of dyad interview, which was also used in the treatment group, and another control group did not receive any interview.</td>
<td>Change in BPSD: a) depressive symptoms: CSDD; b) behavioral disturbances and c) psychotic symptoms: MOUSEPAD</td>
</tr>
<tr>
<td><strong>Mador 2004 (96)</strong></td>
<td>Randomized clinical trial</td>
<td>Hospital setting; mean age 83</td>
<td>71 patients with dementia</td>
<td>Active group: Staff Training Hospital Behavior Advisory Service Control group: Usual Care</td>
<td>Pittsburgh Agitation Scale (PAS)</td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Participants</td>
<td>Intervention details</td>
<td>Comparison outcomes</td>
<td></td>
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<tr>
<td>-------------------------------------------</td>
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<tr>
<td>McCurry 2005 (97) (care giver based)</td>
<td>RCT</td>
<td>36 dyads</td>
<td>Nighttime Insomnia Treatment and Education for Alzheimer’s Disease and training care givers to implement treatment; six, 1-hour sessions at home, over 2-months. Control group: general dementia education and care giver support</td>
<td>Night time and sleep behavior, daytime sleepiness and depression (RMBPC) of care recipients. The number of awakenings and the total time awake at night, as well as daytime sleepiness, all significantly diminished. Depression was significantly reduced post-intervention, but not at 6 month follow-up.</td>
<td></td>
</tr>
<tr>
<td>Moniz-Cook 2008 (98) (care giver based)</td>
<td>Controlled clinical trial</td>
<td>113 dyads</td>
<td>Care givers assisted by community mental health nurses to manage problematic behavior of dementia patients and to cope with stress; home visits 1x/week for 4 weeks plus addition contact as needed over 18 months. Control group: usual care</td>
<td>Frequency of problem behavior and difficulty managing problematic behavior by care giver: adapted-Gilleard Problem Checklist. Problem behaviors significantly decreased over 18 months, but a post-hoc analysis demonstrated the effect was dependent on care managers.</td>
<td></td>
</tr>
<tr>
<td>Nobili 2004 (99) (care giver based)</td>
<td>RCT</td>
<td>69 dyads</td>
<td>A psychologist (60 min visit) and an occupational therapist (90 min visit) gave information and advice to care givers; Control group: helpline and information on community services and legal and economic features of caregiving</td>
<td>Frequency of problem behaviors in care recipient: Spontaneous Behavior Interview – Section C. Problem behaviors and frequency of delusions significantly decreased.</td>
<td></td>
</tr>
<tr>
<td>Proctor 1999 (100)</td>
<td>Randomized trial</td>
<td>105 participants with dementia (in 12 nursing and residential homes); mean age of 83</td>
<td>Active group: Staff training and Education Intervention including psychosocial management of resident’s behavioral problems; Control group: usual care</td>
<td>Crichton Royal Behavioral Rating Scale (CRBRS). No statistical difference for the outcome severity of problem behaviors (-0.02 [-0.41 to 0.36])</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Intervention</td>
<td>Outcome measures</td>
<td>Findings</td>
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<tr>
<td>Teri 1997(101)</td>
<td>RCT</td>
<td>72 dyads</td>
<td>Two behavioral therapy interventions. One comprised education and discussing and planning strategies to manage problem behavior and to maximize cognitive function of the care recipient (increase pleasant events plus self-care strategies). The other intervention included the aforementioned elements, but substituting problem solving for the pleasant events; 60- minsession, 1x/week for 9 weeks:</td>
<td>Hamilton Depression Rating Scale, CSDD and Beck Depression Inventory</td>
<td>Depression significantly improved with both behavioral interventions. No significant difference between either active treatment.</td>
</tr>
<tr>
<td>Teri 2003 (102) (care giver based)</td>
<td>RCT</td>
<td>153 dyads</td>
<td>Exercise for care recipients and care givers taught behavioral management techniques and given education on dementia; 12 hour sessions 2x/week for 3 weeks, followed by sessions 1x/week for 4 weeks, then sessions 2x/week for 2 weeks. Control group: usual care</td>
<td>Hamilton Depression Rating Scale and CSDD; RMBPC (delays in institutionalization related to problem behavior and associated care giver distress)</td>
<td>Depression significantly reduced at 3 months, but no significant difference at 24 months. (Care recipients with higher initial depression maintained improvements.). Trend for significantly decreased institutionalization due to problem behaviors at 24 months.</td>
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<tr>
<td>Study</td>
<td>Methodology</td>
<td>Sample Size</td>
<td>Intervention Details</td>
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</tr>
<tr>
<td>Teri 2003</td>
<td>Controlled clinical trial</td>
<td>95 dyads</td>
<td>Care givers taught behavioral management techniques and communication strategies; increased care giver support. Pleasant events also increased for care recipients; home sessions 1x/week for 8, then monthly telephone calls for 4 months. Control group: usual care</td>
<td>NPI, RMBPC Severity and frequency of behavior problems significantly declined.</td>
<td></td>
</tr>
<tr>
<td>Ulstein 2007</td>
<td>RCT</td>
<td>171 dyads</td>
<td>Care givers taught problem solving and communication techniques, in addition to usual care; four and a half months. Control group: usual care</td>
<td>NPI No significant difference in care recipient behavioral symptoms. (Post-hoc analysis revealed behavioral symptoms significantly improved in female care recipients.)</td>
<td></td>
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</table>

CSDD = Cornell Scale for Depression in Dementia
Table 13. Characteristics of Multicomponent Interventions for behavioral disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Brodaty 2003 (104)</td>
<td>RCT</td>
<td>N=86 with dementia, female 62, mean age 83 years, control group: usual care</td>
<td>1. Psychogeriatric case management: psychological, social and pharmacological treatment supervised by a geriatric psychiatrist and administered by a multidisciplinary team; one team member is case manager. 2. Psychiatric consultation: management plans provided to NH-staff and general practitioner.</td>
<td>AMTS, BEHAVE-AD, EBAS-DEP, FAST, CSD, NPI, SAPS, GDS, CRI, HRS-D/HAM-D, CIRS, DSM-IV</td>
<td>Improvement in depression and psychosis in all 3 groups</td>
</tr>
<tr>
<td>Opie 2002 (105)</td>
<td>RCT</td>
<td>N=99 with dementia, female 72, mean age 84 years</td>
<td>Individually tailored medical, pharmacological, psychosocial and nursing interventions targeting specific behaviors</td>
<td>MMSE, CMAI, BAGS, GDS</td>
<td>Decline in restlessness, physical aggression and verbal disruption; still detectable in 75% of subjects after 1 month</td>
</tr>
<tr>
<td>Proctor 1999 (100)</td>
<td>RCT</td>
<td>N=105 with dementia, female 87, mean age 83 years</td>
<td>Staff training and education</td>
<td>AGECAT organic, AGECAT depression, Chrichton scale, Barthel index</td>
<td>Significantly improved scores for depression and cognition</td>
</tr>
<tr>
<td>Rovner 1996 (106)</td>
<td>RCT</td>
<td>N=81 with dementia and somatic illness, female 63, mean age 82 years</td>
<td>Activity program, psychotropic drug management and weekly educational meetings with a psychiatrist</td>
<td>MMSE, CMAI, PGDRS, DSM-III-R, RUGS</td>
<td>Significant decrease of behavior disorders, restraint use and antipsychotic use in intervention group</td>
</tr>
</tbody>
</table>

MMSE=Mini-Mental State Examination; CMAI=Cohen-Mansfield Agitation Inventory; PGDRS=Psychogeriatric Dependency Rating Scale; DSM-III-R=Diagnostic and Statistic Manual of Mental Disorders (III-R=third edition revisited; IV=fourth edition); RUGS= Resource Utilization Groups; AGECAT= Automatic Geriatric Examination for Computer-Assisted Taxonomy; BAGS=Behavior Assessment Graphical System; GDS=Geriatric Depression Scale; AMTS=Abbreviated Mental Test Score; BEHAVE-AD=Behavioral Pathology in Alzheimer’s Disease Rating Scale; EBAS-DEP=Even Briefer Assessment for Depression; FAST=Functional assessment Staging CSD=Cornell Scale for Depression in Dementia; NPI=NeuroPsychiatric Inventory; SAPS=Scale for the Assessment of Positive symptoms; CRI=Resident Classification Index; HRS-D/HAM-D=Hamilton Depression Rating Scale; CIRS=Cumulative Illness Rating Scale
**Table 14. Exercise-based intervention for behavioral disturbances in patients with dementia**

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burgener 2008 (107)</td>
<td>repeated-measures randomized design</td>
<td>43 people with early stage dementia referred (self-referred or by the physician); female 20; mean age 77;</td>
<td>Multimodal intervention (Tai Chi exercise, cognitive-behavioral therapies and support group) on; Duration 1 hour x 3 times a week for 40 weeks</td>
<td>Geriatric depression scale (GDS 15)</td>
<td>At 20 weeks: GDS increased (worsened) by 0.4 in intervention and 0.9 in control (difference not significant)</td>
</tr>
<tr>
<td>Rolland 2007 (108)</td>
<td>single-blind, parallel group, randomized controlled trial</td>
<td>134 ambulatory subjects with AD living in nursing homes</td>
<td>Exercise program (aerobic, strength, flexibility, and balance training). Duration 1 hour x 2 times a week for 40 weeks Walking was required for at least half of the session. A circular walking trail was created and adapted for each exercise group</td>
<td>Montgomery-Asberg Depression Rating Scale (MADRS)</td>
<td>At 12 months: MADRS 13.4 (+/-8.0) in intervention and 14.8 (+/-7.2) in control (difference not significant)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Description</td>
<td>Intervention</td>
<td>Outcomes</td>
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<tr>
<td>Teri 2003</td>
<td>Randomized</td>
<td>153 community dwelling patients meeting National Institute of Neurological and Communicative Disease and Stroke/Alzheimer Disease and Related Disorders Association criteria for Alzheimer disease; 63 female; mean age 78;</td>
<td>Combined exercise - Aerobic, endurance, strength, balance and flexibility training - and caregiver training program, Reducing Disability in Alzheimer Disease; Duration 1/2 hour x 7 times a week for 12 weeks</td>
<td>Cornell scale for depression: At 2 years: mean difference, 2.14; 95% CI, 0.14–4.17; p&lt;0.04</td>
<td></td>
</tr>
<tr>
<td>Steinberg 2009</td>
<td>Randomized</td>
<td>27 home dwelling patients with Alzheimer’s (MMSE&gt;10); 21 female; mean age 78;</td>
<td>Active group: Daily program of aerobic, balance and flexibility, and strength training, shown to patients and caregivers, to be done at home; Control: homesafety assessment</td>
<td>Depression and apathy measured with NPI and the Cornell Scale for Depression in Dementia: No statistical difference between groups</td>
<td></td>
</tr>
<tr>
<td>Van de Winckel 2004</td>
<td>Randomized</td>
<td>25 female residents; mean age 81; NINCDS-ARDA criteria used for probable or possible Alzheimer’s disease and MMSE score lower than 24/30 (MMSE 11);</td>
<td>Active group: daily physical exercises (strength, balance and flexibility) supported by music for 30 min/session Duration 1/2 hour x 7 times a week for 12 weeks Control group: daily conversation</td>
<td>Beoordelingsschaalvoor Oudere Patienten/Evaluation scale for older patients: At 3 months: no significant difference in depressive behavior subscale</td>
<td></td>
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References


# PRISMA 2009 Checklist

<table>
<thead>
<tr>
<th>Section/topic</th>
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<th>Checklist item</th>
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<tbody>
<tr>
<td><strong>TITLE</strong></td>
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</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
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<tr>
<td><strong>ABSTRACT</strong></td>
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<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>2</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
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<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>5-6</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>6</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
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<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>doi:10.1136/bmjopen-2014-007488</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>7</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>7</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>7</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>7</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>8</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>8</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>Not used</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>Not measured</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.</td>
<td>Data not pooled</td>
</tr>
</tbody>
</table>
### PRISMA 2009 Checklist

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>Not performed</td>
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<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>Not performed</td>
</tr>
</tbody>
</table>

### RESULTS

| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 9 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 9-47 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | NA |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 9-47 Supplemental file |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | NA |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |

### DISCUSSION

| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 48-50 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 50 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 51-52 |

### FUNDING

| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 52 |

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Systematic review of systematic reviews of non-pharmacological interventions to treat behavioral disturbances in older patients with dementia. The SENATOR-OnTop series

<table>
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<td>Date Submitted by the Author</td>
<td>05-Sep-2016</td>
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<td>Complete List of Authors</td>
<td>Abraha, Iosief; Italian National Research Center on Aging (IRCCS-INRCA), Geriatrics and Geriatric Emergency Care Rimland, Joseph; Italian National Research Center on Aging (INRCA), Geriatrics and Geriatric Emergency Care Trotta, Fabiana; Italian National Research Center on Aging (INRCA), Geriatrics and Geriatric Emergency Care Dell'Aquila, Giuseppina; Italian National Research Center on Aging (INRCA), Geriatrics and Geriatric Emergency Care Cruz-Jentoft, Alfonso; Hospital Universitario Ramón y Caja, Servicio de Geriatría Petrovic, Mirko; Ghent University, Department of Internal Medicine (Geriatrics) Gudmundsson, Adalsteinn; Landspitali University Hospital Reykjavik Soiza, Roy; NHS Grampian, Geriatric Medicine O'Mahony, Denis; University College Cork, Department of Medicine (Geriatrics) Guaita, Antonio; &quot;Golgi Cenci&quot; Foundation Cherubini, Antonio; Italian National Research Center on Aging (INRCA), Geriatrics and Geriatric Emergency Care</td>
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<td>Secondary Subject Heading</td>
<td>Neurology, Mental health</td>
</tr>
<tr>
<td>Keywords</td>
<td>Non-pharmacological intervention, Dementia &lt; NEUROLOGY, Alzheimer's disease, Behavioral and psychological symptoms in dementia, BPSD</td>
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Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series

Iosief Abraha, Joseph M Rimland, Fabiana Mirella Trotta, Giuseppina Dell’Aquila, Alfonso Cruz-Jentoft, Mirko Petrovic, Adalsteinn Gudmundsson, Roy Soiza, Denis O’Mahony, Antonio Guaita, Antonio Cherubini

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e-mail: iosief_a@yahoo.it
Abstract

Objective To provide an overview of non-pharmacological interventions for behavioural and psychological symptoms in dementia (BPSD).

Design Systematic overview of reviews


Eligibility criteria Systematic reviews (SRs) that included at least one comparative study evaluating any non-pharmacological intervention, to treat BPSD.

Data extraction Eligible studies were selected and data extracted independently by two reviewers. The AMSTAR checklist was used to assess the quality of the SRs.

Data analysis Extracted data were synthesised using a narrative approach.

Results Thirty-eight systematic reviews and 142 primary studies were identified, comprising the following categories of non-pharmacological interventions: (a) Sensory Stimulation Interventions (12 SR, 27 primary studies) that encompassed: acupressure, aromatherapy, massage/touch therapy, light therapy, sensory garden; (b) Cognitive/Emotion-oriented Interventions (33 SRs; 70 primary studies) that included cognitive stimulation, music/dance therapy, dance therapy, snoezelen, transcutaneous electrical nerve stimulation, reminiscence therapy, validation therapy, simulated presence therapy; (c) Behaviour Management Techniques (6 SRs; 32 primary studies); and (d) other therapies (5 SR, 12 primary studies) comprising exercise therapy, animal-assisted therapy, Special Care Unit and Dining Room Environment-based interventions.

Music therapy was effective in reducing agitation (SMD, -0.49; 95% confidence interval (CI), -0.82 to -0.17; p=0.003), and anxiety [SMD, -0.64; 95% CI, -1.05 to -0.24; P=0.002]. Home-based behavioural management techniques, caregiver-based interventions or staff training in
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communication skills, person-centred care or dementia care mapping with supervision during implementation were found to be effective for symptomatic and severe agitation.

Conclusions

A large number of non-pharmacological interventions for BPSD were identified. The majority of the studies had great variation in how the same type of intervention was defined and applied, the follow-up duration, the type of outcome measured, usually with modest sample size. Overall, music therapy and behavioural management techniques were effective for reducing BPSD.

Strengths and limitations of this study

- Non-pharmacological interventions have gained increasing attention in recent years as an alternative first-line approach to treat Behavioural and Psychological Symptoms in Dementia (BPSD).

- The strength of this review is its extensive, comprehensive systematic search of studies that investigated non-pharmacological interventions for BPSD. It provides a compendium of the types of non-pharmacological interventions, including the component of each single intervention, the dosage (when available), and the duration of the treatment.

- Primary studies were generally of limited sample size; there was substantial variation in the characteristics of the intervention and the authors of primary studies reported different conceptual frameworks, and sometimes broad, and quite generic descriptions, of the interventions.
Introduction

Dementia is a neuropsychiatric syndrome characterized by cognitive decline and progressive
deterioration of daily function, often associated with behavioural disturbances.

The prevalence of dementia in older subjects is reported to be approximately 6% worldwide \(^1\) and,
with global population ageing, it is expected to rise, although some recent studies have suggested
descending trends in dementia frequency \(^2\). Dementia presents a considerable burden to families and
caregivers and is becoming a major challenge for all healthcare systems, as well as for society at
large \(^3\)\(^4\). Alzheimer’s disease (AD) is the most common form of dementia in older people,
accounting for 60 percent of cases.

Approximately 5 out of every 6 patients with dementia, including those living at home, will develop
behavioural and psychological symptoms during the course of the disease \(^5\)\(^8\). Behavioural and
psychological symptoms of dementia (BPSD) are defined as signs and symptoms of disturbed
behaviour, mood, thought, or perception \(^9\). These disturbances, namely agitation, depression,
elation, delusions and hallucinations are strongly correlated with each other \(^10\)\(^11\). Twenty percent of
those initially without symptoms will manifest them within 2 years of dementia diagnosis \(^12\),
whereas 50% to 80% of those with clinically important symptoms remain agitated for several
months \(^13\). In addition, at least 50% of patients with dementia present with significant BPSD on a
monthly basis \(^14\). Agitation, together with depression, hinder activities and relationships, cause
feelings of helplessness and distress in families and formal caregivers \(^15\) and are strong predictors
for poor quality of life \(^16\), as well as nursing home admission \(^17\).

Currently, options for treating BPSD include both pharmacological and non-pharmacological
therapies \(^18\)\(^19\). Psychotropic medications are often used to reduce the frequency and severity of
BPSD, but in the majority of patients, they provide only modest symptom control \(^20\)\(^22\). A recent
trial reported that the addition of citalopram to psychosocial support significantly reduced agitation
and caregiver distress \(^23\). However, their adverse effects are common and problematic, in particular
the increased risk of falls and fractures \(^{24}\) stroke and even mortality \(^{25}\). In addition, there is some evidence that the use of benzodiazepines to treat agitation in patients with dementia may increase cognitive decline \(^{24}\) and may expose patients to an immediate risk of injurious falls \(^{26}\). Finally, memantine and cholinesterase inhibitors are considered to be of very limited value to improve agitation in subjects with AD \(^{27,28}\).

In general, non-pharmacological interventions are considered a preferable alternative to psychotropic pharmacotherapy for treating BPSD \(^{29}\). However, there is conflicting evidence concerning the efficacy and practicality of non-pharmacological interventions to improve BPSD, particularly agitation \(^{9,30}\).

The purpose of the present overview is to assess the evidence supporting these non-pharmacological interventions with a view to providing a working compendium for the non-drug management of BPSD.

The present overview updates the evidence on the same theme gathered by a previous systematic overview published in 2011 \(^{31}\).
Methods

This work is part of the ONTOP (Optimal Evidence-Based Non-drug Therapies in Older People) project, a workpackage of a European Union funded FP7 research named SENATOR (Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older peRsons). The ONTOP aim is to undertake a literature search of systematic reviews and provide clinical recommendations concerning evidence-based non-pharmacological treatments of several prevalent medical conditions affecting older people, including delirium\textsuperscript{32,33}, pressure ulcers \textsuperscript{33-35}, falls\textsuperscript{36,37}, stroke and heart failure. A protocol that describes the search strategy, screening and inclusion criteria, has been previously published\textsuperscript{38}. Briefly, to obtain the evidence regarding the non-pharmacological interventions, we first identified published SRs using a systematic search across several databases. After processing eligible SRs, we identified and obtained primary studies from these SRs to generate the compendium of non-pharmacological interventions. In a subsequent work will present the assessment of the body of evidence and provide recommendations according to the GRADE approach\textsuperscript{38}.

Search Strategy and Inclusion Criteria for Systematic Reviews

The search sources included the Cochrane Database of Systematic Reviews, PubMed, PsycINFO, and CINAHL (Appendix 1). Two criteria were considered for further evaluation of an abstract: a) a paper defined as a review or a meta-analysis; b) the use of any non-pharmacological intervention to treat behavioural disturbances in patients with dementia. The publication years ranged from 2009 to March 2015.

Subsequently, full-texts of relevant abstracts were obtained and screened to identify systematic reviews of interest based on: a) the use of at least one medical literature database; b) the inclusion of at least one primary study; and c) the use of at least one non-pharmacological intervention to treat behavioural disturbances in people aged 60+ years.
We assessed the methodological quality of each SR using the AMSTAR (A Measurement Tool to Assess Reviews) instrument that contains 11-items. Final grading of the methodological quality of each SR was based on the overall score and reported as either "high" (score ≥ 8), "medium" (score 4-7) or "low" (score ≤ 3). Two reviewers independently assessed the quality of the SRs and disagreements were resolved by consensus.

**Data extraction and management**

From each SR, the following data were collected: the publication year, the databases searched, the study population, the non-pharmacological interventions, the number of primary studies included, the outcome measures and the AMSTAR score. Pairs of reviewers independently screened titles, abstracts and full-texts of articles. Disagreements were resolved by discussion or, where necessary, by consulting another author.

**Outcome measures**

We focused on reviews that considered BPSD, as a primary outcome, measured by (a) multi-domain scales (e.g. Neuropsychiatric Inventory (NPI), Brief Psychiatric Rating Scale (BPRS)), (b) scales specific to agitation (e.g. Cohen-Mansfield Agitation Inventory (CMAI)), and (c) scales specific to depression or anxiety (e.g. Cornell Scale for Depression in Dementia (CSDD)).

