Efficacy and Feasibility of Non-Pharmacological Interventions for Neuropsychiatric Symptoms of Dementia in Long-Term Care: A Systematic Review

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ABSTRACT:

Background: Non-pharmacological therapies are often recommended as a first-line treatment for neuropsychiatric symptoms of dementia (NPS) in long-term care (LTC). However, little is known about which non-pharmacological interventions are most effective for NPS in LTC or the feasibility of treatments given the availability of resources in typical LTC environments.

Methods: We searched the electronic databases MEDLINE, EMBASE and PsycInfo (1980 – 2010) using key words and medical subject heading for randomized, controlled trials evaluating non-pharmacological interventions for NPS conducted in LTC settings. Change in severity of NPS symptoms was evaluated through the NPS outcomes measures reported in studies. We assessed study quality and described the feasibility of interventions based on various aspects of study design.

Results: A total of 40 studies met inclusion criteria. Sixteen of forty included studies (40%) reported statistically significant results in favour of non-pharmacological interventions on at least one measure of NPS. These interventions included: staff training in NPS management strategies; mental health consultation and treatment planning; exercise; recreational activities; and, music therapy or other forms of sensory stimulation. Many of the studies had methodological limitations which placed them at potential risk of bias. The majority of interventions (N=30, 75%) required significant resources from services outside of LTC or significant time commitments from LTC nursing staff for implementation.

Conclusion: There are several non-pharmacological interventions that may be effective for NPS in LTC although there are a limited number of large-scale, high quality studies in this area. The feasibility of some interventions will be limited in many LTC settings and further research into practical and sustainable interventions for NPS in LTC is required in order to improve utilization of these important treatments.

INTRODUCTION:

Neuropsychiatric symptoms of dementia (NPS), also known as behavioral and psychological symptoms of dementia, are common among older adults with dementia in long-term care (LTC)[1, 2]. NPS can include symptoms such as agitation, psychotic symptoms including delusions or hallucinations, or aggressive behavior directed towards staff or co-residents[3, 4]. In long-term care (LTC) or nursing home settings the prevalence of dementia and NPS is high. Approximately 60% of individuals in LTC have underlying dementia[1] and the majority of individuals with dementia will develop NPS at some point in their illness[1, 5]. NPS among community dwelling older adults is a risk factor for LTC placement[6] and NPS are associated with increased costs of care[7], decreased quality of life for individuals with dementia[8] and their caregivers[8, 9]. NPS are also associated with greater cognitive and functional decline[10, 11] and increased mortality[10].

Interventions to treat NPS of dementia can include both non-pharmacological and pharmacological interventions. Psychotropic use is common in LTC with a high prevalence of antipsychotics[12-17], and benzodiazepines or other sedatives[12, 15, 18] which are all frequently used for NPS. Some classes of psychotropic medications such as antipsychotics[19] and antidepressants[20] have evidence to support their use in NPS however their effects are generally modest and serious adverse effects such as cerebrovascular accidents[21] and an increased risk of mortality[22-24] highlight the need for non-pharmacological alternatives for these symptoms.

Guidelines for NPS of dementia[25, 26] recommend non-pharmacological treatments for NPS as initial therapy for NPS or to be used as adjuncts to pharmacological treatments. However there are a number of possible non-pharmacological treatments for NPS[27] and the evidence which supports their use is often unclear. Previous reviews on non-pharmacological interventions

for NPS of dementia have been conducted[27-39] although only a few reviews have applied rigorous methods for evaluating the quality of studies[28, 29, 31, 37]. In addition, many of these reviews have also included studies conducted in settings other than LTC such as the community or hospital inpatients where the severity of NPS symptoms, degree of cognitive impairment, and availability of resources may differ significantly from LTC. Finally, there have been no reviews which have systematically evaluated the potential feasibility of interventions in various LTC settings with respect to the requirements for specialized geriatric mental health providers, time required for staff to receive training or to implement the interventions, or monetary costs. Identifying aspects of study design which may serve as potential barriers to implementation of non-pharmacological interventions in some LTC settings is important to understand interventions that may be more readily translated from research settings to typical LTC environments. Therefore, the objective of our study was to systematically review the evidence for non-pharmacological interventions for NPS in LTC, and to assess both the quality of studies and feasibility of interventions. A better understanding of the efficacy and feasibility of non-pharmacological interventions will help identify effective interventions for NPS and identify strategies to enhance implementation of these important treatments.

METHODS:

Search Strategy:

We followed the PRISMA guidelines for conducting systematic reviews to guide the review process[40]. We searched the electronic databases Medline (1980 - 2010) and EMBASE (1980 - 2010) using free text search terms and medical subject headings for potentially relevant articles. We combined terms for dementia (*dementia, Alzheimer*), LTC (*nursing homes, long*

term care, nursing homes, residential care institutions, assisted living, homes for the aged) behavioral symptoms (*behavioral problems, behavioral disorders, affective disorders, perceptual disturbances, psychiatric symptoms, behavioral and psychological symptoms of dementia, BPSD, neuropsychiatric symptoms*) and non-pharmacological interventions (*psychotherapy, physical therapy, psychotherapeutic counselling, exercise, physical activity, aromatherapy, recreation therapy, occupational therapy, music therapy*) using free-text searches and medical subject headings. Google Scholar was also searched for additional articles using key words and citation lists of key articles. We hand-searched the reference lists of retrieved articles, previous reviews on NPS, and NPS guidelines for additional articles not identified by the initial search of electronic databases.

Study Selection:

Preliminary lists of potentially relevant titles and abstracts were screened by two authors to identify studies meeting inclusion criteria. We included all randomized, parallel group, clinical trials comparing any non-pharmacological interventions to either usual care, a medication, or other non-pharmacological control group for LTC residents with dementia. We included all English language publications in the review along with abstracts that provided sufficient information for data extraction. We excluded studies that only used pre-post comparisons of participants without a control group and also excluded studies that used a crossover study design given the high placebo-response rate noted in some NPS studies[19]. We only included studies that were conducted in LTC settings exclusively or if conducted in a mix of LTC and other populations (such as outpatients or hospitalized patients) when the proportion of individuals who were in LTC formed the majority (>50%) of study participants. All retrieved full text articles

were reviewed for meeting inclusion criteria by two study authors and discrepancies were resolved thru further discussion.

Data Extraction:

Data were extracted in duplicate by two authors and reviewed for consistency. We extracted information from articles on the following characteristics where provided by studies: description of the intervention and control group; mean age or participants; gender distribution; study setting; severity of cognitive impairment (as measured by Mini-mental Status Exam Score or other cognitive test); method for diagnosing dementia; and, duration of study. We included the following information on change in symptoms of NPS. For studies utilizing continuous measures of NPS symptoms we reported the baseline score, score at study endpoint, change in NPS symptoms and associated test statistics where these were reported. For studies using binary outcomes the proportion of participants satisfying the outcome measure of improvement was reported. In studies which did not specify a primary outcome or endpoint we reported the change in total NPS symptom scores if a NPS symptoms rating scale was identified or on other measures of NPS. Where multiple endpoints were reported without specification of a primary endpoint we included the first endpoint following conclusion of the active treatment period as the primary endpoint.

Assessment of Study