**Inclusion criteria for primary studies and assessment**

From the included SRs, we obtained any experimental comparative study, either randomised or nonrandomised, that investigated any non-pharmacological intervention to treat BPSD in older patients. Observational studies or before-after studies, with historical controls, were excluded. As outlined in our protocol, we extracted data from primary studies to perform meta-analyses and heterogeneity was addressed using the Cochrane Collaboration approach.

**Risk of bias assessment and grading the quality of evidence**

We used the Cochrane Collaboration method to evaluate the risk of bias. The domains considered were random sequence generation, allocation concealment, blinding of participants, personnel, or
outcome assessor\textsuperscript{40}, incomplete outcome data\textsuperscript{41}, selective reporting\textsuperscript{42} and other potential biases (e.g., balance in baseline characteristics). The overall quality of evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology that takes into account the risk of bias, consistency of results across the studies, precision of the results, directness, and likelihood of publication bias\textsuperscript{43}. Results regarding the risk of bias assessment, and grading the quality of evidence, will be provided in a companion paper.
Results

Our search strategy identified 4,392 abstracts of which 2,549 were duplicates and were subsequently removed. After abstract screening, 67 records were identified for full-text assessment. Of these, 38 reviews were included in this overview. From these SRs, we obtained 142 primary studies from which we abstracted details of the non-pharmacological interventions. Figure 1 shows the study screening process. Table 1 depicts the basic characteristics of the included SRs. The characteristic of relevant primary studies are reported in Appendix 2 as electronic Tables (eTable). The AMSTAR evaluation are summarized in Appendix 3

The interventions in this overview were classified according to the following categories: (a) Sensory Stimulation Interventions that encompass acupuncture, aromatherapy, massage therapy, light therapy, sensory garden intervention, cognitive stimulation, music/singing and dance therapy, snoezelen and transcutaneous electrical nerve stimulation (TENS) therapy; (b) Cognitive/Emotion-oriented Interventions that include reminiscence therapy, validation therapy, simulated presence therapy; and (c) Behavioural management technique and (d) Other interventions, such as exercise therapy, pet-therapy or special care unit.

Sensory Stimulation Interventions

Shiatsu and acupressure

Only one SR was identified. Robinson 2011\textsuperscript{44} (AMSTAR=7) investigated the evidence available for shiatsu and acupressure in BPSD. Shiatsu is a form of complementary medicine primarily developed in Japan, which employs gentle manipulations, stretches and pressure with the fingers, elbows, knees and feet. Acupressure is similar, but exerts pressure for longer on specific meridian points according to traditional Chinese medicine or acupoints of the human body in order to “balance energy fields”.

The authors identified 40 RCTs, 8 controlled clinical trials, 5 crossover trials, 6 within-subjects studies, 1 observational study, 10 uncontrolled studies and one prospective study. Only one
randomised trial (n=133 participants) using acupressure in dementia subjects was relevant for our assessment. The authors reported that agitation, aggression and physically non-aggressive behaviour all declined significantly in demented subjects.

**Aromatherapy**

Aromatherapy is proposed as a complementary intervention, to treat a wide range of health problems, including lack of sleep and behavioural symptoms for people with dementia. Aromatherapy is based on the use of plant products or aromatic plant oils to produce essential oils and blends of aromatic compounds. Aromatherapy can be delivered through massage or topical application, inhalation and water immersion.

Our systematic search identified 3 SRs that considered aromatherapy as an intervention to treat agitated behaviours and other outcomes in patients with dementia. The AMSTAR scores ranged from 6 to 8 across the reviews. The range of included primary studies varied from 4 to 13.

The most recent SR was a Cochrane review, which had the highest AMSTAR quality score (8). The review included only randomised trials and launched its last search strategy in January 2013. Seven studies with 428 participants were identified. The types of interventions included lavender-based (4 studies), Melissa-based (two studies) and lemon balm oil (1 study) aromatherapy. However, only two of these had usable data for pooling. The first study (n=71) reported a favourable treatment effect on measures of agitation (MD -11.1, 95% CI -19.9 to -2.2) and behavioural symptoms (MD -15.8, 95% CI -24.4 to -7.2), whereas the second trial (n=63) did not detect any difference in agitation (MD 0.00, 95% CI -1.36 to 1.36) or behavioural symptoms (n = 63, MD 2.80, 95% CI -5.84 to 11.44). The review authors remarked that the published studies used different scales to assess the behavioural symptoms and were limited both in sample size and methodological quality, particularly because of selective reporting bias.
The second review by Seitz \textsuperscript{29} consisted of any non-pharmacological interventions, including aromatherapy, to treat outcomes relevant to patients with dementia. The review reported data in a narrative way and cited only one study of aromatherapy \textsuperscript{53}, which was also included in the Cochrane review above \textsuperscript{48}. The review received an AMSTAR score of 6.

The third study was a review by Fung et al \textsuperscript{47}, which considered only aromatherapy as a non-pharmacological intervention. The review was judged to have moderate methodological quality (AMSTAR score=6). After performing a comprehensive search in several electronic databases, 11 studies were identified, with a total of 405 patients in different settings, including long-term care (LTC) homes, clinical centres and general and old age psychiatry. In addition to the trials included in the above cited Cochrane review, the review by Fung et al. \textsuperscript{47} included one randomised trial \textsuperscript{55} which was excluded in the Cochrane review because the route of administration was not reported and there was no mention of the type of the aromatherapy, in addition to 5 controlled clinical trials \textsuperscript{56-60}. Moreover, the Fung et al review \textsuperscript{47} did not include the two trials \textsuperscript{49,61,51} that were evaluated in the Cochrane review. The controlled clinical trials could not be included in a meta-analysis because of heterogeneity. The review highlighted the methodological limitations of the studies and reported promising results of aromatherapy. eTable 1 describes the type of interventions, the outcomes and the results of the primary studies included in the Aromatherapy reviews.

**Massage Therapy**

Massage and touch therapy have been proposed as non-pharmacological interventions to be used in dementia to offset manifestations of cognitive decline and behavioural disturbances, including related psychological problems, such as depression and anxiety, and to improve quality of life \textsuperscript{62}.

Two reviews were identified. The first was a Cochrane review \textsuperscript{63} that was included in the review by O’Neil\textsuperscript{31}. This review assessed the efficacy of Massage and Touch therapy for the treatment of BPSD. Its last search strategy was launched in 2006. The aim of the overview was to evaluate the effects of a range of massage and touch therapies on conditions associated with dementia, such as
anxiety, agitated behaviour and depression, to identify any adverse effects, and to provide recommendations for future trials. The review considered only randomised trials. The primary outcome measures were changes in the frequency and severity of various types of agitated behaviour, as observed by staff or investigators (short-term and long-term using any rating method), and the emotional well-being and the quality of life of the patients (rated by staff, investigators and/or patients themselves using any method).

Remington (2002) \(^{64}\) assessed the effect of music and massage in 68 nursing home residents with dementia (Alzheimer's disease, multi-infarct dementia or senile dementia). The subjects were randomly allocated into 4 groups: calming music, hand massage, simultaneous calming music and hand massage, and no intervention. The intervention lasted 10 minutes, and was given to each patient once.

The efficacy of treatment on 'agitation level' was evaluated with a modified version of the Cohen-Mansfield Agitation Inventory (CMAI) administered by trained research assistants who were blinded to treatment allocation when possible. The method of randomisation was unclear and to conceal allocation, sealed envelopes, without further explanation, were used. However, patients could have been excluded after allocation (if they had a CMAI score of 0 at baseline) and consequently the study was considered to have high risk of selection bias.

The trial found that agitated behaviour decreased, more so in the group receiving hand massage than in the group receiving no treatment. This treatment effect was consistently found, compared to baseline, for measurements taken during treatment, immediately after treatment, and one hour after treatment, and it was practically identical among the three groups receiving treatment (hand massage, calming music or both). The mean agitation score was in favour of massage therapy immediately after treatment [MD 7.83 (4.30 to 11.36)] and 1-hour after treatment [MD 12.12 (6.58, 17.66)].

The second review by Moyle et al. \(^{65}\) conducted a search in 10 databases in October 2011. The authors identified 13 studies that evaluated massage therapy for the treatment of behavioural
disturbances in patients with dementia, but only one study with a high methodological score, using the Validity Rating Tool, was identified. The included study, performed by Hollyday-Walsh, was a prospective before-after study in which 52 participants (39 women and 13 men; mean age 90 years) from two skilled nursing facilities in Northeastern Minnesota, USA, were enrolled. Patients were cognitively impaired and had a history of agitated behaviour confirmed by the facility staff. The intervention consisted of a 10- to 15-minute massage of the upper extremities (including the head, shoulders and hands), undertaken by a physical therapy assistant, during a 1-hour period identified by caregivers as the time the participant was usually most agitated (individualised for each participant). The outcomes of interest were assessed with a scale that used the five Behavioural Symptoms from the minimum data set; a) wandering; b) verbally abusive behavioural symptoms; c) physically abusive behavioural symptoms; d) socially inappropriate/disruptive behaviour; and e) resistance to care.

Methodologically, the study was considered at high risk of selection and performance bias given the study design and the nature of the intervention. In addition, it was unclear whether the outcome assessor was blinded. Massage therapy was significantly associated with improvement for 4 of the 5 outcomes examined, including wandering (0.38 vs. 0.16, P<0.001), verbally agitated behavioural symptoms (0.59 vs. 0.49, P=0.002), physically agitated behavioural symptoms (0.82 vs. 0.40, P<0.001), and resistance to care (0.10 vs. 0.09, P=0.022). eTable 2 describes the type of interventions, the outcomes and the results of the primary studies included in the Massage therapy reviews.

**Light therapy**

Rest-activity and sleep-wake cycles are controlled by the endogenous circadian rhythm generated by the suprachiasmatic nucleus (SCN) of the hypothalamus. Degenerative changes in the SCN appear to be a biological cause of circadian rhythm disturbances in people with dementia. In addition to the internal regulatory loss, older people (especially those with dementia) experience a reduction in sensory input, due to less visual sensitivity to light and less exposure to bright
environmental light. Evidence suggests that circadian rhythm disturbances may be reversed by stimulation of the suprachiasmatic nucleus with light.\textsuperscript{67}

Four reviews considered the use of bright light therapy to treat behavioural problems in patients with dementia.

The first was a Cochrane review\textsuperscript{67} (AMSTAR=10) with the aim of evaluating the effectiveness of light therapy to improve cognition, ADLs, sleep, challenging behaviour, and psychiatric disturbances associated with dementia. The search strategy was launched in January 2014. The included studies were randomised trials that compared any bright light therapy, including dim red light or dim, low-frequency blinking light less than 300 lux, to usual care. The primary outcome measures included cognition (global or single domain, e.g. memory), ADLs, sleep-wake disturbances, challenging behaviour (e.g. agitation), psychiatric disturbances (e.g. depression), and adverse effects. Secondary outcomes were rates of institutionalisation and overall cost of care. The authors identified eleven studies, but stated that three of the studies could not be included in the analyses either because the data were insufficient or could not be retrieved from the trial authors. Only four of the included studies considered challenging behaviour as an outcome, but the sample sizes were limited and the outcome measures were not the same across the studies.\textsuperscript{68-71} A meta-analysis of challenging behaviour however was performed and no substantial heterogeneity was found, although the results were not statistically in favour of bright light therapy.

The second review aimed to identify which non-pharmacological interventions were most effective for BPSD in long-term care\textsuperscript{29}. Only two studies\textsuperscript{68,69} were included in the review (which were already included in the Forbes review\textsuperscript{67}), but were not assessed in detail. The review received 4 points in the AMSTAR rating system.

The third review\textsuperscript{72} aimed to assess the role of physical environment in supporting person-centred dining in long-term care. Only one study that evaluated the effect of ambient bright light in activity
and dining areas among institutionalised people with dementia was identified\(^{73}\). This study was not included in the previous two reviews.

The fourth review\(^{74}\) that addressed the effectiveness of environment-based interventions for people with Alzheimer's disease or dementia, identified a cluster-unit crossover trial\(^{75}\). The trial was conducted in two geriatric units in a state-operated psychiatric hospital and in a dementia-specific residential care facility in Oregon, USA and enrolled 66 older adults with dementia to evaluate the effectiveness of ambient bright light therapy, delivered through a high-intensity, low-glare lighting system installed in the public areas of study units at both sites, at reducing depressive symptoms. Each lighting condition was provided for multiple 3-week periods in a predetermined sequence. The CSDD was used to assess depressive symptoms. Results did not support the use of ambient bright light therapy as a treatment for depressive symptoms in people with dementia\(^{75}\). eTable 3 describes the type of interventions, the outcomes and the results of the primary studies included in the Light therapy reviews.

**Sensory garden and horticultural activities**

Whear 2014\(^{76}\) (AMSTAR=7) investigated the impact of gardens and horticultural therapy on the mental and physical wellbeing of residents with dementia, in nursing homes and specialised dementia care facilities. This approach uses either “sensory” gardens to stimulate the 5 senses (sight, vision, hearing, smell and touch), or plants and plant-related activities to improve well-being (horticultural therapy or therapeutic horticulture). Eighteen studies were identified: ten were quantitative studies (two RCTs (n=34), six pre-post studies, one crossover study, one prospective cohort study), seven qualitative and one used mixed methods. In one of the RCTs\(^{77}\) there was a non-statistically significant decline in verbal and physical aggression and non-verbal aggression, and total CMAI score (eTable 4).

Gonzalez et al.\(^{78}\) (AMSTAR=3) examined the effects of sensory garden and horticultural activities in dementia care. Sixteen studies were identified, including 2 RCTs (n=149), one of which was
cluster randomised, 11 pre-post studies, 2 case studies and one survey. In the smaller of the two
RCTs, verbal agitation significantly decreased in the outdoor horticultural group compared to the
indoor horticultural group, while in the larger trial, the effect of subjects in the horticultural group
did not differ from the traditional activity group. (Connell et al. was included in both systematic
reviews.)

eTable 4 describes the type of interventions, the outcomes and the results of the primary studies
included in the Sensory Garden and Horticultural activities reviews.

**Music and dance therapy**

Music therapy is the application of music and/or its elements (melody, rhythm, harmony, sound) by
a qualified musical therapist, in order to support and stimulate various aspects of cognitive,
emotional, social and physical needs, such as expression, communication, learning and forming
relationships. Subjects can passively listen to music or actively participate by singing, playing an
instrument or moving. Dance therapy is a psychotherapeutic intervention that uses movement to
“further the emotional, cognitive, physical and social integration of the individual”.

Six SRs that evaluated music therapy, and one review that assessed live singing to people
affected with dementia, were identified.

The number of included primary studies in the reviews varied from 3 to 18 and the AMSTAR
scores of the reviews ranged from 2 to 7.

The review by Ueda, received the highest score (AMSTAR=7) and included 9 randomised
trials and 9 controlled clinical trials that evaluated one music-related experience or a combination of
music-related experiences, such as singing, listening, performing, rhythmic exercising, and
improvising. Uncontrolled before-and-after studies and case studies were excluded.

Participants were allocated to music therapy (mean of 36 min/day, 2-3 days/week for 10 weeks
(range 1 day to 11 months)) or usual care for BPSD assessment. The music therapy comprised
listening (86-94), moving/dancing (86 88 89 95-98), singing/playing a musical instrument (86 88 89 93 96 97), and in some occasion was administered in combination with exercise (104) and reminiscence therapy (89 100 102).

Music therapy was effective in reducing behavioural symptoms (6 RCTs + 5 CTs; 397 participants) [SMD = −0.49 (95% CI −0.82 to −0.17)], despite a moderate and statistically significant heterogeneity [I²=58%, P=0.009]. The same intervention achieved a statistically significant reduction on depression (4 RCTs + 5 CTs; 250 participants) [SMD = -0.32 (95% CI -0.68 to -0.04); I² = 44%, P=0.08] and anxiety (SMD -0.64, 95% CI -1.05 to -0.24; I²=55%; eight studies; 258 participants).

Whear et al (85) investigated the effectiveness of mealtime interventions, including music, on BPSD in people with dementia in residential nursing homes or care homes. Eleven studies were identified: one controlled trial, three before/after studies and seven repeated measure time series studies. The results of the studies were described narratively. One before/after study with 22 participants found that music played at mealtime improved physical and verbal, aggressive and non-aggressive, behaviour using the CMAI.

Seitz (29) (AMSTAR=6) identified 40 RCTs of non-pharmacological interventions, of which 3 studies with 133 participants (97 98 105) evaluated music therapy for BPSD of dementia in long-term care facilities. Due to the heterogeneity of the studies (study design, patient populations, interventions, treatment duration and outcomes measured), the authors did not perform a meta-analysis. The behavioural outcome was measured either with a modified CMAI, Behavioural Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD) or the NPI. In one study, the music therapy was performed with movement, in a group, for 30 minutes, twice/week for 4 weeks (98). In a second study, the music intervention lasted 30 minutes, 3 times/week for 6 weeks (105). And in a third trial, the duration and frequency of individual sessions were not specified, but the therapy lasted 14 weeks (97). Two of the three studies employing music found a statistically significant difference between...
treatment and control groups, but all three were at risk of randomisation bias and 2 had unclear bias of incomplete outcome data. All the studies were included in Ueda’s review 82.

The review by McDermott 81 (AMSTAR=4) searched MEDLINE, EMBASE, PsycINFO, CINAHL, the Cochrane Library, Web of Science, Journal of Music Therapy, and Nordic Journal of Music Therapy and identified 18 studies of which 6 were RCTs (the remaining were non-randomised controlled studies (n=4), before-and-after studies (n=5) and qualitative and mixed-method studies (n=3)). Two trials 97,101 and the case-control study 105 were already included in the reviews described above 29,82. Three RCTs (n=165), two of which were carried out by the same group, measured BPSD using either the NPI or BEHAVE-AD. In one trial, the music therapy (patients and music therapist play musical instruments to express emotions and interact) was performed for 30 minutes, 3 times/week for one month, followed by a one month interruption, over 6 months (Raglio 2010). In another study by the same group, the music therapy (singing and body movement with music to stimulate communication) was administered for 30 minutes, 30 times over 16 weeks 97. In the third trial, the therapy was executed for 30 minutes, 3 times/week for 6 weeks (Svansdottir 2006). McDermott et al concluded that evidence for reduction of behavioural disturbance was consistent, but there were no high-quality longitudinal studies that demonstrated long-term benefits of music therapy. Of note, five of the RCTs included in the review were not included in the review by Ueda 82.

Unlike the previous review, Vasionyte 83 (AMSTAR=4) provided a meta-analysis of the effects of music interventions (median=8 weeks; range 2-53 weeks) in patients with dementia, differentiating between different types of interventions (listening, active music therapy, recorded music, live music, selected music, individualised music, classical/relaxation music, popular/native music and group and individual interventions). This SR included 18 studies comprised of 6 RCTs 87,91,106-109, 6 CCTs 88,92,99,103,110 and 6 pre-post-test studies. The outcomes evaluated were behaviour (measured with the CMAI, NPI-Q, Multidimensional Observation Scale For Elderly Subjects (MOSES), an
agitation checklist or a behavioural chart), affect, cognition and physiology. There was no 
statistically significant effect on behaviour (Effect Size (ES) 1.16, 95% CI -0.65 – 2.98; 8 studies, 
n=217) or affect (ES 0.38, 95% CI -0.56 – 1.32; 6 studies, n=109), while cognition (ES 1.56, 95% 
CI 1.11 – 2.01; 4 studies, n=63) and physiology (ES 0.72, 95% CI 0.36 – 1.08; 4 studies, n=88) 
were affected. Three of the RCTs, and four of the controlled trials, in this review, were also 
included in Ueda.

The review by Wall included 13 studies that were presented narratively. The review was of low 
quality (AMSTAR score 2).

The review by Chatterton et al evaluated the efficacy of 'live' singing to people with dementia for 
cognitive, behavioural, physiological, and social outcomes. The study received an AMSTAR score 
of 1.

An additional SR that aimed to assess the role of the physical environment in supporting person-
centred dining in long-term care, identified four non-randomised studies, with different designs, that 
evaluated the effect of music on the incidence of agitated behaviours during mealtimes, among 
older adults with dementia, residing in special care units. The results of these studies showed 
that playing music during mealtime reduced the incidence of agitated behaviour.

eTable 5a describes the type of interventions, the outcomes and the results of the primary studies 
included in the Music therapy reviews.

**Dance therapy**

Two reviews evaluated dance therapy in patients with dementia. The first review’s objective 
was to evaluate the evidence concerning dancing interventions in physical and mental illnesses 
compared to other types of interventions or non-specific interventions. The review received 3 
points in the AMSTAR scoring system and identified 13 small studies reporting results from 11 
randomised trials of which only one considered patients with dementia. The trial that considered
subjects with dementia included 29 participants (mean age 79 years, SD 7.7; 75% female) in a nursing home and evaluated the efficacy of dance and movement therapy delivered in nine sessions, lasting 30 to 45 minutes each, once-a-week. The outcome measures included the word list savings score, the Clock drawing test (for visual spatial ability), the Cookie Theft picture description task from the Boston Diagnostic Aphasia test and the Nurses’ Observation Scale for Geriatric Patients (NOSGER). The results did not show any important differences in favour of dance therapy.

The second SR aimed to evaluate the effects of dance (movement) therapy and ballroom dancing, compared to usual care, for adults with physical and mental illnesses. The review received only 1 point on the AMSTAR scale and identified only one study that investigated the intervention in a population affected by dementia and which was also included in the review above.

Snoezelen Multisensory Stimulation Therapy

Snoezelen Multisensory Stimulation Therapy (SMST) comprises multiple stimuli and is aimed at stimulating the primary senses of sight, hearing, touch, taste and smell. The intervention is provided in specially designed rooms, which provide diverse sensory-stimulating effects/material including music, aroma, bubble tubes, fiber optic sprays and moving shapes projected across walls. SMST was investigated by two reviews.

The first was an overview of reviews and its evidence for SMST was based on a Cochrane review that included three studies. The inclusion criterion was any randomised trial that assessed the efficacy of SMST and/or multi-sensory stimulation to treat people over 60 years of age suffering from dementia. The outcomes of interest included behaviour, mood, cognition, physiological indices, and client-carer communication, as well as short-term effects measured during the sessions or post-session, and longer-term benefits measured post-intervention and at follow-up.
The three included primary studies evaluated a total of 311 patients with dementia, aged 60 or older. The first was a randomised trial that compared eight standardised multi-sensory programmes with eight standardised activity sessions. Both programmes were implemented on a one-to-one basis, twice-a-week, with each session lasting 30 minutes. Fifty subjects (25 female, mean age 78) with a diagnosis of Alzheimer's disease (N=33), vascular dementia (N=7) or a mixed diagnosis (N=10) were enrolled. The objectives of the trial were the immediate effects of SMST on the behaviours of older people with dementia, the carryover effects of SMST on mood and behaviour to day hospitals and home environments, and the maintenance effects of SMST on mood, behaviour, and cognition over time. The effects of SMST on behaviour were measured by INTERACT. The generalization effects were measured by three outcome measures: the carryover effect of day-hospitals was measured with the General Behaviour and Community Skills sub-scales of REHAB (Baker 1988); the carryover effect to home, at mid- and post-intervention, was measured with the Behaviour and Mood Disturbance Scale (BMD) and the Behaviour Rating Scale (BRS) of the Clifton Assessment Procedures for the Elderly (CAPE). The maintenance effect (at the one-month post-intervention follow-up) on behaviours and cognition were measured by REHAB, BMD, the Cognitive Assessment Scale (CAS) of CAPE and MMSE. No significant effects on any scale of behavioural symptoms were found either immediately after intervention or at one-month follow-up.

The second study was a quasi-experimental pre- and post-test design with cluster randomisation performed at a ward level, which compared a 15-month, 24-hour individualised care plan that was integrated with SMST, with 15-month usual care. The study included 136 subjects diagnosed with Alzheimer's, vascular or mixed dementia from 3 different countries (UK = 94 day patients, the Dutch sample = 26 inpatients. Swedish sample = 16 inpatients). There was a significant group difference in mean baseline MMSE scores (data from the UK and the Dutch only) between the SMST group (9.4) and the control group (6.7) (p=0.01). All subjects attended eight, 30-minute sessions on a one-to-one basis according to their group assignment. The sessions were conducted by
the same key workers throughout the study period. The following outcomes measured the short-
term effects of SMST on behaviours: (1) INTERACT (22-item) measured behaviours during the
sessions; (2) INTERACT (12-item) measured behaviours 10 minutes before and 10 minutes after
the sessions; and (3) Behaviour Observation Scale for intramural psychogeriatrics (GIP) measured
behaviours that were videotaped during the sessions in the Netherlands sample.

The study showed significant effects on two behavioural items of INTERACT during sessions:
enjoying oneself (MD = -0.74; 95% CI (-1.29, -0.19); z = 2.62, P = 0.01) and bored/inactive (MD =
-0.56; 95% CI (-1.11, -0.01); z = 1.99, P = 0.05). There were no longer-term treatment effects of the
integrated SMST-care programme on behaviour.

The third study assessed the effects of SMST when integrated into 24-hour daily care on
nursing home residents with dementia. One hundred twenty-five patients with moderate or severe
dementia and care dependency were recruited from 6 old age psychiatry wards for pre-test. A
cluster randomised design was used to assign the wards to either experimental (integrated SMST
care programme) or control (usual activity) conditions. Twelve old age psychiatry wards in six
nursing homes (out of 19 homes) were recruited to the study. At baseline, 125 subjects (female
79%, mean age 84) were recruited and were assigned to experimental or control conditions
according to the ward in which they stayed. For the experimental group, subjects were given a
stimulus-preference screening in 10 weekly one-hour sessions to identify their preferred sensory
stimuli. Subsequently, individual SMST care plans were developed for each participant based on
their life history, stimulus preference, and discussions from multidisciplinary conferences. Certified
nursing assistants (CNAs) used multisensory stimuli in the 24-hour care of the experimental
subjects. Subjects in the control group were provided with individual usual care. A minimum period
of three months was used for both experimental and control conditions.

The short-term effects of the integrated SMST-care programme on behaviours were measured using
a modified version of INTERACT, in which six items were deleted and eight new items were added
during morning care sessions. The long-term effects of integrated SMST-care programmes on
behaviours, mood, and interaction were evaluated at the 18-month follow-up using the eight items of GIP for apathy, anxiety and disoriented behaviours, the Dutch version of CMAI for agitated behaviours, physically non-aggressive behaviour and verbally agitated behaviours, and the Cornell Scale for Depression for depressive symptoms. In terms of behavioural disturbances, when compared to the control, the 24-hour integrated SMST-care programme showed a significant effect on two behavioural items of INTERACT during sessions: enjoying self (MD = -0.74; 95% CI (-1.29, -0.19); z = 2.62, P = 0.01) and bored/inactive (MD = -0.56; 95% CI (-1.11, -0.01); z = 1.99, P = 0.05). There were no longer-term treatment effects of the integrated SMST-care programme on behaviour. In terms of mood, there were significant improvements in one mood item of INTREACT during sessions: the SMST group was happier and more content than the control group (MD = -0.84; 95% CI (-1.39, -0.29); z = 2.98, P = 0.003). There were no significant effects of the 24-hour integrated SMST at post-intervention. The fourth review scored 6 in the AMSTAR evaluation and investigated different non-pharmacological interventions including SMST for the treatment of BPSD. The review identified only one study that was included in the above cited review.

eTable 6 describes SMST-based interventions, outcomes and results of the primary studies included in the reviews.

**Transcutaneous electrical nerve stimulation**

Transcutaneous electrical nerve stimulation (TENS) is a simple, non-invasive, non-pharmacological intervention commonly used for pain control and occasionally for neurological and psychiatric conditions such as drug/alcohol dependency, headaches, and depression. TENS consists of attaching electrodes to the skin and applying an electrical current, whose frequency can vary from low (< 10 Hz) to high (> 50 Hz).

Two reviews were identified.
One review that evaluated current treatment options for sleep disturbance in Alzheimer’s dementia scored 3 in the AMSTAR evaluation. Different non-pharmacological interventions were considered, including bright light therapy, behavioural and multi-faceted interventions (combined increased daytime physical activity and exercise, decreased daytime in-bed time, daily sunlight exposure, structured bedtime routine, and decreased night-time noise and light) and TENS. For the latter intervention, only one randomised trial of 19 nursing home residents was identified. The study did not evaluate behavioural outcomes.

A Cochrane review that was included in O’Neil’s review was also considered. The review was focused only on RCTs that enrolled inpatients and outpatients of any age (with or without caregivers), with a diagnosis of dementia. The outcomes of interest included visual and verbal short- and long-term memory, semantic verbal fluency, circadian rest-activity rhythm, affect/depression, level of independent functioning, adverse effects, and drop outs due to inefficacy. The review identified and included 9 trials that were performed in Japan and the Netherlands. The Dutch studies were performed by the same group of authors. These studies were randomised placebo-controlled trials and the participants were chosen from a group of 350 to 500 residents of a residential home for older people. The age range of the subjects was approximately 70 to mid-90 years and were mostly female (>80%). All subjects met NINCDS-ADRDA criteria for the clinical diagnosis of probable AD; most subjects had early AD, but some had moderate AD. Subjects generally had scores of 17 or less on the Hamilton Depression Rating Scale. All included studies used a similar TENS protocol, except the most recent one published in 2002, which addressed cranial electrostimulation.

The remaining 3 publications were performed by a group of authors from Japan and describe the results of the same study. The study design was a double-blind crossover and, in contrast to the Dutch studies, subjects were thought to have multi-infarct dementia or Alzheimer’s disease and were selected on the basis of irregular sleep-wake patterns in conjunction with nocturnal behaviour.
disorders and/or dementia. Twenty-seven subjects completed the study. The intervention used a HESS-10 stimulator with rectangular pulse waveforms at a frequency of 6-80 Hz, a pulse duration of 0.2 ms maximum, 256 µAmps and an amplitude of 6-8 V. The outcomes evaluated were sleep disorder, motivation, behaviour disorder, intelligence, emotion, language, neurological signs, subjective complaints and activities of daily life. All of these were rated on a 5-point scale: absence of the related symptom, 0; mildly disturbed, 1; moderately disturbed, 2; markedly disturbed, 3; and severely disturbed, 4. Of the 9 studies, only 3 could be included in a meta-analysis for a combined total of 63 subjects. Two of these studies were conducted in the Netherlands, and one was conducted in Japan. Results, however, were inconclusive. It should be noted that none of the other studies mentioned adverse effects, although it is unclear if adverse events were monitored.

eTable 7 describes TENS-based interventions, outcomes and results of the primary studies included in the reviews.
Cognitive/Emotion-oriented Interventions

Cognitive stimulation

Cognitive stimulation involves a variety of pleasurable activities, such as word games, puzzles, music, cooking, gardening and discussing past and present events and is usually carried out by trained personnel with small groups of 4-5 people. It lasts for 45 minutes, minimally 2 times per week. It is based on Reality Orientation, which was developed in the 1950s to counteract the confusion and disorientation of older people during hospitalizations. Seven reviews were identified

Woods 2012 (AMSTAR score=10) was a Cochrane review that identified 15 RCTs that used cognitive stimulation for people with dementia. The authors stated that most of the studies were of low quality, but that generally, investigators had taken measures to protect against the risk of allocation concealment bias. In a meta-analysis of 3 trials (n=190 participants), the intervention had no effect on problem behaviours (SMD -0.14, 95% CI -0.44 – 0.17; I²=0%, P=0.57).

The review by Aguirre et al. in 2013 (AMSTAR score =5) evaluated the effectiveness of cognitive stimulation in patients with dementia and identified 9 RCTs. Three trials that considered behaviour-related outcomes were identified. These trials were already included in Woods’s review and reached the same conclusion.

Alves et al. in 2013 (AMSTAR score =4) identified 4 RCTs of cognitive interventions for AD patients. Only one trial that measured BPSD as an outcome was identified. The study population was composed of 32 patients with a score between 10 and 24 on the Mini Mental State Examination, no history of antidepressant medication, and a total Neuropsychiatric Inventory score greater than 5 points arising from at least 2 domains of behaviour. The cognitive stimulation intervention was administered individually and focused on a set of tasks requiring executive
functions and working memory. The study found a statistically significant reduction of BPSD (MD -2.06; 95% CI -2.91 to -1.21).

The study of Carrion et al. in 2013 (AMSTAR score =4) found 17 RCTs of cognition-oriented interventions (reality orientation and skills training) for dementia sufferers. Challenging behaviour was evaluated in only 2 trials (n=156 and n=44, respectively) that employed the two categories of cognitive interventions, using the Neuropsychiatric Inventory and the Revised Memory and Behaviour Problems Checklist. In both RCTs, the intervention group had a smaller increase in change from baseline compared to the control group. Due to the heterogeneity among the studies, the authors decided a meta-analysis was inappropriate.

Yu 2009 (AMSTAR=3) included 15 studies (9 RCTs, 5 CCTs and 1 before-after study), in addition to 5 case studies and 3 undefined studies, all of which investigated different types of cognitive interventions for AD and dementia. The only study, a CCT (n=32 with early stage AD), that evaluated the effect of cognitive stimulation on behavioural disturbances, showed larger improvement than the cognitive training group.

Olazarán et al. in 2010 (AMSTAR =4) identified 179 RCTs of diverse types of non-pharmacological interventions for Alzheimer’s Disease patients and examined problem behaviour, mood, QoL, cognition, ADLs, mechanical restraint and institutionalisation of patients, and mood, psychological well-being and QoL of CGs. The authors performed a meta-analysis of three low quality RCTs to determine the effect of cognitive stimulation on problem behaviour and mood. There was a non-statistically significant reduction in problem behaviour (group session cognitive stimulation (ES=0.61; 95% CI 0.09-1.12)). The primary study by Baines et al., was included in the Woods review above, while the study by Robichaud et al. was included in the review by Kim which examined Behaviour Management Techniques described below.

Thirty-three RCTs, employing cognitive interventions for cognitively impaired individuals (dementia and mild cognitive impairment), were identified in Kurz et al. (AMSTAR score =2).
Twelve of these trials examined behavioural disturbances, but only 3 studies found a significant
effect of the intervention.

Zientz et al. \(^{142}\), (AMSTAR score=2) identified 3 studies (2 RCTs and 1 RCT or CCT; n=124
participants) of caregiver-administered cognitive stimulation for individuals with AD. One of the
randomised trials (n=16) found that individuals who received the intervention displayed fewer
behavioural problems compared to those who had not been given the intervention.

**cTable 8** describes Cognitive stimulation-based interventions, outcomes and results of the primary
studies included in the reviews.

**Reminiscence therapy**

Reminiscence therapy is a non-pharmacological intervention that involves the discussion of past
experiences, events and activities with family members or other groups of people. The intervention
uses materials such as photographs, books, old newspapers and familiar items from the past to
inspire reminiscences and facilitate people to share and value their experiences. Three reviews
assessed reminiscence therapy as a non-pharmacological intervention to treat agitated behaviour in
patients with dementia \(^{29, 149, 150}\).

The first review \(^{29}\) received the highest score (AMSTAR score of 6) and considered all non-
pharmacological interventions to treat relevant outcomes in patients with dementia. The review
identified two small studies involving a total of 107 patients \(^{151, 152}\) performed in care facilities. The
NPI and the Clifton Assessment Procedures for the Elderly-Behavioural Rating Scale (CAPE-BRS)
were used to measure BPSD. Seitz et al.\(^{29}\) reported that this outcome was unaffected in one study
\(^{152}\), while the effect of the intervention was unclear in the other study \(^{151}\).

The second review \(^{150}\) was focused only on reminiscence therapy as a sole treatment of behavioural
outcomes for patients with dementia. The review was of low methodological quality (AMSTAR
score=3). The results were presented in a narrative synthesis. The review included 5 trials with a
before-after design, containing 258 patients affected by dementia. The studies considered different interventions. Two studies (one with 31 participants [Haight 2006] and the other with 17 participants [Morgan 2010]) assessed a life review or story approach and found significant improvements in depression, communication, positive mood and cognition. The third study (101 participants [Lai 2004]) evaluated specific reminiscence, which produced a life-story book using personalised triggers for each person's life history. No significant differences were observed between groups except for outcomes such as well-being and social engagement. The remaining two trials (involving 73 participants and 36 participants) evaluated individual reminiscence approaches. One study used six weekly sessions, which focused on a particular life phase, such as childhood or family life, while the other study used a basket of visual and auditory activities, based on five themes, such as musical instruments, designed to stimulate reminiscence. No significant differences were observed between the groups in terms of behavioural outcomes.

The third review focused on whether reminiscence therapy could alleviate depressive symptoms in adults with dementia, but its methodological quality was extremely low (AMSTAR score=1). Four primary studies with a pre-post test design, were included and were described individually, three of which were randomised trials and one of which comprised a single group.

eTable 9 describes Reminiscence therapy interventions, outcomes and results of the primary studies included in the reviews.
Validation Therapy

Validation therapy is based on the general principle of the acceptance of the reality and personal truth of another person’s experience and incorporates a range of specific techniques. Validation therapy is intended to give the individual an opportunity to resolve unfinished conflicts by encouraging and validating the expression of feelings. The specific interventions and techniques are based on a synthesis of behavioural and psychotherapeutic methods. The approach can be used as a structured therapeutic activity in a group setting, usually lasting several weeks, or it can be conducted individually as part of an ongoing approach to facilitate communication as a supplement to group work. The validation therapy techniques comprised non-threatening, simple concrete words; speaking in a clear, low and empathic tone of voice; rephrasing and paraphrasing unclear verbal communication; responding to meanings through explicit and implicit verbal and non-verbal communication; and mirroring verbal and non-verbal communication.

One Cochrane review that evaluated the effectiveness of validation therapy to reduce BPSD was identified (AMSTAR score=7). The review included only randomised trials of subjects over 65 years of age, diagnosed with Alzheimer's disease, dementia or other forms of cognitive impairment, according to ICD 10, DSM IV or comparable criteria. The outcomes of interest were cognition, behaviour, emotional state and activities of daily living. The review, updated in 2005, included 3 randomised trials (n=155 participants). Another SR that evaluated the effective characteristics of residential long-term care settings for people with dementia identified one trial that was included in the Cochrane review.

Primary studies

The first study (n=31) was performed in a nursing home and used an intervention (30 minutes once-per-week for 6 weeks) that included activities such as discussion of a previously agreed subject, singing and movement, followed by a closing ritual and refreshments. Behaviour was measured with the Behaviour Assessment Tool. The control groups consisted of reminiscence
therapy, which followed the guidance of a reality orientation manual (cues such as flannel boards and calendars were used to promote orientation) and usual care. At 6 weeks, validation therapy was associated with a decrease of problem behaviours (MD=-5.97, 95% CI -9.43 – -2.51; P<0.001; based on an analysis of subjects who completed the study).

The second study \(^{160}\) enrolled 36 patients with moderate to severe disorientation of which 25 had a diagnosis of dementia. The study was performed in a long-term care institution in the USA. The validation therapy was performed twice-a-week for nine months; details of the validation therapy were not given. Agitation was measured using the Minimal Social Behaviour Scale (MSBS; Farina 1957) where a reduction in score indicated improvement. No effects on behaviour were detected.

The last study \(^{161}\) was carried out in ‘skilled-care nursing homes’ in the USA. In this study, patients were included if they had at least a moderate level of dementia (assessed by the Short Portable Mental Status Questionnaire – SPMSQ – and the Validation Screening Instrument), and displayed problem behaviours, such as physical aggression. Validation therapy (four meetings lasting 30 minutes per week for 52 weeks) was composed of groups divided into 4 sessions of 5-10 minutes each. The first session included introductions, salutations and singing. The second session involved conversation regarding a subject of interest; recalling past events was promoted. The third session comprised an activity programme and singing or poetry. The fourth session involved refreshments and individual goodbyes. Agitation was measured with the CMAI\(^{163}\), carried out as CMAI(N) nurse observed and CMAI(O) non-participant observed. The authors reported that depression (MOSES) decreased at 12 months (MD -4.01, 95% CI -7.74 – - 0.28; P=0.04, based on an analysis of participants (66 out of 88) who completed the study. **Table 10** describes validation therapy interventions, outcomes and results of the primary studies included in the reviews.

### Simulated Presence Therapy

Simulated presence therapy (SPT) involves the use of video/audiotapes made by family members containing scripted ‘telephone conversations’ about cherished memories from earlier parts of a
person’s life, in an effort to stir remote memory, improve behavioural symptoms, and enhance the quality of life among people with dementia. Two SRs were identified.

The first review was written by only one reviewer and scored 3 on the AMSTAR scale. The review was aimed at investigating the effectiveness of SPT for challenging behaviours in dementia. The review searched PubMed, PsycINFO and the Web of Science, conducted hand searches of relevant articles and considered for inclusion, studies that reported pre-test and post-test, or pre-test and during-test data for SPT for challenging behaviours. The SPT consisted of audio or videotapes prepared by a spouse, family members, the caregiver, a psychologist, a surrogate or researchers. Of the seven included primary studies, only the data from four could be pooled, showing an overall mean effect of 0.70, with a 95% confidence interval of 0.38–1.02, but with statistically significant heterogeneity ($I^2=71\%, P=0.02$).

The second review examined the efficacy of any non-pharmacological intervention (including SPT) to reduce BPSD in patients with dementia. After searching the databases MEDLINE, CINAHL, PsycINFO, EMBASE, Dissertations International, and the Cochrane Database of Systematic Review, from 1974 to May 2008, the review identified only 2 studies that were included in the Zetteler review above. eTable 11 describes SPT, outcomes and results of the primary studies included in the reviews.
Behavioural management techniques

There is a multitude of behavioural interventions that constitute Behavioural Management Techniques, which include behavioural or cognitive-behavioural therapy, functional analysis of specific behaviour, individualised behavioural reinforcement strategies, communication training, and other therapies such as habit training, progressive muscle relaxation, and token economies.

These behavioural interventions can be realised either with the patient or by training caregivers to perform the intervention with the patient.

One overview of reviews and four SRs that considered behavioural interventions were identified. The overview of reviews by O’Neil 2011 identified three SRs, and after performing additional searches of primary studies, included nine randomised trials. The overview authors’ conclusions were in support of behavioural management techniques as effective interventions for behavioural symptoms of dementia although they admitted there were mixed results. In addition, the authors highlighted some concerns regarding the variety of specific interventions and methodological limitations in many studies, and advocated additional research with carefully assessed outcomes.

A Health Technology Assessment (HTA) report that aimed to evaluate the clinical and cost-effectiveness of sensory, psychological and behavioural interventions to manage agitation in older adults with dementia, systematically searched and identified 4 randomised trials. The intervention in all 4 trials was caregiver-based. The HTA authors concluded that the evidence in favour of the behavioural management techniques was limited.

A Cochrane review aimed to assess the effects of functional analysis-based interventions for people with dementia (and their caregivers) living in their own home or other settings and identified 18 randomised trials. The development of the intervention was driven by various approaches and theories, including knowledge and/or training approaches, the stress-coping model, the Progressively Lowered Stress Threshold model and problem solving approaches. In addition, the
time frame in which the intervention was delivered varied from 9 days to 18 months and the number of sessions used to deliver the intervention varied widely, from 1-2 sessions to more than 10 sessions. Of the 18 studies included the authors were able to meta-analyse data from 4 trials, of which one contained unpublished data. There were no significant reductions in the incidence of challenging behaviours reported post-intervention in four family care studies (SMD 0.02, 95% CI -0.13–0.17, P= 0.80, N=722).

Among 179 RCTs of diverse types of non-pharmacological interventions for Alzheimer’s Disease patients, identified by Olazarán 2010 (AMSTAR score =4), the authors performed a meta-analysis of three low quality RCTs of behavioural interventions (analysis and modification of antecedents and consequences of behaviour) and found a statistically significant reduction in problem behaviour (ES=0.57, 95% CI 0.21-0.92; 3 trials; n=167). The same authors carried out another meta-analysis of four low quality RCTs of care staff training in behavioural management and found a reduction in problem behaviour (ES=0.22, 95% CI 0.02-0.43; 4 trials; n=370).

Two primary studies examined emotion-oriented care. The first study was a RCT of NH residents (n=146 older residents with AD, mixed AD and vascular dementia and dementia syndrome; mean age 84). The intervention of emotion-oriented care was associated with less anxious behaviour in the group of residents who needed less assistance/care compared to similar residents in the usual care group. The second study was a cluster randomised study of residential care homes (n=16 homes; n=151 residents). The authors reported that there was no statistically significant effect of the intervention on any behavioural outcome, including behavioural problems. Teri 2000 was included in the Health Technology Assessment; Gormley 2001 and Teri 2005 were included in the Brodaty 2012 review, Gonyea 2006 was included in reviews in Behaviour Management Techniques, McCallion 1999 and Teri 2005 were included in Eggenberger.
Eggenberger 2013 (AMSTAR score = 3) aimed to evaluate interventions that were designed to enhance communication or interaction in dementia care, in any setting. Review authors identified 12 studies (7 randomised trials, 2 controlled clinical trials and 3 before-after studies) that focused on communication training for staff in institutions and family caregivers at home. In institutional settings, the results on challenging behaviour, of residents with dementia, were not consistent. Four studies reported a significant reduction of challenging behaviour. McCallion et al., for instance, demonstrated a decrease of physically aggressive behaviour (15.16 (SD 9.81) to 12.21 (SD 8.31), p<0.001)), and a reduced mean occurrence of verbally aggressive behaviour in patients with dementia (16.22 (SD 10.31) to 12.88 (SD 8.39), p<0.001)). In addition, one trial demonstrated a significant decrease of residents’ agitation during care routines (F(1.7=5.12, p<0.05)). Conversely, three studies reported no effect on challenging behaviour of people with dementia.

Only one trial was included in the Brodaty 2012 review.

Kim et al., conducted a review to assess the effectiveness of occupational therapy on behavioural problems and depression in patients with dementia. MEDLINE, CINAHL, ProQuest and The Cochrane Library were searched up to the end of March 2011. The AMSTAR score was 7. The authors defined occupational therapy as an application of ‘activity analysis, caregiver training, sensory stimulation, behaviour control skill teaching, physical and social environmental modification, cognitive training, and purposeful activity’. The review identified nine randomised trials with a total of 751 participants. Based on the type of intervention, the authors categorised four studies as sensory stimulation, three studies as functional task activities, and 2 studies as environmental modification. The authors performed a meta-analysis of the trials with occupational therapy-based sensory stimulation and found an effect size of 0.32 (95% CI, 0.04–0.59; 250 participants; no significant heterogeneity). No significant effect was detected for
OT-based functional task activities (0.15, 95% CI, -0.17–0.47; 203 participants) or environmental modification (0.13, 95% CI, -0.09–0.36; 298 participants).

**Primary studies**

Overall 22 trials were evaluated in the 6 reviews that were included. Except for one study performed in Taiwan, all the studies were carried out in Europe, the US and Australia. Thirteen studies were performed in family care settings. Three studies with a total of 740 residents were conducted in care homes. Finally, one study was located in an assisted living setting and the other in a hospital setting.

Characteristics of the interventions varied greatly across the trials. Fifteen trials were focused on enhancing communication skills in family and formal caregivers. Eighteen trials focused on functional activity, of which four were described as a Behavioural Management intervention. The intervention in one trial involved caregiver training on verbal or non-verbal communication focused on activities of daily living. Another trial was dedicated to teaching participants the basic technique for progressive muscle relaxation. Time delivery of the intervention also varied widely. However, as noted by Moniz-Cook, the intervention delivery was determined by setting: the interventions in care homes were provided weekly and lasted for six months. In one family care study, the intervention was provided in just 4 sessions over eight weeks. Follow-up data varied from a few weeks to 24 months.

**Setting based description**

**Family care.** In this setting, family caregivers assisted people with dementia at home, with or without support from formal caregivers, healthcare workers and adult day care centres. Thirteen trials were conducted in a family care setting. Six of these trials investigated an intervention that was focused on enhancing communication skills of the caregiver. The duration of the intervention ranged from 3 weeks to 12 months. The
number of weekly sessions administered were, according to a classification proposed by Moniz-Cook 2012, high (> 10 session) in three trials, moderate-high (6-10 sessions) in one trial, moderate (3 to 5 sessions) in one trial and minimal (1 to 2 sessions) in one trial. The subjects that delivered the interventions varied from trial to trial: occupational therapists; trained nurses or social workers; professionals specialised in the REACH programme; healthcare professionals supervised by an old age psychologist; psychologists or trial investigator together with an experienced nurse.

Four of the 13 trials in the family care setting investigated a behavioural intervention that was focused on providing support to the caregiver. The interventions lasted from 5 weeks to 18 months, with the number of sessions that varied from 4 to 8 sessions, with home visits and associated with or followed by telephone contacts. Overall, the intervention dosage was high for three trials, medium-high in one trial and moderate in one trial. The interventions were delivered by different healthcare experts: Community Mental Health Nurses; therapists; occupational therapists; community consultants trained by an old age psychologist.

The remaining two trials evaluated behavioural management techniques. Teri 2000 compared the intervention consisting of 8 weekly and 3 biweekly sessions (high intensity intervention) with pharmacological interventions or placebo. The intervention was provided by a therapist with a master’s degree and one-year clinical experience, but was not reported in detail. The post-intervention evaluation started at 4 months and the follow-up lasted beyond 12 months. The second study did not completely describe the intervention for behavioural management. The intervention was delivered in 4 sessions (moderate intensity) over 8 weeks by the trial investigator.

In terms of results, no statistically significant change in the incidence of challenging behaviours was observed in any of the studies. Moniz-Cook 2012 meta-analysed data of four studies (N=722), but did not find any difference among the groups (SMD 0.02, 95% CI -0.13 to 0.17, P=0.80; I²=0%)
At follow-up of six months, two studies did not show any significant effect of behavioural management techniques. When the frequency of challenging behaviours was examined, none of the studies detected a significant difference even when a meta-analysis, using the data from 10 studies, was performed (SMD -0.05, 95% CI -0.17–0.07).

**Assisted Living.** In this setting, people with dementia lived in a residence, did not require full time nursing care, but needed assistance with some ADLs, such as bathing, dressing or eating. Family members could still act as intermittent caregivers during visits by providing different types of support for ADLs, Instrumental ADLs (e.g., laundry washing, room cleaning, transportation to a doctor’s office), socio-emotional support (e.g., talking, reminiscing, socialising), monitoring care provision or advocating. One study evaluated a behavioural management intervention to improve caregiver training to manage residents with dementia. The intervention intensity was medium-high, delivered by a clinical psychologist and graduate nursing students who performed 2 half-day group workshops and 4 individualised sessions with a follow-up 2 months after the termination of the intervention. Results for residents showed a statistically significant effect, in intent-to-treat analyses, in favour of the STAR-caregivers (STAR-C) intervention, general behavioural disturbance (measured by the Revised Memory and Behaviour Problems Checklist (RMBPC), NPI and ABID) and depression.

**Residential care.** This setting referred to both assisted living residences and nursing homes. The latter included facilities for people with dementia who needed significant nursing care. Three cluster randomised trials were conducted in residential care with a total of 743 residents.

In 15 residential care sites across metropolitan areas in Sydney (Australia), Chenoweth et al. examined the efficacy of person-centred care vs usual care. The intervention was a high intensity, person-centred care, based on the needs-driven model in which staff, selected by managers,
administered training sessions to caregivers. The topics covered during the sessions were derived from Bradford University's training manual. The duration of the intervention was 4 months and the overall follow-up was 8 months. The total number of residents enrolled was 289. During follow-up, the mean agitation score (measured with the CMAI) in the person-centred care group decreased significantly, from 47.5 (9.1) at baseline, to 37.2 (9.1) at six months (P = 0.01), compared to usual care in which agitation increased from 50.3 (6.8) at baseline to 57.7 (6.8) at six months (P value not reported).

In 12 residential homes, Fossey 2006 allocated 346 residents to an intervention that consisted of training and support delivered to nursing home staff over 10 months, focusing on person-centred care and skill development for the management of agitated behaviour in dementia. The comparison intervention was usual care. The high intensity intervention was delivered during the whole period of follow-up (12 months) by a psychologist, an occupational therapist or a nurse supervised weekly by the trial investigators. The study’s main outcome measure was mean levels of agitated and disruptive behaviour measured with the CMAI, but no significant difference between the groups was detected.

In 10 residential homes, Proctor 1999 allocated 120 patients to a staff-based intervention or usual care. The intervention, of high-medium intensity, consisting of training on “psychosocial management of residents”’ behavioural problems, was delivered through seven, one-hour seminars by members of the hospital outreach team and psychiatric nurse during the whole period of follow-up (6 months). The seminars covered topics that the staff had identified to improve their knowledge and skills (e.g., management of dementia, aggression, etc.). The Crichton Royal Behavioural Rating scale was used to assess behavioural characteristics of residents (0=no problems, 38=severe problems). In addition, the geriatric mental state schedule and the diagnostic algorithm AGECAT (Automatic Geriatric Examination for Computer-Assisted Taxonomy) was used to assess the effect of the intervention on residents’ organic and depressive symptoms. Despite the control group
having mean scores on the Crichton scale higher than the intervention group at follow-up, this
difference was not statistically significant [mean score -0.7 (-3.0–1.6)].

Although the clustered trials reported different types of interventions, intensities, durations and
follow-up times, Moniz-Cook et al. attempted an analysis using two studies and found a
significant reduction in behavioural disturbances [SMD, -0.21, 95% CI -0.39 – -0.03; P=0.02;
I²=9%].

eTable 12 describes Behavioural Management Technique-based interventions, outcomes and results
of the primary studies included in the reviews.
Multicomponent interventions

Integrated interventions combining psychiatric and nursing home care
Collet 2010 (AMSTAR score=5) carried out a SR in Medline, PsycINFO and Pubmed to determine the efficacy of interventions that combined psychiatric and nursing home care in nursing home residents. The authors identified 4 RCTs (n=371 participants), 1 retrospective cohort study and 3 prospective case studies. All the studies used tailored treatment plans that combined psychosocial, nursing, medical and pharmacological interventions. The results of the RCTs were described narratively. Three out of the four randomised trials reported an improvement in behaviour and mood, while one trial found no difference among the groups (eTable 13).

Combination of environmental sensory stimulation
A SR that evaluated the effective characteristics of residential long-term care settings for people with dementia, identified one controlled clinical trial. The intervention in this trial was provided in five nursing homes and consisted of 15 agitated participants with dementia taking showers, 15 agitated participants with dementia taking walks in an environment where natural elements, such as large bright pictures coordinated with audio, including bird songs, bird pictures, the sound of water flowing gently, as well as food (such as banana, pudding or soda). The control group consisted of 15 other agitated participants with dementia that received only usual care. Agitation was measured with a modified version of CMAI. The analysis showed a significant decline in agitation in the treatment group with respect to the comparison group.

Combination of music and hand massage
Another review that aimed to assess the role of physical environment in supporting person-centred dining in long-term care, identified another trial that was not included in the previous reviews. This trial applied an experimental 3x3 repeated measures design and included 41 residents with dementia living in three special care units. Participants were mostly female (78.0%), with a mean age of 84.5 years (SD=6.0). Residents in the treatment group received each of three
treatments (hand massage, favourite music, and the combination of both) with each treatment lasting 10 minutes; the control group did not receive any treatment. The CMAI was used to measure agitation. The results showed that each single and combined treatment, were effective in significantly decreasing agitation immediately following the intervention and one-hour post-intervention.

eTable 13 describes Multicomponent Interventions, outcomes and results of the primary studies included in the reviews.
Other interventions

Exercise therapy

The systematic search identified 2 reviews\textsuperscript{212,213} that evaluated the efficacy of only exercise as a therapeutic intervention.

The review by Potter et al.\textsuperscript{212} received 6 points in the AMSTAR assessment and identified 13 randomised trials that evaluated the effects of physical activity on physical functioning, quality of life and depression in older people with dementia. Only four of these trials investigated depression as an outcome using four different rating scales (Geriatric Depression Scale (GDS15); Montgomery-Asberg Depression Rating Scale (MADRS); a Dutch Evaluation scale for older patients (subscale used); and the Cornell scale for Depression in Dementia) and two trials measured behavioural disturbances (Neuropsychiatric Inventory and Stockton Geriatric Rating Scale).

The review authors stated that the methods of randomisation were clear and adequate in six of the trials with only three of these also providing methods of allocation concealment; eight of the trials reported information regarding losses to follow-up and six trials declared intention-to-treat analysis.

The first study, Burgener 2008\textsuperscript{214}, was a small trial (n=43) carried out in community-dwelling older people with dementia. The intervention was multimodal comprising Tai Chi (sitting and standing; 60 mins, 3 times-a-week for 40 weeks) and cognitive behavioural therapies. Depressive symptoms were measured with the GDS15. The authors reported that at 20 weeks of observation, there were no statistical differences between the groups.

The second study, Rolland 2007\textsuperscript{215} was a larger trial (n=134) carried out in nursing homes. Participants performed exercises including stretching, walking, strength, flexibility and balance training, for 60 mins, 2 times/week for 40 weeks. Depression was evaluated using the MADRS.

After 12 months of observation, the MADRS score (13.4±8.0) was higher in the intervention group than in the control group (14.8±7.2), but without any statistical difference.

The third study\textsuperscript{104} was also a small study (n=25) conducted in a psychiatric hospital. The invention was composed of strength, balance and flexibility exercises with music, 30 mins daily for 12 weeks.
Depression was measured in older patients with the sub-scale *Beoordelijnschaal voor Oudere Patienten*. At 3 months follow-up, no significant difference in depressive behaviour was observed. The last study, was a larger trial (n=153) that enrolled community-dwelling patients and their caregivers. The exercise intervention, for patients, comprised aerobic, endurance, strength, balance and flexibility training, 30 minutes twice weekly, reducing to twice monthly, for 23 weeks.

Caregivers were given training in behavioural management techniques. The Cornell scale for depression in dementia was used to assess depression. At a 2 year follow-up, the mean difference was 2.14 (95% CI, 0.14–4.17) and statistically significant in favour of the intervention. The four trials used different types of interventions, outcome measures and follow-up times that hindered the possibility of performing meta-analyses.

The two randomised trials that considered behavioural disturbances used the Neuropsychiatric Inventory and Stockton Geriatric Rating Scale, respectively.

The second review by Thuné-Boyle received an AMSTAR score of 2 and included 6 studies comprising 2 small randomised trials (n=31), 2 prospective design and 2 repeated measures studies that examined the effect of exercise on BPSD. In the first trial (Hokkanen 2003), the exercise intervention consisted of 16 sessions of dance and rhythmic movement lasting 30–45 minutes, once-a-week. This trial was already discussed in the dance section. The second trial aimed to assess the efficacy of a home-based exercise intervention programme to improve the functional performance of patients with Alzheimer's Disease. The intervention consisted of a daily programme of aerobic, balance and flexibility, and strength training, given to patients and caregivers.

Depression and apathy were measured using NPI and the Cornell Scale for Depression in Dementia at 6 and 12 weeks. *Table 14* describes Exercise therapy, outcomes and results of the primary studies included in the reviews.
Animal-assisted therapy

One review\(^{218}\), performed a comprehensive literature search in PubMed, EMBASE, and PsycINFO to identify pertinent studies that evaluated the efficacy of Animal-Assisted Therapy (AAT) in older patients with dementia or other psychiatric disorders. The authors identified 23 eligible studies of which 18 recruited patients with dementia, but only 10 studies investigated the effect of AAT on BPSD. The design of the studies was as follows: 3 case-control and 7 repeated measures (e.g., interrupted time series analysis) studies. Overall, the authors concluded that animal-assisted therapy may have positive influences on patients with dementia by reducing the degree of agitation and improving the amount and quality of social interaction. However, they advocated more research examining the issue of optimal AAI duration, frequency of sessions, and suitable target group.

Primary studies

Churchill et al.\(^{219}\) included 28 residents of three special care units with dementia (25% women; mean age 83.8 years; dementia evaluated with Bourke Dementia Rating Scale). The authors administered pet-therapy visits during the difficult ‘sundown’ time to examine the effect on residents with a history of agitated ‘sundowning’ behaviour. The active group was exposed to 30-minutes interaction with an investigator and a dog, which ameliorated agitated/aggressive behaviour measured with the Agitated Behaviours Mapping Instrument scale. However, the study did not report the P-values. In addition, the variability in resident response over time after the departure of the dog was not explored.

The effect of dog-based AAT was also evaluated in another special care unit. McCabe et al.\(^{220}\) enrolled 22 subjects with dementia (women 68%; mean age 83.7, range 68-96 years). The study introduced a resident dog and agitated behaviour was measured using the Nursing Home Behaviour Problem Scale. Data were collected 1 week before and for the first 4 weeks after introduction of the dog. The authors reported a significant reduction in daytime behavioural disturbances among residents, but not during evening shift.
In a small pilot study, Richeson et al. evaluated visiting therapy dogs in 15 residents with dementia (14 women; age range 63-99 years; dementia MMSE mean score: 3.9; 26% with depression). The session with visiting therapy dogs lasted 1 hour daily for 3 weeks. Agitated behaviour, measured with the CMAI, decreased significantly after 3 weeks and increased significantly after 2 weeks washout subsequent to the end of AAT.

Libin and Cohen-Mansfield assessed the efficacy of a robotic cat (NeCoRo) and a soft toy cat in reducing agitated behaviour in 9 women with moderate dementia in nursing homes. The intervention consisted of two, 10-minute interactive sessions on different days. The robotic cat produced a significant increase in pleasure and interest, but did not reduce agitation. Conversely the soft toy cat significantly reduced agitation.

Motomura et al. included 8 women (mean age 84.8 years) residing in a nursing home and evaluated the efficacy of animal-assisted therapy, consisting of two dogs visiting for 1 hour, over 4 consecutive days, to reduce apathy or irritability. The outcomes were measured using the Geriatric Depression Scale, Physical Self-Maintenance Scale and MMSE. The intervention did not show any significant change on any of the outcomes evaluated.

Sellers et al. included 4 residents with dementia to evaluate the efficacy of a visiting dog. Agitation was measured with the Agitated Behaviours Mapping Instrument and Social Behaviour Observation Checklist. The authors reported that the intervention reduced agitated behaviour during treatment and increased observed social behaviour, but data and p-values were not reported.

**Dining Room Environment**

Two small (n=38) pre-post studies included in Whear’s review examined the effect of improved lighting and table-setting contrast in a dining room environment. One study (Brush 2002; n=25) found a positive effect on problem behaviours using the Meal Assistance Screening Tool, while the other study found a statistically significant reduction in daily agitation.
Special Care Units

In a Cochrane review, Lai 2009 (AMSTAR=8) examined Special Care Units (SCUs) for dementia individuals with behavioural problems. SCUs are characterised by trained staff, special care programmes, an altered physical environment, and involvement of families. This SR included one quasi-experimental study and seven observational studies (6 prospective cohort studies and 1 prospective case-controlled study). The absence of randomised trials is likely a consequence of important practical and ethical issues in applying this methodology in older subjects with dementia and behavioural problems. Only one case-controlled study evaluated agitation and used NPI and CMAI to measure the outcome in 65 participants with dementia. The results showed no significant changes in outcomes at three months; however, there were small, but significant improvements in the NPI score in favour of the SCU group at 6 months (WMD -4.30 (95% CI -7.22 - -1.38), 12 months (WMD -4.30 (95% CI -7.22 - -1.38)), and 18 months (WMD -5.40 (95% CI -9.16 - -1.65)). The same study also evaluated the effect of SCU on mood at three months and the results showed a small significant effect in favour of SCU [WMD -6.30 (95% CI -7.88 - -4.72)].
Discussion

Given the well-known negative side effects of commonly prescribed drugs to control behavioural disturbances (BPSD) in patients with dementia, non-pharmacological interventions have gained increasing attention in recent years as an alternative first-line approach to treat BPSD. This overview addresses the evidence supporting the efficacy of these interventions in community and residential care settings. We identified a number of SRs, which often focused on single interventions although, in several instances, multicomponent interventions were also examined. With the present study, using the primary studies included in the SRs, we have created a compendium of the types of non-pharmacological interventions, including the component of each single intervention, the dosage (when available), and the duration of the treatment.

In the absence of a validated taxonomy, we categorised the interventions according to the following classification: sensory stimulation interventions; cognitive/emotion-oriented interventions; behaviour management techniques (further subdivided according to the recipient of the intervention, i.e. the person with dementia, the caregiver or the staff); Multicomponent interventions and other interventions, such as exercise and animal-assisted therapies.

Among sensory simulation interventions, the only convincingly effective intervention for reducing behavioural symptoms (specifically agitation and aggressive behaviour) was music therapy. According to the most comprehensive review of music therapy, this treatment also reduced anxiety. However, the evidence supporting the effectiveness of music therapy was limited by moderate, but significant, heterogeneity, probably related to the variability of the intervention (e.g., type of music, active involvement, such as singing/playing a musical instrument and dancing, or passive involvement, such as listening) and the heterogeneity of the patient population in terms of the severity of dementia and the type of dementia. The efficacy of Aromatherapy and Massage therapy, both associated with conflicting results, remains unknown. Light therapy and SMST therapy did not show any noteworthy effect for clinical practice.
The body of evidence concerning cognitive/emotion-oriented interventions, which include Reminiscence Therapy, Simulated Presence Therapy and Validation Therapy, had important methodological limitations. The quality of the primary studies was low, as reported by the review authors, and the sample size of the studies was not powered to detect statistically significant effects. Even when it was possible to combine studies in a meta-analysis, for example, for Simulated Presence Therapy, the pooled estimated effect was not statistically significant. Added to these shortcomings was the variability in the length and type of the interventions and the multitude of outcomes measured. Overall, convincing evidence supporting the effectiveness of these psychological interventions was lacking.

The most frequently assessed intervention in several trials was Behavioural Management techniques. The elements in this type of intervention included behavioural or cognitive-behavioural therapy, functional analysis of specific behaviour, individualised behavioural reinforcement strategies, communication training, and other therapies, such as habit training, progressive muscle relaxation, and token economies. The body of evidence supporting the effectiveness of Behavioural Management techniques includes both positive and negative studies. Among the types of Behavioural Management techniques which aimed to enhance communication skills, formal caregiver training, and dementia mapping provided in residential care, were found to be effective at reducing agitation. The evidence was convincing when the intervention was supervised by healthcare professionals, with the effectiveness possibly persisting for 3 to 6 months.

There is some evidence that multicomponent interventions that use a comprehensive, integrated multidisciplinary approach combining medical, psychiatric and nursing interventions can reduce severe behavioural problems in nursing home patients.

Other interventions such as animal-assisted and exercise therapy did not show any convincing effect on any BPSD.
Strengths of this overview

The present overview represents a substantial update of a previous overview, using a search strategy launched in 2009, that provided a comprehensive synthesis of the evidence about non-pharmacological interventions on BPSD. We systematically searched reviews available in 4 electronic databases and systematically collected the evidence regarding non-pharmacological interventions for the treatment of behavioural disturbances in patients with dementia. To allow the identification of SRs of all potential non-pharmacological interventions, we used a highly sensitive search strategy by avoiding the inclusion of any specific name of non-pharmacological interventions. We also assessed the methodological quality of the reviews using the AMSTAR criteria. Another strength of the present overview was the adoption of a systematic and transparent method, and the use of duplicate, independent reviewers who performed the phases of study selection, data abstraction and data interpretation separately.

Limitations of the interpretation of the results

Overall, the SRs had a number of methodological limitations that could have affected the confidence in the reported results. First, the heterogeneity of the types and characteristics of the interventions, even within the same class of non-pharmacological interventions, was the most significant problem that emerged from the present study. One implication is that there are serious methodological issues that question the correctness, in our opinion, of combining studies in a meta-analysis, as some authors have previously done. Moreover, in some studies, the description of the interventions is too vague to allow a complete understanding of what was actually done. In addition, even in cases in which the intervention is well characterised, the dosage of the intervention, and the means used for its delivery, varied considerably. For example, in the case of music therapy, music interventions such as listening to music via headphones, based on participants’ musical preferences, differed from listening, playing percussion instruments, singing, movement or dance and was observed across all 9 trials combined in the meta-analysis. In the case of aromatherapy, there were several essential oils that were used in the primary studies, but in some instances, even when similar
components were used (e.g., Melissa essential oil), the mode of administration differed among trials. Similarly, there was great variation in the intensity (from 2,500 to 10,000 lux), duration (1 to 9 hours), frequency of exposure (10 days to 10 weeks), and type of device used (Dawn-Dusk Simulator)²², when light therapy was investigated for behavioural problems in dementia.

The variation in the characteristics of the interventions was particularly pronounced in the trials ascribed to Behavioural Management techniques. The trials used different conceptual frameworks, and sometimes broad and quite generic descriptions, to describe the interventions that at times were difficult to interpret and which influenced the content and quality of evidence of the SRs. In this area, it is therefore difficult to produce a satisfactory classification, which implies that different SRs did not consider the same group of studies, even when they clearly investigated non-pharmacological interventions specifically designed to improve behavioural management.

Finally, the arbitrary age cut-off of the patients (more than 60 years of age) and the exclusion of reviews published before 2009, constitute other limitations of the present overview. We did not evaluate the methodological quality of the primary studies included in the reviews, as this will be the scope of our next publication, in which we will apply the GRADE criteria³⁸.

**Conclusion**

This overview succeeded in providing a complete and up-to-date compendium of non-pharmacological interventions in older people with dementia, using recently published SRs and meta-analyses. The most promising treatments appeared to be Music therapy and some Behavioural Management techniques, particularly those involving caregiver-oriented and staff-oriented interventions. Despite the considerable number of published articles included in this overview, the evidence supporting the efficacy of non-pharmacological interventions is limited due to methodological quality and sample size and to the presence of important variations in the taxonomy of the non-pharmacological interventions, the outcomes assessed and the tools used to evaluate the outcomes.
Footnotes

Contributors IA, JMR, AC, RS, ACJ and DO conceived and designed the study. The manuscript of this protocol was drafted by IA, JMR, AC, RS, ACJ, AdG, and BHM and revised by MP, AnG, FMT and GDA. IA and JMR designed the search strategies; IA, JMR, FMT, and GDA performed the search, screening and assessment independently. AC arbitrated disagreements during the review. All authors contributed to data analysis and critical revision of the paper; additionally, every author approved the final version.

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Competing interests

No conflicts of interest.

Data Sharing

There are no additional data.
Title of Figures and Tables

**Table 1.** Characteristics of Included Systematic Reviews/Meta-analyses.

**Figure 1** Study screening process
Table 1. Characteristics of Included Systematic Reviews/Meta-analyses.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Databases searched</th>
<th>Population</th>
<th>Non-pharmacological intervention</th>
<th>Primary studies</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aguirre 2013</td>
<td>MEDLINE, Embase, Cinahl, PsycINFO, the Cochrane Library, Lilacs, trial registers, grey literature</td>
<td>Participants who had a diagnosis of dementia (Alzheimer’s disease, vascular dementia mixed Alzheimer’s and vascular dementia, other types of dementia), including all levels of cognitive impairment</td>
<td>Cognitive stimulation</td>
<td>15 RCTs</td>
<td>Mood, quality of life, well-being, ADL, communication, behaviour, neuropsychiatric symptoms and social interaction</td>
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<tr>
<td>Alves 2013</td>
<td>MEDLINE, PsycINFO, Cochrane Library, EMBASE, metaRegister of Clinical Trials, OVID all, EBM Reviews</td>
<td>Patients diagnosed with Alzheimer’s disease (without mild cognitive impairment, mixed Alzheimer’s disease, vascular dementia, and other types of dementia such as frontotemporal dementia or dementia with Lewy bodies)</td>
<td>Memory-Training Program; Attention-Stimulating Activities; Computerized “Cognitive Training”;</td>
<td>4 studies</td>
<td>Cognitive functioning; ADL; Memory Complaints; Finger Tapping Test; Depressive Symptoms; QoL; Reaction time; Screening of mental status; Neuropsychiatric Symptoms</td>
</tr>
<tr>
<td>Bernabei 2013</td>
<td>MEDLINE, Embase, PsycINFO</td>
<td>Elderly patients affected by dementia or psychiatric disorders</td>
<td>Animal-assisted interventions</td>
<td>10 studies on BPSD (3 case-control and 7 repeated measures design)</td>
<td>Any psychiatric disorder</td>
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<tr>
<td>Blake 2013</td>
<td>PubMed, Science Direct, the Cochrane Library and Web of Knowledge</td>
<td>Adults diagnosed with dementia who have depressive symptoms</td>
<td>Reminiscence group therapy</td>
<td>4 studies</td>
<td>Change in level of depressive symptoms</td>
</tr>
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<td>Carrion 2013</td>
<td>MEDLINE, EMBASE, PASCAL, the Cochrane Library, National Guidelines Clearinghouse, Trip database, HEALTHSTAR, CINHAL and PsycINFO</td>
<td>Older people diagnosed as having Alzheimer’s disease or probable Alzheimer’s disease</td>
<td>Cognition-oriented care approaches: 1. Reality Orientation; 2. Skills Training</td>
<td>Reality Orientation: 9 RCTs; Skills Training: 8 RCTs</td>
<td>Cognitive function; behavioural symptoms and mood</td>
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<td>Chaudhury 2013</td>
<td>MEDLINE, CINAHL, Ageline, Web of Science, and Simon</td>
<td>Long-term facility residents with dementia</td>
<td>Supportive dining environment</td>
<td>21 studies included: light</td>
<td>Physiological and socio-psychological</td>
</tr>
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<td>Study (Year)</td>
<td>Databases used</td>
<td>Population of the intervention</td>
<td>Interventions</td>
<td>Outcome Measures</td>
<td>Findings</td>
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<td>Collet 2010</td>
<td>MEDLINE, PsycINFO and Pubmed</td>
<td>Nursing home patients suffering from either somatic illness or dementia combined with psychiatric disorders or severe behavioural problems</td>
<td>Psychiatric care and nursing home care combination</td>
<td>8 RCTs</td>
<td>Psychosis and depression, Increase in Global functioning, behaviour disorders, cognition and ADL</td>
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<td>Eggenberger 2013</td>
<td>MEDLINE, AMED, EMBASE, PsycINFO, CINAHL, The Cochrane Library, Gerolit, Web of Science</td>
<td>People with dementia; professional and family caregivers’ communication skills training by means of face-to-face interaction</td>
<td></td>
<td>12 RCTs</td>
<td>QoL, social interactions</td>
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<tr>
<td>Forbes 2014</td>
<td>MEDLINE, EMBASE, The Cochrane Library, CINAHL, PsycINFO, LILACS+ several Registries, proceedings + other sites</td>
<td>People with dementia</td>
<td>Light therapy</td>
<td>5 studies met the inclusion criteria - only 3 were included in the analyses because of inappropriate reported</td>
<td>Sleep, behaviour, mood, and cognitive disturbances associated with dementia</td>
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<tr>
<td>Forrester 2014</td>
<td>MEDLINE, EMBASE, the Cochrane Library, CINAHL, PsycINFO, LILACS+ several Registries, proceedings + other sites</td>
<td>People with dementia</td>
<td>Aromatherapy</td>
<td>2 RCTs</td>
<td>Agitation, behavioural symptoms, quality of life, and adverse effects</td>
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<td>Fung 2012</td>
<td>MEDLINE, CINAHL, Cochrane Library, PsycINFO, Social Sciences Citation Index, SCOPUS</td>
<td>Participants with dementia</td>
<td>Aromatherapy</td>
<td>11 studies (5 RCTs; 6 controlled trials)</td>
<td>Behavioural problems</td>
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<td>Gonzalez 2014</td>
<td>MEDLINE, AMED, CINAHL, ISI Web of Knowledge, Embase and Scopus</td>
<td>People with dementia</td>
<td>Sensory gardens and horticultural activities</td>
<td>2 RCTs</td>
<td>Agitation levels; cognitive status</td>
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<td>Guzman-Garcia 2013</td>
<td>MEDLINE, AgeInfo, EBM Reviews EBSCO-CINAHL, EMBASE, ISI Web, LILACS, SCOPUS ZETOC; reference lists; EthOS-Beta; ACER;</td>
<td>People with dementia living in long-term care homes.</td>
<td>Dance movement therapy; dance therapy; Psychomotor dance-based; Social dancing</td>
<td>10 studies (1 RCT)</td>
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</tr>
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<td>Database Search Terms</td>
<td>Participants</td>
<td>Intervention</td>
<td>Study Design</td>
<td>Outcomes</td>
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<td>Kiepe 2012</td>
<td>MEDLINE and PsycINFO</td>
<td>Patients with mental illness</td>
<td>Dance therapy</td>
<td>1 study (RCT) for dementia</td>
<td>Any physical and mental outcomes</td>
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<td>Kim 2012</td>
<td>MEDLINE, CINAHL, ProQuest Medical Library, and Cochrane and OT</td>
<td>Persons with dementia</td>
<td>Occupational therapy</td>
<td>9 studies</td>
<td>Behavioural problems and depression</td>
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<td>Kverno 2009</td>
<td>MEDLINE, CINAHL, PsycINFO, EMBASE</td>
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<td>Any non-pharmacological intervention</td>
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<td>Lai 2009</td>
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<td>Patients with a confirmed diagnosis of dementia or Alzheimer’s disease or related disorders</td>
<td>Special care units</td>
<td>8 non-randomised studies (0 RCT)</td>
<td>Behavioural problems, mood, use of restraints and psychotropic medication</td>
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<td>Livingston 2014</td>
<td>MEDLINE; Web of Knowledge; EMBASE; British Nursing Index; the Health Technology Assessment programme database; PsycINFO; NHS Evidence; System for Information on Grey Literature</td>
<td>Subjects with dementia</td>
<td>Sensory, psychological and behavioural interventions</td>
<td>160 primary studies</td>
<td>Agitation</td>
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<td>McDermott 2013</td>
<td>MEDLINE, EMBASE, PsycINFO, CINAHL, Cochrane Library, Web of Science, J Music Therapy, and Nordic Journal of Music Therapy</td>
<td>Subjects with dementia</td>
<td>Music therapy</td>
<td>15 studies (6 RCTs; 4 non-randomised trials; 5 before-after studies)</td>
<td>Behavioural, psychological aspects, hormonal and physiological changes, social and relational aspects of music therapy</td>
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<td>Moniz-Cook 2012</td>
<td>MEDLINE, EMBASE, CINAHL, PsycInfo and LILACS;+</td>
<td>People with dementia, irrespective of its cause or diagnostic subtype, with reported BPSD or ‘behaviours that challenge’, receiving support or treatment from mental health workers, care staff or family or other informal caregivers</td>
<td>Formulation-led individualised interventions targeting reduction in the person’s distress and/or resolution of the caregivers’ management difficulties, Challenges in caregiver self-report of reaction to challenging behaviours.</td>
<td>18 trials</td>
<td>Challenging behaviours (e.g. verbal and physical aggression, restlessness) and mood (depression); Changes in caregiver self-report of reaction to challenging behaviours.</td>
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<tr>
<td>Study</td>
<td>Databases Used</td>
<td>Population</td>
<td>Intervention</td>
<td>Studies Identified</td>
<td>Results</td>
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<td>Moyle 2013</td>
<td>MEDLINE, CINHAL, PsycINFO, Cochrane Library, Scopus, Web of Science, Health Reference Center Academic</td>
<td>Older people with dementia:</td>
<td>Massage therapy</td>
<td>Of 13 studies identified only 1 satisfied the quality of the inclusion criteria</td>
<td>Agitated behaviour</td>
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<td>O’Neill 2011</td>
<td>MEDLINE, the Cochrane Library, PsycINFO</td>
<td>Adults with mild, moderate, or severe dementia</td>
<td>Non-pharmacological treatments</td>
<td>26 systematic reviews</td>
<td>Behavioural symptoms of dementia</td>
</tr>
<tr>
<td>Olazaran 2010</td>
<td>MEDLINE, PsycINFO, CINAHL, Embase, Lilacs and the Cochrane Dementia and Cognitive Improvement Group Specialized Register.</td>
<td>People with Alzheimer's disease and related disorders</td>
<td>Any non-pharmacological intervention</td>
<td>213</td>
<td>Cognition; Institutionalization; ADL; behaviour; mood; QoL; psychological well-being;</td>
</tr>
<tr>
<td>Padilla 2011</td>
<td>MEDLINE, the Cochrane Library, AgeLine, CINAHL, PsycINFO, EMBASE, and HealthSTAR, OT Seeker, and Allied and Complementary Medicine + reference list</td>
<td>People with Alzheimer's Disease and related dementias</td>
<td>Environment-based interventions; Multisensory Approaches; other interventions</td>
<td>1 cross-over trial (environmental-based intervention)</td>
<td>Performance, affect, and behavior</td>
</tr>
<tr>
<td>Potter 2011</td>
<td>MEDLINE, EMBASE, CINAHL, PsycINFO, AMED, the Cochrane Library, the UK National Research Register, Current Controlled Trials</td>
<td>Older people with dementia</td>
<td>Strength and flexibility; strength and balance Tai Chi classes sitting and standing; walking; stretching; seated exercises; balance training; endurance; aerobic training</td>
<td>13 RCTs</td>
<td>Physical functioning, quality of life and depression</td>
</tr>
<tr>
<td>Robinson 2011</td>
<td>MEDLINE; EBM reviews; AMED; BNI; CINAHL; EMBASE;</td>
<td>Not specified</td>
<td>Acupressure</td>
<td>1 RCT (of 71 acupressure studies)</td>
<td>Any outcome</td>
</tr>
<tr>
<td>Salami 2011</td>
<td>MEDLINE, EMBASE, and the Cochrane Central Register</td>
<td>People with Alzheimer's disease</td>
<td>Any treatment option for sleep disturbance not attributable to other clinical conditions</td>
<td>9 RCTs</td>
<td>Sleep disturbance</td>
</tr>
<tr>
<td>Seitz 2012</td>
<td>MEDLINE, EMBASE, PsycINFO, the Cochrane Library and Google Scholar</td>
<td>People with dementia</td>
<td>Any non-pharmacological intervention</td>
<td>40 studies</td>
<td>Neuropsychiatric symptoms</td>
</tr>
<tr>
<td>Subramaniam 2012</td>
<td>MEDLINE, PsycINFO, CINAHL, the Cochrane Library, EMBASE and Web of Knowledge</td>
<td>People with dementia</td>
<td>Reminiscence therapy</td>
<td>5 RCTs</td>
<td>Psychosocial benefits</td>
</tr>
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</tr>
<tr>
<td>Thune-Boyle 2012</td>
<td>MEDLINE, EMBASE, PsycINFO</td>
<td>People with dementia</td>
<td>Exercise therapy</td>
<td>2 RCTs</td>
<td>Behavioural and psychological symptoms</td>
</tr>
<tr>
<td>Ueda 2013</td>
<td>MEDLINE, CINAHL, PsycINFO</td>
<td>People with dementia</td>
<td>Music therapy</td>
<td>18 of 20 studies considered agitation or anxiety (9 CCT; 9 RCTs)</td>
<td>Behavioral and psychological symptoms; ADL; cognitive function</td>
</tr>
<tr>
<td>Vasionytė 2013</td>
<td>JSTOR, EBSCO, ERIC, SCIRUS, MEDLINE, PsycINFO, Cochrane Library and ProQuest, the journal databases SAGE PUB and Cambridge journals</td>
<td>Patients with dementia</td>
<td>Music therapy</td>
<td>3 RCTs</td>
<td>Affective, behavioural, cognitive and physiological outcomes</td>
</tr>
<tr>
<td>Vasse 2010</td>
<td>Pubmed, PsycINFO, Web of Science and the Cochrane library</td>
<td>People with dementia</td>
<td>A walking program combined with conversation, group validation therapy, life review programs, cognitive stimulation therapy, activity therapy and staff education</td>
<td>9 RCTs</td>
<td>Communication between residents with dementia and care staff; neuropsychiatric symptoms of residents with dementia.</td>
</tr>
<tr>
<td>Wall 2010</td>
<td>MEDLINE, CINAHL, PsycINFO</td>
<td>Older people with dementia</td>
<td>Music therapy</td>
<td>4 RCTs</td>
<td>Behaviour and wellbeing</td>
</tr>
<tr>
<td>Whear 2014</td>
<td>MEDLINE, PsycINFO, Embase, HMIC, AMED; Cochrane Library; CINAHL; British Nursing Index; ASSIA; Social Science Citation Index; ETHOS; Social Care Online and OpenGrey November 2012.</td>
<td>Elderly residents with dementia</td>
<td>Mealtime interventions categorized into 4 types: music, changes to food service, dining environment alteration, and group conversation</td>
<td>11 studies (7 time series repeated measures; 3 pre-post study design; 1 controlled clinical trial)</td>
<td>Behavioural symptoms (anxiety, agitation, aggression)</td>
</tr>
<tr>
<td>Woods 2012</td>
<td>MEDLINE, the Cochrane Library, EMBASE, PsycINFO,</td>
<td>People with dementia and their caregivers</td>
<td>Cognitive stimulation</td>
<td>15 RCTs</td>
<td>Cognitive functioning; mood;</td>
</tr>
<tr>
<td>Database(s)</td>
<td>Population</td>
<td>Intervention</td>
<td>Study Design</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>CINAHL and LILACS, ongoing trial databases and grey literature sources</td>
<td>QoL; ADL; behavioural symptoms; neuropsychiatric symptoms</td>
<td>Yu 2009 MEDLINE (PubMed), CINAHL, PsycINFO, and the Cochrane Library People with early-stage Alzheimer’s disease and dementia</td>
<td>Cognitive training</td>
<td>7 RCTs Any dementia symptoms in early-stage Alzheimer’s disease and related dementia.</td>
<td></td>
</tr>
<tr>
<td>Zimmermann 2013 MEDLINE, EMBASE, the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature, AgeLine, and PsycINFO People with dementia in nursing homes and other residential long-term care settings</td>
<td>Effective characteristics of residential long-term care</td>
<td>14 studies: 4 prospective cohort studies, 9 RCTs, 1 non-randomized controlled trial</td>
<td>Health and psychosocial outcomes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ADL, Activities of Daily Living; QoL, Quality of Life; RCT, randomised controlled trial
References


Figure 1. Study screening process

Potentially relevant reviews identified: 4392
- Medline (Pubmed): 1908
- Embase: 3511
- The Cochrane Library: 160
- DARE: 646
- CINAHL (EBSCO): 719
- PsycINFO: 703

Reviews excluded based on abstract evaluation: 4308

Reviews identified for full-text evaluation: 84

Reviews excluded with reason: 23
- Behavioral outcomes not considered: 12
- Caregiver related outcomes: 8
- Non-pharmacological interventions not considered: 2
- Participants did not have dementia: 1

Systematic review/meta-analysis included: 38

Primary studies included for evaluation: 142

Figure 1. Study screening process

186x190mm (300 x 300 DPI)
Appendix 1. Search strategies

1. Medline (via Pubmed)
   ("dementia"[MeSH Terms] OR "dementia"[All Fields] OR dement*[tiab] OR "Alzheimer"[All Fields] OR "cognitive impairment"[tiab])
   MEDLINE[Title/Abstract] OR (systematic AND review[Title/Abstract] OR meta-analysis[Publication Type])

2. EMBASE
   #1 'dementia'/exp OR 'dementia'
   #2 'alzheimers disease'
   #3 cognitive AND impairment
   #4 'systematic review'
   #5 'meta analysis'
   #6 #1 OR #2 OR #3
   #7 #4 OR #5
   #8 #6 AND #7
   #9 #6 AND #7

3. CINAHL
   S1 (MH Dementia OR Alzheimer OR dementia)
   S2 (systematic review OR meta-analysis OR AB medline)
   S3 S1 AND S2

4. Cochrane Library
   #1 MeSH descriptor: [Dementia] explode all trees
   #2 dementia
   #3 alzheimer
   #4 cognitive impairment
   #5 MeSH descriptor: [Mild Cognitive Impairment] explode all trees
   #6 #1 or #2 or #3 or #4 or #5

5. PsychInfo (via Ovid)
   #1. (exp dementia/) OR (dementia.mp.) OR ( alzheimer*.mp.) OR (exp alzheimer's disease/)
   #2. (systematic review.mp.) OR (exp Meta Analysis/) OR (MEDLINE.ab.)
   #3. #1 AND 2
Appendix 2. Characteristics of included primary studies by type of intervention

eTable 1. Aromatherapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akhondzadeh 2003 (1)</td>
<td>Placebo controlled, randomized trial</td>
<td>N=42; female 18; mean age 73; Diagnosis of AD, ADAS &lt;=2, CDR &gt;= 2 satisfied the NINCDS/ADRDA criteria</td>
<td>Intake of 60 drops of Melissa officinalis extract, daily for 4 months</td>
<td>Alzheimer's disease assessment scale- cognitive subscale</td>
<td>Proportion of participants with agitation was significantly less in the treatment arm</td>
</tr>
<tr>
<td>Ballard 2002 (2)</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>N=72, female 43, mean age 78; agitation as defined on CMAI or NPI</td>
<td>10% blended Melissa oil in lotion; application on face and arms; 2 times/day for 4 weeks</td>
<td>CMAI, NPI BI, DCM, CDRS</td>
<td>Significant improvement in the CMAI score</td>
</tr>
<tr>
<td>Burns 2011 (3)</td>
<td>3-arm, double-blind parallel-group placebo-controlled randomized trial</td>
<td>N=114; female 48; mean age 85; agitation for 4 weeks minimally, CMAI &gt;39, satisfied the NINCDS/ADRDA criteria for possible Alzheimer disease</td>
<td>Arm 1: 10% Melissa oil in base lotion massage into the hands and upper arms, 1–2 min 2 times/day by carer of participants for 12 weeks. Arm 2: 5 mg donepezil daily for 1 month and increased to 10 mg afterwards, plus10% of placebo oil (sunflower) massage</td>
<td>NPI, PAS</td>
<td>No significant improvement.</td>
</tr>
<tr>
<td>Cameron 2011 (4)</td>
<td>Cross-over, double-blind placebo-controlled randomized trial</td>
<td>N=18; sex not reported; mean age not reported; inclusion criteria not clearly reported (moderate to severe dementia) (setting not reported)</td>
<td>Intervention group: &lt;2% lemon balm oil</td>
<td>CMAI, PAS, NPI</td>
<td>Gradual, but not statistically significant, reduction in scores in all outcome measures</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>Inclusion Criteria</td>
<td>Intervention</td>
<td>Measurement</td>
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</tr>
<tr>
<td>Fu 2013 (5)</td>
<td>Single-blind parallel-group placebo-controlled randomized trial</td>
<td>N=67; female 40; mean age 84; MMSE &lt;=24/30; AD according to American Psychiatric Association DSM-IV-TR; a documented history of a minimum of two weeks of agitation or aggression in total (consecutively or 14 single days), within the past three months</td>
<td>Arm 1: 3% lavender mist (75 drops); Am 2: 3% lavender mist (75 drops) plus and massage twice a day for 10 days; each hand massaged for 2.5 minutes</td>
<td>CMAI</td>
<td>Significant less aggressive behaviour in the arms that used active treatment</td>
</tr>
<tr>
<td>Gray 2002 (6)</td>
<td>Placebo controlled clinical trial</td>
<td>N=13; females 6; subjects that have “difficult-to-manage behaviours”</td>
<td>Intervention group: A mix of lavender, sweet orange, tea tree oil soaked into a cotton ball and taped to the lapel of each subject by caregiving staff; Total application: 16 times</td>
<td>Subjects were videotaped and rated by trained observers for frequency of resistive behaviours</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Holmes 2002 (7)</td>
<td>Placebo controlled clinical trial</td>
<td>N=15; females 7; diagnostic criteria based on ICD-10 for severe dementia and on a minimum score of 3 points on the PAS; NINCDS/ADRDA criteria for possible Alzheimer’s Disease</td>
<td>Intervention group: Diffusion of 2% lavender oil for 10 sessions; each session lasted 2 h (16.00–18.00 hours) and was followed by placebo (water) for another 2 h; aroma-streams were used for diffusion</td>
<td>PAS</td>
<td>Nine patients (60%) showed an improvement, five (33%) showed no change and one patient (7%) showed a worsening of agitated behaviour during aromatherapy</td>
</tr>
<tr>
<td>Lin 2007(8)</td>
<td>Placebo-controlled crossover randomized trial</td>
<td>N=70; female 41; mean age 78; participants with dementia diagnosed with DSM-IV, with clinically significant agitation identified using Chinese version CMAI</td>
<td>Intervention group: Inhalation of essential oils in cosmetic cotton containing lavender diffused by aroma diffuser. Diffusers were placed at each side of the pillow during sleep at night for at least 1 h.</td>
<td>Chinese version CMAI, NPI,</td>
<td>Significant improvement in NPI and CMAI</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Observation</td>
<td>Outcome</td>
</tr>
<tr>
<td>-------------</td>
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</tr>
<tr>
<td>O'Connor 2011</td>
<td>Cross-over, single-blind placebo-controlled randomized trial</td>
<td>N=66; female 39; mean age 78; Clinical Dementia Rating scale; physically agitated behaviour;</td>
<td>Intervention group: 30% lavender (<em>Lavandula angustifolia</em>) in jojoba oil</td>
<td>Observation of behaviour, CMAI, Philadelphia Geriatric Center Affect Rating Scale</td>
<td>No statistical difference between the groups</td>
</tr>
<tr>
<td>Smallwood 2001</td>
<td>3-arm, single-blinded randomized, controlled trial</td>
<td>N=21; Participants with dementia diagnosed by a psychiatrist</td>
<td>Arm 1: lavender oil massage; Arm 2: plain oil massage; Arm 3: conversation and lavender oil diffusion; All 3 arms received treatment twice in a specific period of the day and twice a week</td>
<td>Video-tapes recording behaviour for 15 min in each specified 4 periods during the day, at baseline, and after treatment. Video recordings were rated by 2 blinded raters.</td>
<td>Only in 1 period (between 15.00–17.00 hours) a consistent reduction in agitation was observed in the lavender oil massage arm than in the other two arms.</td>
</tr>
<tr>
<td>Snow 2004</td>
<td>Placebo controlled clinical trial</td>
<td>N=28; females 26; mean age 86; Probable AD with “marked agitation”; CMAI applied by nursing staff</td>
<td>Arm 1: 2 drops of undiluted oil containing lavender, thyme, and unscented grape-seed oil was placed every 3 h on an absorbent fabric sachet pinned near the clavicular part of each subject’s shirt. Arm 2: 3 applications/day</td>
<td>CMAI (rated every 2 days); Severe Impairment Rating Scale;</td>
<td>No evidence of reduction of agitation</td>
</tr>
</tbody>
</table>

CDRS, Clinical Dementia Rating Scale; CMAI, Cohen-Mansfield Agitation Inventory; DCM, Dementia Care Mapping; DSM, Diagnostic and Statistical Manual of Mental Disorders; NINCDS/ADRDA, National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer’s Disease and Related Disorders Association; NPI, Neuropsychiatric Inventory; PAS, Pittsburgh Agitation Scale
eTable 2 describes the type of interventions, the outcomes and the results of the primary studies included in the Message therapy reviews.

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hollyday-Walsh (12)</td>
<td>Before-after study</td>
<td>N=52 participants (39 women and 13 men; mean age 90 years)</td>
<td>Intervention group: 10- to 15-minute massage of the upper extremities; Control group:</td>
<td>Behavioral Symptoms from the Minimum Data Set; a) wandering; b) verbally abusive behavioural symptoms; c) physically abusive behavioural symptoms; d) socially inappropriate/disruptive behaviour; and e) resistance to care</td>
<td>Massage therapy was significantly associated with improvement for 4 of the 5 outcomes</td>
</tr>
<tr>
<td>Remington 2002 (13)</td>
<td>Randomized trial</td>
<td>N=42 nursing home residents with a diagnosis of &quot;Chronic organic brain syndrome&quot;</td>
<td>Intervention group: hand massage; Frequency: One treatment of 10 min.; Control group: no touch</td>
<td>a) agitation (CMAI)</td>
<td>Agitation reduced: Mean difference; 7.83 (4.30, 11.36)</td>
</tr>
</tbody>
</table>

CMAI, Cohen-Mansfield Agitation Inventory;
### eTable 3. Characteristics of Bright light therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancoli-Israel 2003 (14)</td>
<td>3-arm, single-blind, randomized controlled trial</td>
<td>N=92 nursing home residents; female; mean age 82; MMSE mean=5.7 (SD 5.6, range 0-22)</td>
<td>Active group: Bright light &gt; 2500 Lux; time of day 9.30-11.30 or 17.30-19.30 daily; Control group: Dim, red light (control)&lt; 300 Lux; time of day 9.30-11.30 daily; Device used: Apollo “Brite-Lite” box placed 1m from resident. Duration of treatment: 10 days</td>
<td>Agitation (ABRS and CMAI); Sleep: sleep duration, sleep efficiency, night-time activity measured after 10 days of treatment</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Barrick (15)</td>
<td>cluster-unit crossover design</td>
<td>N=66 participants in two residential care settings</td>
<td>Active group: AM bright light (7-11 AM); PM bright light (4-8 PM); All Day bright light (7 AM – 8 PM); Control group: Standard light (i.e. the baseline condition).</td>
<td>CMAI</td>
<td>Ambient bright light resulted not effective in reducing agitation and may exacerbate behavioural symptoms</td>
</tr>
<tr>
<td>Burns 2009 (16)</td>
<td>Single-blinded randomized trial</td>
<td>N=48 nursing home residents, female 32; mean age 83; any type of dementia</td>
<td>Active group: Bright light 10,000 lux from 10.00 hrs - noon (Brite-Lite box placed in front of resident); Control group: Standard fluorescent tube light at 100 lux from 1000 hrs – noon Received treatment daily for two weeks; Duration of treatment: 14 days (weeks 2 and 3)</td>
<td>Agitation (CMAI); depression (CSDD)</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design</td>
<td>N =</td>
<td>Characteristics</td>
<td>Intervention Details</td>
<td>Outcomes</td>
</tr>
<tr>
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</tr>
<tr>
<td>Dowling 2005 (17)</td>
<td>Randomized controlled trial</td>
<td>70 nursing home residents; female 57; mean age 84; MMSE 0-23 (mean=7, SD 7)</td>
<td>Active group 1: Bright light exposure &gt;2500 lux morning (9:30-10:30 am) Active group 2: Bright light exposure &gt;2500 lux afternoon (3:30-4:30 pm) or supplemented using Apollo Brite Lite IV box placed at least 4 feet from resident Control group: The control group received usual indoor light (150-200 lux) and participated in their regular activities Frequency: Daily, Monday through Friday Duration: 10 weeks</td>
<td>agitation, depression (NPI)</td>
<td>No significant effects in favor of light therapy</td>
</tr>
<tr>
<td>Hickman (18)</td>
<td>Cluster-unit crossover trial</td>
<td>66 older adults with dementia</td>
<td>Active group: morning bright light, evening bright light, all-day bright light (2,000 to 2,500 lux). Control group and 500 to 600 lux</td>
<td>Depression (CSDD)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Riemersma 2008 (19)</td>
<td></td>
<td>199 nursing home patients; mean age 85; any type of dementia</td>
<td>Active group 1: light exposure (using Plexiglas diffusers mounted in ceiling) 1000 lux; Active group 2: light exposure (using Plexiglas diffusers mounted in ceiling) 400 lux + melatonin Active group 3: melatonin only Light exposure frequency: from 9:00 - 18:00 Control group: inactive light</td>
<td>Agitation (CMAI); sleep duration and sleep latency; psychiatric symptoms (NPI); depression (CSDD)</td>
<td>No significant different between the groups</td>
</tr>
</tbody>
</table>

ABRS, Agitated Behavior Rating Scale; CMAI, Cohen-Mansfield Agitation Inventory; CSDD, Cornell Scale for Depression in Dementia; NPI, Neuropsychiatric Inventory
# eTable 4. Characteristics of Sensory Garden and Horticultural activities for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calkins 2007 (20)</td>
<td>Pre-post</td>
<td>N=17 nursing home residents</td>
<td>Garden</td>
<td>Agitation (CMAI), sleep</td>
<td>No results were available</td>
</tr>
<tr>
<td>Cohen-Mansfield 1998 (21)</td>
<td>Pre-post</td>
<td>N=12 nursing home residents</td>
<td>Garden</td>
<td>Mood, Agitation (CMAI)</td>
<td>Statistically significant decrease in physically non-aggressive and aggressive behaviours</td>
</tr>
<tr>
<td>Connell 2007(22)</td>
<td>RCT</td>
<td>N=20 nursing home residents</td>
<td>Horticultural therapy</td>
<td>Agitation (CMAI), sleep</td>
<td>Non-statistically significant effects on aggression and physical and verbal agitation</td>
</tr>
<tr>
<td>Detweiler 2008(23)</td>
<td>Pre-post</td>
<td>N=34 Dementia Units residents</td>
<td>Garden</td>
<td>Inappropriate behaviours (CMAI)</td>
<td>Statistically significant decline in total CMAI</td>
</tr>
<tr>
<td>Jarrott and Gigliotti 2010(24)</td>
<td>RCT, cluster randomized</td>
<td>N=129 with dementia, female not specified, mean age not specified, control group: traditional activities</td>
<td>Horticultural activities for at least 25 minutes, but neither frequency nor total duration specified</td>
<td>Affect (AARS); social engagement (MPES)</td>
<td>No difference in affect.</td>
</tr>
<tr>
<td>Luk 2011(25)</td>
<td>RCT</td>
<td>N=14 nursing home residents</td>
<td>Horticultural activities were conducted outside for 30 mins twice per week.</td>
<td>Agitation (CMAI)</td>
<td>Non-significant decline in aggressive and non-aggressive behaviour and CMAI</td>
</tr>
<tr>
<td>Vuolo 2003(26)</td>
<td>Pre-post</td>
<td>N=50 NH residents</td>
<td>Horticultural therapy</td>
<td>Agitation</td>
<td>Statistically significant reduction in physically non-aggressive behaviour</td>
</tr>
</tbody>
</table>

AARS, Apparent Affect Rating Scale; CMAI, Cohen-Mansfield Agitation Inventory; MPES, Menorah Park Engagement Scale;
### eTable 5a. Music therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi 2009 (27)</td>
<td>CT</td>
<td>N=20; mean age 75, dementia (Alzheimer’s, vascular, other)</td>
<td>Singing song, analysis of libretto, making musical instruments, playing piano and hand bells, song drawing and writing; 50 min/3x per week for 5 weeks;</td>
<td>MMSE, GDS, Gqol,NPI-Q</td>
<td>Reduced behavioural symptoms and depression</td>
</tr>
<tr>
<td>Clark 1998 (28)</td>
<td>RCT</td>
<td>N=18; all types of dementia</td>
<td>Listening to music individually, 2 weeks duration, Agitation (unclear checklist)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cooke 2010 (29)</td>
<td>RCT</td>
<td>N=24; early to mid-stage dementia</td>
<td>Singing, playing music, listening to music in a group, 8 weeks;</td>
<td>GDS</td>
<td></td>
</tr>
<tr>
<td>Goka 2005 (30)</td>
<td>CT</td>
<td>N=22; mean age 78, mild to moderate Alzheimer’s dementia</td>
<td>Combined music and reminiscence therapy. Singing songs associated with memories of the participants; 60 min/1x per week for 10 weeks;</td>
<td>MMSE, HDS-R,DAD, NPI, TORS</td>
<td>non statistically significant reduction of behavioural symptoms</td>
</tr>
<tr>
<td>Groene 1993 (31)</td>
<td>RCT</td>
<td>N=30, mean age 78, Alzheimer’s dementia</td>
<td>Listening, playing percussion instruments, singing, movement or dance. Music based on personal references; 7 sessions, 15 min each;</td>
<td>Wandering behaviour, seating/proximity behaviour, MMSE</td>
<td>no change in wandering behaviour</td>
</tr>
<tr>
<td>Guétin 2009 (32)</td>
<td>RCT</td>
<td>N=30, mean age 86, mild to moderate Alzheimer’s dementia</td>
<td>Listened to music based on participants’ music preferences via headphones; 20 min/1x per week for 24 weeks; control group: rest and reading</td>
<td>Hamilton Scale, GDS</td>
<td>reduced depression</td>
</tr>
<tr>
<td>Ikeda 2006 (33)</td>
<td>RCT</td>
<td>N=12, mean age 86, severe senile dementia</td>
<td>One on one rhythm exercise. Shake hands and clap in rhythm to music based on participant’s music preferences with a familiar song; 15 min/5x per week for 7 weeks;</td>
<td>MMSE, GBS,ROM-T, D-EMS</td>
<td>non statistically significant reduction of depression</td>
</tr>
<tr>
<td>Irish 2006 (34)</td>
<td>CT, repeated measures</td>
<td>N=10 with mild Alzheimer’s dementia</td>
<td>Listening to classical music individually, 2 weeks, State-Trait Anxiety Inventory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledger 2007 (35)</td>
<td>CT</td>
<td>N=45, mean age 85, mild to moderate senile Alzheimer’s dementia</td>
<td>Listening to music played by the therapist, singing, playing instruments, moving to music and discussing feelings and memories; 30-45 min/1x per week for at least 42 weeks to 1 year;</td>
<td>CMAI-long</td>
<td>non statistically significant increase of behavioural symptoms</td>
</tr>
<tr>
<td>Mihara 2004 (36)</td>
<td>CT</td>
<td>N=19, mean age 86, dementia</td>
<td>Greeting, gentle stretching exercise and breath control, singing familiar music, playing a musical instrument and rhythm activity; 30-45 min/1x per week for 8 weeks;</td>
<td>AR-MCL, TORS,JSS-D, JSS-E, VI</td>
<td>non statistically significant reduction of depression</td>
</tr>
<tr>
<td>Miura</td>
<td>CT</td>
<td>N=31, mean age 78, mild</td>
<td>Opening song, rhythm exercise, singing, music</td>
<td>BI, GDS, MMSE,SKT,</td>
<td>non statistically</td>
</tr>
<tr>
<td>Year</td>
<td>Study Type</td>
<td>Sample Description</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Summary</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>---------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>2005(37)</td>
<td></td>
<td>Alzheimer’s, vascular, frontotemporal and Lewy body and other dementia</td>
<td>appreciation and reminiscence; &lt;60 min/1x per week for 8-10 weeks;</td>
<td>ZBI, SPECT,D-EMS, D-EMS</td>
<td>significant increase of depression</td>
</tr>
<tr>
<td>Nair 2010(38)</td>
<td>Randomized, cross-over</td>
<td>N=37,</td>
<td>Listening to classical music in a group, 12 weeks duration,</td>
<td>Behavior chart</td>
<td>No change in behaviours.</td>
</tr>
<tr>
<td>Hokkanen 2008(39)</td>
<td>RCT</td>
<td>29 nursing home residents, female 22, mean age 82, dementia (Alzheimer’s, vascular, other)</td>
<td>Dance movement therapy; 30-45 min/1x per week for 9 weeks; control group: regular nursing home activities</td>
<td>The word list savings score; Clock drawing test; Cookie Theft; NOSGER</td>
<td>Reduction of behavioural symptoms; non statistically significant reduction of depression</td>
</tr>
<tr>
<td>Raglio 2008(40)</td>
<td>RCT</td>
<td>N=59, mean age 85, Alzheimer’s, mixed and vascular dementia</td>
<td>Singing and body movement with music to promote communication; 30 sessions of 30 min/session for 16 weeks; control group: educational and entertainment activities</td>
<td>MMSE, BI, NPI,MTCS</td>
<td>Non statistically significant reduction of depression</td>
</tr>
<tr>
<td>Raglio 2010(41)</td>
<td>RCT</td>
<td>N=20, female 15, mean age 86</td>
<td>Improvisation-based music therapy: two 30-minsession/week for 15 weeks; control group: educational and occupational activities</td>
<td>NPI</td>
<td>NPI: no change; NPI sub-score: depression improved</td>
</tr>
<tr>
<td>Raglio 2010(42)</td>
<td>RCT</td>
<td>N=60, female 55, mean age 85, Alzheimer’s, mixed and vascular dementia</td>
<td>Patients and music therapist express their emotions playing musical instruments and interacting; 30 min/3x per week for 12 weeks; control group: educational support and entertainment activities</td>
<td>NPI</td>
<td>Non statistically significant reduction of behavioural symptoms and depression</td>
</tr>
<tr>
<td>Remington 2002(43)</td>
<td>RCT</td>
<td>N=34, mean age 82, mild to severe senile dementia</td>
<td>Listening to music with a slow tempo via a portable CD player; 1 session for 10 min;</td>
<td>CMAI</td>
<td>Reduced behavioural symptoms</td>
</tr>
<tr>
<td>Sung 2006a(44)</td>
<td>RCT</td>
<td>N=36, mean age 78, dementia</td>
<td>Body and limb movement to participant’s familiar music with moderate tempo via a CD player; 30 min/2x per week for &gt;4 weeks; control group: usual care</td>
<td>CMAI</td>
<td>Non statistically significant reduction of behavioural symptoms</td>
</tr>
<tr>
<td>Sung 2006b(45)</td>
<td>RCT</td>
<td>N=57, mean age not reported, dementia</td>
<td>Listened to music based on personal references; 30 min/2x per week for 6 weeks;</td>
<td>CMAI</td>
<td>Reduction of behavioural symptoms</td>
</tr>
<tr>
<td>Sung 2010(46)</td>
<td>CT</td>
<td>N=52, mean age 80, moderate and severe senile dementia</td>
<td>Listened to music based on participant’s music preferences in via CD players; 30 min/2x week for &gt;6 weeks;</td>
<td>Anxiety (RAID)</td>
<td>Preferred music listening reduced significantly the anxiety score at six weeks (F = 12.15, p = 0.001)</td>
</tr>
<tr>
<td>Suzuki 2004(47)</td>
<td>CT</td>
<td>N=23, mean age 84, Alzheimer’s and vascular dementia</td>
<td>Opening song, singing songs based on personal references, playing hand-held drums; 60 min/2x per week for 8 weeks;</td>
<td>MOSES</td>
<td>MOSES: ‘irritability’ sub-score improved significantly</td>
</tr>
<tr>
<td>Suzuki 2007(48)</td>
<td>CT</td>
<td>N=16, mean age 86, Alzheimer’s and vascular dementia</td>
<td>The greeting song, singing songs from subjects’ historical background and preference, hand-bell performance, and listening to flute and piano; 60</td>
<td>BEHAVE-AD</td>
<td>Non statistically significant reduction of behavioural symptoms</td>
</tr>
</tbody>
</table>
For peer review only

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Population</th>
<th>Type of Intervention, Dose, Route of Administration in Active Group</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>N=16, age range 84-104, moderate to severe senile dementia</td>
<td>Listening to songs accompanied by different kinds of musical instruments, singing songs, playing exercise with listening to songs and playing musical instruments. Music was relaxing western and Chinese traditional music; 45 min/3x per week for 3 weeks;</td>
<td>CMAI, NPI</td>
<td>Reduction of behavioural symptoms</td>
</tr>
<tr>
<td>RCT</td>
<td>N=25, mean age 82, Alzheimer’s and multiple infarct dementia</td>
<td>Exercise training with music adapted to the age-range of the participants; 30 min daily for 3 months;</td>
<td>BOP scale</td>
<td>Non statistically significant increase of behavioural symptoms</td>
</tr>
</tbody>
</table>

BEHAVE-AD, Behavior Pathology in Alzheimer’s Disease Rating Scale; BOP, Beoordelingsschaal voor Oudere Patient/Evaluation Scale for Elderly; CMAI, Cohen-Mansfield Agitation Inventory; CHF, congestive heart failure; CT, Controlled clinical trial; HRV, heart rate variability; MOSES, Multidimensional Observation Scale for Elderly Subjects; NPI, Neuropsychiatric Inventory; RCT Randomized controlled trial; RAID, Rating Anxiety in Dementia

Table 5b. Dance therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Population</th>
<th>Type of Intervention, Dose, Route of Administration in Active Group</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>N=29 nursing home residents, female 22, mean age 82, dementia (Alzheimer’s, vascular, other)</td>
<td>Dance movement therapy; 30-45 min/1x per week for 9 weeks; control group: regular nursing home activities</td>
<td>The word list savings score; Clock drawing test; Cookie Theft; NOSGER</td>
<td>No change in behaviours.</td>
</tr>
</tbody>
</table>

NOSGER (Nurses’ Observation Scale for Geriatric Patients)

eTable 6. Snoezelen Multisensory Stimulation Therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Population</th>
<th>Type of Intervention, Dose, Route of Administration in Active Group</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>N=50 subjects with Alzheimer’s disease, vascular dementia or mixed diagnosis; mean age 78; female 25</td>
<td>Eight standardized multi-sensory programs.</td>
<td>INTERACT (22-item); INTERACT (12-item); Carry-over and long-term effect Behavioral: REHAB (general behaviour subscale and deviant behaviour subscale) Behavior Rating Scale (BRS) of CAPE</td>
<td>No significant effects on any scale of behavioural symptoms were found either immediately after intervention or at one-month post-follow-up</td>
</tr>
<tr>
<td>Randomized</td>
<td>N=136 subjects diagnosed with</td>
<td>Eight multi-sensory</td>
<td>INTERACT (22-item); INTERACT</td>
<td>There were no longer-term</td>
</tr>
<tr>
<td>Year</td>
<td>Study</td>
<td>Type</td>
<td>Sample</td>
<td>Intervention</td>
</tr>
<tr>
<td>------</td>
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</tr>
</tbody>
</table>
| 2003 | (52)  | Trial | Alzheimer’s, vascular or mixed dementia; mean MMSE scores snoezelen group (9.4) and the control group (6.7) (p=0.01) | Programs (12-item); Carry-over and long-term effect Behavioral: REHAB (general behaviour subscale and deviant behaviour subscale) Behavior Rating Scale of CAPE | Treatment effects of the integrated snoezelen-care program on behaviour. |}

van Weert 2005 (53)

CT

N=125, female 101, mean age 84, dementia (DSM-III-R)

Snoezelen; 18 months, control group non specified

CMAI (Cohen-Mansfield Agitation Inventory);

Improvement in intervention group for short term period but not for long follow-up

DSM, Diagnostic and Statistical Manual of Mental Disorders
### eTable 7. Transcutaneous electrical nerve stimulation therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hozumi 1996 (54)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Country: Japan N=27 subjects with multi-infarct dementia with irregular sleep-wake patterns and nocturnal behaviour disorders and/or delirium; 15 female; age 58 - 86 years</td>
<td>Stimulator type: HESS-10 Waveform: rectangular pulses Frequency: 6 - 80 Hz Pulse duration: 0.2 ms maximum, rms of 256 microA Amplitude: 6 - 8 V Electrode location: transcranial with electrodes attached to the &quot;forehead and inion with a head-band&quot; Treatment duration: 20 minutes daily for 2 weeks Placebo treatment: same as experimental but electrodes disconnected from the device.</td>
<td></td>
<td>Behavior disorder improved p &lt; 0.05</td>
</tr>
<tr>
<td>Scherder 1998 (55)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Country: Holland N=18 subjects in a residential home, mean age 82 (70 – 91); Shortened MMSE mean 4.4/12.7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances. NINCDS-ADRDA criteria</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental except no current delivered.</td>
<td>BOP scale</td>
<td>Behavioral disorder not improved</td>
</tr>
<tr>
<td>Scherder 1999 (56)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Country: Holland N=18 subjects, 9 expt, 9 control Lived in a residential home for elderly people. Age: 70 - 91yrs, mean 81.7 Shortened MMSE mean 4.4/12.7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances. Met NINCDS-ADRDA criteria for clinical diagnosis of dementia of Alzheimer's type, GDS stage 6 (mid-stage) with symptoms present at least 6 months, all scored 17 or less</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental</td>
<td>BOP scale</td>
<td>Behavioral disorder not improved</td>
</tr>
<tr>
<td>Scherder 1999 (57)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>N=15 subjects, 8 experimental, 7 control (16 initially, one from the control group did not tolerate the actigraphic assessment and was therefore excluded from the study)</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes between T1 and T5 on 2cm from the spine. Poles switched daily. Treatment duration: 30 min/day, 5 days/week, 6 weeks Placebo intervention: Same as experimental except no current delivered.</td>
<td>Rest–activity rhythm (assessed using actigraphy)</td>
<td>Improvement in the rest–activity rhythm</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------------</td>
<td>--------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Scherder 1999 (58)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Lived in a residential home for elderly people. Meeting NINCDS-ADRDA criteria for clinical diagnosis of probable dementia of Alzheimer’s type, GDS stage 6 (midstage) with symptoms.</td>
<td>Stimulation not described except that Premier 10s stimulator used. Study 1: TENS for 6 hours/day, therapist present throughout Study 2: TENS for 30 min/day, therapist present throughout Study 3: TENS without therapist present (called “isolated TENS” in the report), duration of treatment not indicated. Study 4: no description of TENS intervention given. Therapist present.</td>
<td>BOP scale</td>
<td>No improvement in behavioural disturbances Behavioural disorder not improved</td>
</tr>
<tr>
<td>Scherder 2000 (59)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Institutionalized elderly persons 17 F, 3 M Age: 82-91 yrs, mean 86.9 Inclusion criterion for shortened MMSE 8-12/12, BUT a range of 7-11, mean of 9.4 described for the experimental group, range 8 - 12, mean 9.7 for controls.</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec. Amplitude: Visible muscle twitches Electrode location: Two 2 x 3 cm electrodes</td>
<td>BOP scale</td>
<td>Need of help subscale only: ns Behaviour inventory: ns</td>
</tr>
<tr>
<td>Scherder 2002 (60)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Institutionalized elderly persons. Mean age: experimental group 87.1, control group 87.67. Mean education: experimental group 3.11, control group 2.88. MMSE experimental group 18.33, control group 19.67. All met NINCDS-ADRDA criteria for the clinical diagnosis of probably AD and stage 5 of the GDS.</td>
<td>Stimulator: Alphastim 100 Waveform: Bipolar asymmetric rectangular waves, Frequency: 0.5 Hz Pulse duration: not given Amplitude: 10 - 600 microA, to just below reported sensation of tingling and/or dizziness or to maximum if no sensation experienced. Electrode Placement: clipped to the earlobes. Treatment duration and frequency: 30 minutes/day between 1500 and 1900 h, 5 days/week, 6 weeks. Placebo intervention: Same as experimental except no current administered.</td>
<td>BOP scale</td>
<td>No improvements or treatment effects on Affective, independent &amp; psychogeriatric behaviour</td>
</tr>
<tr>
<td>Scherder 2003 (61)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Lived in a residential home for elderly people. Age: 70 - 91yrs, mean 81.7 Shortened MMSE mean 4.4/12. 7 or less/12 on this scale, (equivalent to 17 or less/20 on regular MMSE) classifies patients as having serious cognitive disturbances. Met NINCDS-ADRDA criteria for clinical diagnosis of dementia of Alzheimers type, GDS stage 5 (midstage) with symptoms present at least 6 months</td>
<td>Stimulator type: Premier 10s 1. Stimulator: Alphastim 100 Waveform: Bipolar asymmetric rectangular waves, Frequency: 0.5 Hz 30mins/day, 5 days a week 2.control appeared the same with electrodes but no current</td>
<td>Rest–activity rhythm (assessed using actigraphy)</td>
<td>No improvement in the rest–activity rhythm</td>
</tr>
<tr>
<td>Van Someren 1998 (62)</td>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Nursing home patients. Diagnosed with early stage probable AD NINCDS-ADRDA Age mean 84 +/- 1.5 Dutch cognitive screening test: mean 10.2 +/- 0.4( = approx 18 on MMSE);</td>
<td>Stimulator type: Premier 10s Waveform: asymmetric biphasic square wave, Burst mode Frequency: Bursts of trains, 9 pulses/burst, pulse freq 160Hz, burst freq 2 Hz Pulse duration: 100 microsec.</td>
<td>Rest–activity rhythm (assessed using actigraphy)</td>
<td>Improvement in the rest–activity rhythm</td>
</tr>
</tbody>
</table>
|                | (initial sample of 19, 14 completed), 6 treated, 8 placebo; | Amplitude: Visible muscle twitches  
Electrode location: Two 2 x 3 cm electrodes between shoulder blades.  
Treatment duration: 30 min/day, 5 days/week, 6 weeks  
Placebo intervention: Same as experimental except no current delivered. |

BOP, Beoordelingsschaal voor Oudere Patient/Evaluation Scale for Elderly; GDS, Global Deterioration Scale; MMSE, Mini-Mental State Examination; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association
<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baines 1987 (63)</td>
<td>Cross-over, randomized trial</td>
<td>15 residents living in care home, female 14; Mean age=81.5. 'Moderate to severe Impairment of cognitive functioning'</td>
<td>Reality orientation (board and discussion of current orientating information through newspapers, photographs, calendars and clocks etc., with materials selected to stimulate all five senses)</td>
<td>Behavior: BRS</td>
<td>No significant difference between the groups in terms of the behavioural disturbances</td>
</tr>
<tr>
<td>Chapman 2004 (64)</td>
<td>Randomized controlled trial</td>
<td>donepezil-plus-stimulation group; n = 26; donepezil-only group; n = 28. mild to moderate Alzheimer's disease (AD; Mini-Mental Status Examination score of 12-28); 54 to 91 years</td>
<td>cognitive-communication stimulation in combination with donepezil</td>
<td>NPI</td>
<td>A group x time interaction for the stimulation plus donepezil- group on irritability compared with the donepezil-only group.</td>
</tr>
<tr>
<td>Ferrario 1991 (65)</td>
<td>Randomized controlled trial</td>
<td>19 elderly residents; female 8; mean age 82 Subjects with cognitive disturbances - MMSE range 18-25</td>
<td>Reality orientation</td>
<td>Behavior problems: MOSES - irritable, withdrawn Mood: MOSES</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Study Design</td>
<td>Participants</td>
<td>Interventions</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
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<td></td>
</tr>
<tr>
<td>Onder 2005 (66)</td>
<td>3-arm, randomized controlled trial</td>
<td>156 home residents with probable Alzheimer’s Disease on Donepezil treatment for at least 3 months; female 113; mean Age 75.8; MMSE 20.1 (sd 3.1)</td>
<td>Current information, topics of general interest, historical events and famous people, attention, memory and visuo-spatial</td>
<td>Behavior problems: NPI</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Niu 2010 (67)</td>
<td>randomized, controlled, rater-blind clinical trial</td>
<td>32 patients with mild to moderate Alzheimer’s disease showing marked BPSD</td>
<td>Cognitive stimulation focused on tasks requiring executive functions and working memory</td>
<td>NPI</td>
<td>Change in Neuropsychiatric Inventory total score (MD -2.06 (95% CI -2.91 to -1.21, P&lt;0.001)</td>
</tr>
<tr>
<td>Spector 2001 (68)</td>
<td>Randomized controlled trial</td>
<td>35 patients in day centers and residential homes; moderate dementia; MMSE: 11.5±4.4 for intervention group; 15.5±4.4 for control group; mean age: 85.7±6.7</td>
<td>Intervention: mixture of reality orientation and other Cognitive learning exercises (15 sessions twice weekly, 45 min/session) Control: usual care</td>
<td>BRS</td>
<td>No statistical difference between the two groups</td>
</tr>
<tr>
<td>Spector 2003 (69)</td>
<td>Randomized controlled trial</td>
<td>201 patients in residential homes or day centers; moderate dementia; (MMSE: 14.4±3.8); Mean age: 85.3±7.0</td>
<td>Intervention: mixture of reality orientation and other cognitive stimulation exercises (14 sessions twice weekly, 45 min/session) Control: usual care</td>
<td>Mood: CSDD, RAID; Behaviour: BRS, (CAPE).</td>
<td>No statistical difference between the two groups</td>
</tr>
<tr>
<td>Tadaka 2004 (70)</td>
<td>Randomized controlled trial</td>
<td>60 community-dwelling older adults with dementia; mean age 83</td>
<td>Intervention: reminiscence and reality orientation (1.5h once-a-week, for 10 weeks)</td>
<td>MOSES</td>
<td>No effect reported on irritability or depression</td>
</tr>
<tr>
<td></td>
<td>Randomized controlled trial</td>
<td>38 long-stay residential patients: mean age: 71.8±16.6 for intervention group; 68.0±15.4 for control group</td>
<td>Severe dementia (RCP mental scale: 34.5±29.9 for intervention group; 37.6±28.9 for control group)</td>
<td>Intervention: reorientation therapy (5 times a week, 30 min/session for 3 months)</td>
<td>Control: occupational therapy, + both individual and group activities</td>
</tr>
</tbody>
</table>

BRS, Behavioral Rating Scale; CSDD, Cornell Scale for Depression in Dementia; CBRS, Crichton Behavior Rating Scale; MOSES, Multidimensional Observation Scale for Elderly Subjects; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; RAID, Rating Anxiety in Dementia
eTable 9 . Reminiscence therapy for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deponte 2007</td>
<td>Randomized trial</td>
<td>N=30, mean age 86.8; dementia diagnosis (unspecified)</td>
<td>Sensorial reminiscence, 3 months</td>
<td>NPI</td>
<td>Unclear</td>
</tr>
<tr>
<td>Haight 2006</td>
<td>Pre-post design, randomized controlled trial</td>
<td>N=31, female?, age range 60-99, dementia</td>
<td>Life review/life story book sessions; 1 hr/1x per week for 8 weeks</td>
<td>CSDD; Alzheimer's mood scale; functional independence scale; communication observation scale; memory and behaviour problems checklist</td>
<td>Significant change in depression, communication, positive mood</td>
</tr>
<tr>
<td>Haslam 2010</td>
<td>Pre-post design, randomized controlled trial</td>
<td>N=73, female?, age range (dementia) 62-93, dementia and non-dementia</td>
<td>Discussion and conversation; 30 min/1x per week for 4 weeks</td>
<td>Addenbrooke's cognitive examination - revised; HADS;</td>
<td>Group reminiscence enhanced memory performance.</td>
</tr>
<tr>
<td>Lai 2004</td>
<td>Pre-post design, randomized controlled trial</td>
<td>N=101, female?, mean age 86, dementia</td>
<td>Stimulate recall during conversation with life story book; 30 min/1x per week for 6 weeks</td>
<td>Social engagement scale, well-being/ill-being scale</td>
<td>Psychosocial well-being improved significantly in the intervention group.</td>
</tr>
<tr>
<td>Morgan 2010</td>
<td>Pre-post design, randomized controlled trial</td>
<td>N=17, female?, mean age 83, dementia</td>
<td>Life review/life story book sessions; 30 min-1 hr/1x per week for 8-12 weeks</td>
<td>GDS; autobiographical memory interview</td>
<td>Improved autobiographical memory and reduced depression</td>
</tr>
<tr>
<td>Politis 2004</td>
<td>Pre-post design, randomized controlled trial</td>
<td>N=36, female?, mean age 84, dementia</td>
<td>Generating questions from a geriatrics network kit and using the responses of participants to initiate conversations; 30 min/3x per week for 4 weeks</td>
<td>NPI, NPI-apathy, Alzheimer's disease-related quality-of-life scale;</td>
<td>No difference between intervention and control groups on NPI and NPI-apathy</td>
</tr>
<tr>
<td>Wang 2009</td>
<td>Randomized trial</td>
<td>N=77, female 37, mean age 79; mild-moderate dementia (clinical dementia rating)</td>
<td>Structured group reminiscence therapy;1x per week for 8 weeks</td>
<td>CAPE-BRS</td>
<td>No difference between intervention and control groups</td>
</tr>
</tbody>
</table>

CAPE-BRS, Clifton Assessment Procedures for the Elderly–Behavioral Rating Scale; CSDD, Cornell Scale for Depression in Dementia; GDS Geriatric depression scale; HADS, hospital anxiety and depression scale; NPI Neuropsychiatric Inventory
**eTable 10. Validation therapy for behavioural disturbances in patients with dementia**

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peoples 1982 (79)</td>
<td>RCT</td>
<td>N=31, female 23, mean age 88</td>
<td>A group leader, song leader or hostess was identified. Activities included discussion on a previously agreed topic, singing and movement activity, and a closing ritual followed by refreshments.; 30 min/1x per week for 6 weeks; control groups: reminiscence therapy and usual care</td>
<td>BAT; TADCE</td>
<td>Behavior improved at 6 weeks.</td>
</tr>
<tr>
<td>Robb 1986 (80)</td>
<td>RCT</td>
<td>N=36 (N=25 with dementia), female?, mean age 80.5</td>
<td>Details of the Validation therapy were not reported; 2x per week for 9 months; control group: usual treatment (e.g. medication)</td>
<td>MSQ; PGCMS; MSBS</td>
<td>No effects detected.</td>
</tr>
<tr>
<td>Toseland 1997 (81)</td>
<td>RCT</td>
<td>N=88, female 66, mean age 87.6; moderate level of dementia (SPMSQ and VSI)</td>
<td>Four sessions, 5-10 minutes each. Session 1. Introductions, greetings and singing. Session 2. Interaction on a topic of interest, reminiscing encouraged. Session 3. Program activity, singing or poetry. Session 4. Refreshments and individual good byes.; 30 min/4x per week for 52 weeks; control groups: social contact group and usual care</td>
<td>CMAI; MOSES; GIPB;</td>
<td>Depression decreased in validation therapy group.</td>
</tr>
</tbody>
</table>

BAT, Behavior assessment tool; CMAI, Cohen Mansfield Agitation Inventory; GIPB, Geriatric Indices of Positive Behavior; MOSES, Multidimensional Observation Scale for Elderly Subjects; MSBS, Minimal Social Behavior Scale; MSQ, Mental Status Questionnaire; PGCMS, Philadelphia Geriatric Center Morale Scale; SPMSQ, Short Portable Mental Status Questionnaire; TADCE, Tool for Assessing the Degree of Confusion in the Elderly; VSI, Validation Screening Instrument
<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camberg 1999 (82)</td>
<td>Latin-square, double-blind</td>
<td>N=54, mean age 83</td>
<td>Audiotape prepared by a family member or a surrogate</td>
<td>SOAPD, visual analog scales, positive affect scales, facial diagrams of mood,</td>
<td>No significant difference for agitation and mood.</td>
</tr>
<tr>
<td>Cheston 2007(83)</td>
<td>within-subjects</td>
<td>N=6, age range 75-91</td>
<td>Audiotape prepared by participant’s spouse</td>
<td>PRS</td>
<td></td>
</tr>
<tr>
<td>Cohen-Mansfield 1997(84)</td>
<td>CT</td>
<td>N=32, mean age 87</td>
<td>Videotape prepared by family members or researchers</td>
<td>CMAI, tape recordings and standardized observations for verbally disruptive behaviours</td>
<td>Verbally disruptive behaviours decreased by 46% during the videotape, and 16% during the no-intervention.</td>
</tr>
<tr>
<td>Garland 2007 (85)</td>
<td>RCT (single blind)</td>
<td>N=30, age range 66-93</td>
<td>Audiotape prepared by a family member and a psychologist</td>
<td>CMAI</td>
<td>Behavioral symptoms significantly reduced in favor of active intervention</td>
</tr>
<tr>
<td>Miller 2001 (86)</td>
<td>quasi-experimental</td>
<td>N=7, age range 68-89</td>
<td>Audiotape prepared by a family member</td>
<td>HRS (first 4 items)</td>
<td>Significant decline in agitation level</td>
</tr>
<tr>
<td>Peak 2002(87)</td>
<td>N-of-1 trials (4 cases studied)</td>
<td>N=4, age range 64-84</td>
<td>Audiotape prepared by participant’s spouse</td>
<td>modified PRS</td>
<td>For two of the four people presented here, SPT improved levels of some of the observed behaviours</td>
</tr>
<tr>
<td>Woods 1995(88)</td>
<td>quasi-experimental</td>
<td>N=8, age range 71-97</td>
<td>Audiotape prepared by caregiver</td>
<td>DBRS</td>
<td>Disruptive behaviour reduced in active treatment group</td>
</tr>
</tbody>
</table>

CMAI, Cohen-Mansfield Agitation Inventory; DBRS, Disruptive Behavior Rating Scale; HRS, Haycox Rating Scale; PRS, Positive Response Schedule for Severe Dementia; SOAPD, Scale for the Observation of Agitation in Persons with Dementia;
**Table 12. Characteristics of Primary studies that assessed Behavioral Management Techniques for behavioural disturbances in patients with dementia**

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burgio 2003 (89)</td>
<td>Randomized controlled trial</td>
<td>Participants with dementia: mean MMSE score 14.53 for white participants and 10.98 for African American participants, with a mean age of 78.83; 70 white + 48 African American primary caregivers</td>
<td>Caregiver Skill Training Intervention based on a manual</td>
<td>RMBPC</td>
<td>No statistical difference between the groups.</td>
</tr>
<tr>
<td>Burns 2003 (90)</td>
<td>Randomized controlled trial</td>
<td>167 Dyads; 66 caregivers</td>
<td>Active group: REACH intervention: behaviour care (individualized educational program on BMT) + individualized care giver stress – coping management training in 8 face-to-face sessions and 30 telephone calls over 24 months Control group: behaviour care only</td>
<td>problem behaviour: RMBPC.</td>
<td>Significant improvement in caregiver bother associated with care recipient behaviours;</td>
</tr>
<tr>
<td>Chenoweth 2009 (91)</td>
<td>(care giver based)</td>
<td>289 residents (15 residential homes) with need-driven behaviours, mean age: 85 years.</td>
<td>Caregiver training and support intervention in either: Person-Centred Care or Dementia Care Mapping</td>
<td>CMAI, NPI, QUALID, QUIS</td>
<td>Significant reduction in agitation</td>
</tr>
<tr>
<td>Farran 2004 (92)</td>
<td>Randomized controlled trial</td>
<td>295 participants with AD or dementia; MMSE &lt; 24, mean MMSE score: 12.6</td>
<td>Intervention: Caregiver skill. Control: Information and Support Orientated Group Intervention</td>
<td>BMS-R, RMPBC</td>
<td>No statistical differences between the two groups</td>
</tr>
<tr>
<td>Fossey 2006 (93)</td>
<td>Cluster randomized controlled trial</td>
<td>346 residents with dementia (12 residential homes); mean age: 82 years.</td>
<td>Active group: Training and Support Intervention for nursing home staff. Control group: treatment as usual</td>
<td>CMAI</td>
<td>No statistical difference (mean difference 0.3, −8.3 to 8.9; P = 0.94).</td>
</tr>
<tr>
<td>Study</td>
<td>Design Type</td>
<td>Sample Description</td>
<td>Interventions</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
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<tr>
<td>Gitlin 2001 (94)</td>
<td>Randomized clinical trial</td>
<td>Active group: Education about dementia and impact of home environment on behavioural problems and daily living deficits; instruction in problem solving and developing strategies, to manage caregiving concerns. Control group: usual care.</td>
<td>- Frequency of behavioural problems: MBPC + 4 other behaviours; - caregiver distress associated with behavioural problems - caregiving self-efficacy assessed by care givers.</td>
<td>No effects on frequency of care recipient behavioural problems (intervention 20.25-17.2; control 18.74-14.43);</td>
<td></td>
</tr>
<tr>
<td>Gitlin 2003 (95) (care giver based)</td>
<td>Randomized clinical trial</td>
<td>Active group: Home environmental skill building program over 5, 90-min home visits and 1, 30-min telephone contact: education, and physical and social environment modifications; similar to (44) (Philadelphia REACH). Control group: usual care (information only).</td>
<td>- Number of disruption-related behaviours: modified RMBPC presence or absence of behaviours rather than frequency; - caregiver upset with disruptive behaviours: RMBPC.</td>
<td>No change in disruptive behaviours for care recipients (intervention 2.14-1.88; control 2.16-1.96);</td>
<td></td>
</tr>
<tr>
<td>Gonyea 2006 (96) (care giver based)</td>
<td>Randomized controlled trial</td>
<td>Active group: Caregiver group based training intervention (Project CARE); Control group: Psychoeducational control group using similar structure to the intervention group.</td>
<td>NPI - severity and distress</td>
<td>No statistical difference for severity of problem behaviours (-0.24 [-0.68 to 0.20]).</td>
<td></td>
</tr>
<tr>
<td>Gormley 2001 (97) (caregiver based)</td>
<td>Controlled clinical trial</td>
<td>Active group: Education and aggressive behaviour management training program for care giver in 4 in-home sessions over 8 weeks. Control group: discussions with care giver and care recipient on a variety of non-specific care-related issues and advice on services.</td>
<td>a) Overall symptomatology and severity of behavioural problems: BEHAVE-AD; b) care recipient aggressive behaviour: Rating Scale for Aggressive Behavior in the Elderly.</td>
<td>- no difference in overall behavioural problems (intervention 8-6.5; control 8-7.8); - no diff in patient’s aggressive behaviour (intervention 9.4-6.9; control 8.8-8.6);</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcomes</td>
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</tr>
<tr>
<td>Graff 2007 (98)</td>
<td>Randomized clinical trial</td>
<td>135 ITT dyads; 132 IA</td>
<td>Active group: Occupational therapy in 10 sessions over 5 weeks: therapist taught care recipient to use compensatory and environmental strategies to improve their performance of daily activities and care giver trained by means of cognitive behavioural treatment. Control group: waitlist</td>
<td>CSDD- care recipient mood</td>
<td>Significantly improved care recipients’ mood (intervention 8.3 -6.2; control 8.1-9.2).</td>
</tr>
<tr>
<td>Huang 2003 (99) (care giver based)</td>
<td>Randomized clinical trial Northern Taiwan.</td>
<td>48 participants with dementia (and their family caregiver); predominantly female; mean age of 76 years; mean MMSE score 13.1. (care givers predominantly female, mean age 56)</td>
<td>Active group: a home-based Caregiver Training Program; Control group: written materials only</td>
<td>Chinese version of CMAI (care recipient Frequency of problem behaviours and caregiver self-efficacy).</td>
<td>No statistical difference in agitation</td>
</tr>
<tr>
<td>Losada-Baltar 2004 (100) (care giver based)</td>
<td>Randomized clinical trial Spain</td>
<td>31 participants with dementia; mean age 80</td>
<td>Active group: Caregiver Problem-Solving Skills Training Intervention Control group: usual care</td>
<td>MBCL - frequency and reaction</td>
<td>No statistical difference for the outcome frequency of problem behaviours0.20 [-0.91 to1.30]</td>
</tr>
<tr>
<td>Marriott 2000 (101) (care giver based)</td>
<td>3-arm, controlled clinical trial</td>
<td>42 dyads</td>
<td>Care giver education, stress management and skills training to manage behaviour of care recipient and coping with change; 1 session every 2 weeks, for a total of 14 sessions. Control groups: one group received one type of dyad interview, which was also used in the treatment group, and another control group did not receive any interview.</td>
<td>Change in BPSD: a) depressive symptoms: CSDD; b) behavioural disturbances and c) psychotic symptoms: MOUSEPAD</td>
<td>At post-treatment, behavioural disturbances significantly decreased, but no significant effects at follow-up.</td>
</tr>
<tr>
<td>Mador 2004 (102)</td>
<td>Randomized clinical trial in hospital setting; mean age 83</td>
<td>71 patients with dementia</td>
<td>Active group: Staff Training Hospital Behavior Advisory Service Usual Care</td>
<td>PAS</td>
<td>Worsening of severity of problem behaviours at post-intervention (SMD 0.89 [0.41-1.38])</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Intervention</td>
<td>Outcomes</td>
<td></td>
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</tr>
<tr>
<td>McCurry 2005 (103) (care giver based)</td>
<td>RCT</td>
<td>36 dyads</td>
<td>Nighttime Insomnia Treatment and Education for Alzheimer’s Disease and training care givers to implement treatment; six, 1-hour sessions at home, over 2-months. Control group: general dementia education and care giver support</td>
<td>Night time and sleep behaviour, daytime sleepiness and depression (RMBPC) of care recipients. The number of awakenings and the total time awake at night, as well as daytime sleepiness, all significantly diminished. Depression was significantly reduced post-intervention, but not at 6-month follow-up.</td>
<td></td>
</tr>
<tr>
<td>Moniz-Cook 2008 (104) (care giver based)</td>
<td>Controlled clinical trial</td>
<td>113 dyads</td>
<td>Caregivers assisted by community mental health nurses to manage problematic behaviour of dementia patients and to cope with stress; home visits 1x/week for 4 weeks plus addition contact as needed over 18 months. Control group: usual care</td>
<td>Frequency of problem behaviour and difficulty managing problematic behaviour by care giver: adapted-Gilleard Problem Checklist. Problem behaviours significantly decreased over 18 months, but a post-hoc analysis demonstrated the effect was dependent on care managers.</td>
<td></td>
</tr>
<tr>
<td>Nobili 2004 (105) (care giver based)</td>
<td>RCT</td>
<td>69 dyads</td>
<td>A psychologist (60 min visit) and an occupational therapist (90 min visit) gave information and advice to care givers; Control group: helpline and information on community services and legal and economic features of caregiving</td>
<td>Frequency of problem behaviour in care recipient: Spontaneous Behavior Interview – Section C. Problem behaviours and frequency of delusions significantly decreased.</td>
<td></td>
</tr>
<tr>
<td>Proctor 1999 (106)</td>
<td>Randomized trial</td>
<td>105 participants with dementia(in 12 nursing and residential homes); mean age of 83</td>
<td>Active group: Staff training and Education Intervention including psychosocial management of resident’s behavioural problems; Control group: usual care</td>
<td>CRBRS. No statistical difference for the outcome severity of problem behaviours (-0.02 [-0.41 to 0.36])</td>
<td></td>
</tr>
<tr>
<td>Teri 1997 (107)</td>
<td>RCT</td>
<td>72 dyads</td>
<td>Two behavioural therapy interventions. One comprised education and discussing and planning strategies to manage problem behaviour and to maximize cognitive function of the care recipient (increase pleasant events plus self-care strategies). The other intervention included the aforementioned elements, but substituting problem solving for the pleasant events; 60-minsession, 1x/week for 9 weeks: Control groups: usual care and wait-list control.</td>
<td>HDRS, CSDD and BDI. Depression significantly improved with both behavioural interventions. No significant difference between either active treatment.</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>Intervention</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Teri 2003 (108) (care giver based)</td>
<td>RCT</td>
<td>153 dyads</td>
<td>Exercise for care recipients and care givers taught behavioural management techniques and given education on dementia; 12 hour sessions 2x/week for 3 weeks, followed by sessions 1x/week for 4 weeks, then sessions 2x/week for 2 weeks. Control group: usual care</td>
<td>HDRS, CSDD and RMBPC</td>
<td>Depression significantly reduced at 3 months, but no significant difference at 24 months. (Care recipients with higher initial depression maintained improvements.) Trend for significantly decreased institutionalization due to problem behaviours at 24 months.</td>
</tr>
<tr>
<td>Teri 2005 (109) (care giver based)</td>
<td>Controlled clinical trial</td>
<td>95 dyads</td>
<td>Caregivers taught behavioural management techniques and communication strategies; increased care giver support. Pleasant events also increased for care recipients; home sessions 1x/week for 8, then monthly telephone calls for 4 months. Control group: usual care</td>
<td>NPI, RMBPC</td>
<td>Severity and frequency of behaviour problems significantly declined.</td>
</tr>
<tr>
<td>Ulstein 2007 (110) (care giver based)</td>
<td>RCT</td>
<td>171 dyads</td>
<td>Caregivers taught problem solving and communication techniques, in addition to usual care; four and a half months. Control group: usual care</td>
<td>NPI</td>
<td>No significant difference in care recipient behavioural symptoms. (Post-hoc analysis revealed behavioural symptoms significantly improved in female care recipients.)</td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory; BEHAVE-AD, Behavioural Pathology in Alzheimer’s Disease Rating Scale; BMS-R, Behaviour Management Skill Revised; CRBRS, Crichton Royal Behavioural Rating Scale; CMAI, Cohen Mansfield Agitation Inventory; CSDD, Cornell Scale for Depression in Dementia; HDRS, Hamilton Depression Rating Scale; MBCL, Memory and Behaviour Check List; MBPC, Memory and Behaviour Problem Checklist; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; PAS, Pittsburgh Agitation Scale; QUALID, Quality of life in late stage dementia; QUIS, Quality interactions schedule; RMBPC, Revised Memory and Behaviour Problem Checklist
**Table 13. Characteristics of Multicomponent Interventions for behavioural disturbances in patients with dementia**

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brodaty 2003 (111)</td>
<td>RCT</td>
<td>N=86 with dementia, female 62, mean age 83 years, control group: usual care</td>
<td>1. Psychogeriatric case management: psychological, social and pharmacological treatment supervised by a geriatric psychiatrist and administered by a multidisciplinary team; one team member is case manager. 2. Psychiatric consultation: management plans provided to NH-staff and general practitioner.</td>
<td>AMTS, BEHAVE-AD, EBAS-DEP, FAST, CSD, NPI, SAPS, GDS, CRI, HRS-D/HAM-D, CIRS, DSM-IV</td>
<td>Improvement in depression and psychosis in all 3 groups</td>
</tr>
<tr>
<td>Opie 2002 (112)</td>
<td>RCT</td>
<td>N=99 with dementia, female 72, mean age 84 years</td>
<td>Individually tailored medical, pharmacological, psychosocial and nursing interventions targeting specific behaviours</td>
<td>CMAI, BAGS, GDS</td>
<td>Decline in restlessness, physical aggression and verbal disruption; still detectable in 75% of subjects after 1 month</td>
</tr>
<tr>
<td>Proctor 1999 (106)</td>
<td>RCT</td>
<td>N=105 with dementia, female 87, mean age 83 years</td>
<td>Staff training and education</td>
<td>AGECAT organic, AGECAT depression, Chrichton scale,</td>
<td>Significantly improved scores for depression and cognition</td>
</tr>
<tr>
<td>Rovner 1996 (113)</td>
<td>RCT</td>
<td>N=81 with dementia and somatic illness, female 63, mean age 82 years</td>
<td>Activity program, psychotropic drug management and weekly educational meetings with a psychiatrist</td>
<td>CMAI, PGDRS, DSM-III-R, RUGS</td>
<td>Significant decrease of behaviour disorders, restraint use and antipsychotic use in intervention group</td>
</tr>
</tbody>
</table>

AGECAT, Automatic Geriatric Examination for Computer-Assisted Taxonomy; AMTS, Abbreviated Mental Test Score; BAGS, Behaviour Assessment Graphical System; BEHAVE-AD, Behavioral Pathology in Alzheimer’s Disease Rating Scale; CIRS, Cumulative Illness Rating Scale; CMAI, Cohen-Mansfield Agitation Inventory; CRI, Resident Classification Index; DSM, Diagnostic and Statistical Manual of Mental Disorders; EBAS-DEP, Even Briefer Assessment for Depression; FAST, Functional Assessment Staging CSD; GDS, Geriatric Depression Scale; HRS-D/HAM-D, Hamilton Depression Rating Scale; NPI, Neuropsychiatric Inventory; PGDRS, Psychogeriatric Dependency Rating Scale; RUGS, Resource Utilization Groups; SAPS, Scale for the Assessment of Positive symptoms.
### eTable 14. Exercise-based intervention for behavioural disturbances in patients with dementia

<table>
<thead>
<tr>
<th>Primary study</th>
<th>Study design</th>
<th>Population</th>
<th>Type of intervention, dose, route of administration, frequency and duration in active group</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burgener 2008 (114)</td>
<td>repeated-measures randomized design</td>
<td>43 people with early stage dementia referred (self-referred or by the physician); female 20; mean age 77;</td>
<td>Multimodal intervention (Tai Chi exercise, cognitive-behavioural therapies and support group) on; Duration 1 hour x 3 times a week for 40 weeks</td>
<td>GDS 15</td>
<td>At 20 weeks: GDS increased (worsened) by 0.4 in intervention and 0.9 in control (difference not significant)</td>
</tr>
<tr>
<td>Rolland 2007 (115)</td>
<td>single-blind, parallel group, randomized controlled trial</td>
<td>134 ambulatory subjects with AD living in nursing homes</td>
<td>Exercise program (aerobic, strength, flexibility, and balance training). Duration 1 hour x 2 times a week for 40 weeks Walking was required for at least half of the session. A circular walking trail was created and adapted for each exercise group</td>
<td>MADRS</td>
<td>At 12 months: MADRS 13.4 (+/- 8.0) in intervention and 14.8 (+/- 7.2) in control (difference not significant)</td>
</tr>
<tr>
<td>Teri 2003 (108)</td>
<td>Randomized controlled trial</td>
<td>153 community dwelling patients meeting National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer Disease and Related Disorders Association criteria for Alzheimer disease; 63 female; mean age 78;</td>
<td>Combined exercise - Aerobic, endurance, strength, balance and flexibility training and caregiver training program, Reducing Disability in Alzheimer Disease; Duration 1/2 hour x 7 times a week for 12 weeks Control group: routine medical care</td>
<td>CSDD</td>
<td>At 2 years: mean difference, 2.14; 95% CI, 0.14 - 4.17; p&lt;0.04</td>
</tr>
<tr>
<td>Steinberg 2009 (116)</td>
<td>Randomized trial</td>
<td>27 home dwelling patients with Alzheimer’s (MMSE&gt;10)</td>
<td>Active group: Daily program of aerobic, balance and flexibility, and strength training, shown to patients and caregivers, to be done at home; Control: home safety assessment</td>
<td>Depression and apathy (NPI and CSDD)</td>
<td>No statistical difference between groups</td>
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<td>Van de Winckel 2004 (50)</td>
<td>Randomized trial</td>
<td>25 female residents; mean age 81; NINCDS-ARDRA criteria used for probable or possible Alzheimer's disease and MMSE score lower than 24/30 (MMSE 11)</td>
<td>Active group: daily physical exercises (strength, balance and flexibility) supported by music for 30 min/session Duration 1/2 hour x 7 times a week for 12 weeks Control group: daily conversation</td>
<td>BOP scale At 3 months: no significant difference in depressive behaviour subscale</td>
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BOP, Beoordelingsschaal voor Oudere Patient/Evaluation Scale for Elderly; CSDD, Cornell Scale for Depression in Dementia; GDS, Geriatric depression scale; MADRS, Montgomery-Asberg Depression Rating Scale; MMSE, Mini-Mental State Examination;
References


Appendix 3. Methodological Quality Assessment of the included systematic reviews

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### AMSTAR Items

All 11-items were scored as “Yes”, “No”, “Can’t Answer” or “Not Applicable”. AMSTAR comprises the following items:

1. ‘a priori’ design provided;
2. duplicate study selection/data extraction;
3. comprehensive literature search;
4. status of publication as inclusion criteria (i.e., grey or unpublished literature);
5. list of studies included/excluded provided;
6. characteristics of included studies documented;
7. scientific quality assessed and documented;
8. appropriate formulation of conclusions (based on methodological rigor and scientific quality of the studies);
9. appropriate methods of combining studies (homogeneity test, effect model used and sensitivity analysis);
10. assessment of publication bias (graphic and/or statistical test); and
11. conflict of interest statement.

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<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
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<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
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<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td>9-47</td>
</tr>
<tr>
<td>Risk of bias within studies</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td>NA</td>
</tr>
<tr>
<td>Results of individual studies</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td>9-47 Supplemental file</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td>NA</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see Item 15).</td>
<td>NA</td>
</tr>
<tr>
<td>Additional analysis</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td>NA</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary of evidence</td>
<td>24</td>
<td>Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</td>
<td>48-50</td>
</tr>
<tr>
<td>Limitations</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td>50</td>
</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td>51-52</td>
</tr>
<tr>
<td>FUNDING</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Funding</td>
<td>27</td>
<td>Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.</td>
<td>52</td>
</tr>
</tbody>
</table>

Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series

Josief Abraha, Joseph M Rimland, Fabiana Mirella Trotta, Giuseppina Dell'Aquila, Alfonso Cruz-Jentoft, Mirko Petrovic, Adalsteinn Gudmundsson, Roy Soiza, Denis O'Mahony, Antonio Gualia and Antonio Cherubini

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The authors would like to thank dr. Reisberg and colleagues for their appreciation and for their valuable comments on our manuscript. Reisberg and colleagues correctly noticed the discrepancy in presentation of the categorization of the non-pharmacological intervention between the main text and the abstract. The authors would like to underline that the categorization of the interventions in the main text is the correct one and therefore the results in the abstract should be modified as follows:

38 SRs and 129 primary studies were identified, comprising the following categories of non-pharmacological interventions: (1) sensory stimulation interventions (25 SRs, 66 primary studies) that encompassed: shiatsu and acupressure, aromatherapy, massage/touch therapy, light therapy, sensory garden and horticultural activities, music/dance therapy, dance therapy, snoezelen multisensory stimulation therapy, transcutaneous electrical nerve stimulation; (2) cognitive/emotion-oriented interventions (13 SRs; 26 primary studies) that included cognitive stimulation, reminiscence therapy, validation therapy, simulated presence therapy; (3) behaviour management techniques (6 SRs; 22 primary studies); (4) Multicomponent interventions (3 SR; four primary studies); (5) other therapies (5 SRs, 15 primary studies) comprising exercise therapy, animal-assisted therapy, special care unit and dining room environment-based interventions.

Please note that the numbers provided are absolute numbers and the following reviews can fall in different categories as they considered different types of non-pharmacological interventions and thus explain any discrepancy in numbers: Seitz 2012\(^1\) that considered aromatherapy, light therapy, music/dance therapy, snoezelen therapy, and reminiscence therapy; O’Neil 2011\(^2\) that considered snoezelen, behavioural management techniques; Chaudhury 2013\(^3\) that considered light therapy and the role of physical environment in supporting person-centred dining in LTC; and Whear 2014\(^4\) that examined the effect of improved lighting and table-setting contrast in a dining room environment. In addition, two primary studies fell in two different categories: Proctor 1999\(^5\) was in reviews that dealt with behavioural management techniques (BMT) and one review that, within the multicomponent interventions, examined the combined effect of BMT with educational intervention; and Teri 2003\(^6\) was considered in the BMT reviews and the exercise-based reviews.

In addition, the authors want to point out the following minor corrections in the main text: page 17 under the paragraph on Behavioural management techniques it should read ‘One review of reviews and five SRs’ instead of ‘One overview of reviews and four SRs’.

page 21, the authors missed describing the seventh study with repeated measures design: “In the a small repeated measures study Mossello et al, evaluated the effect of animal assisted therapy in ten patients attending an Alzheimer Day Care Centre. The design consisted in 2 weeks' pre-intervention, 3 weeks' control activity with plush dogs, and 3 weeks' animal assisted therapy. NPI was used to assess BPSD and CMAI to assess mood; both outcomes remained unchanged across the study. Anxiety measured with NPI decreased during animal assisted therapy (p=0.04)\(^7\).”

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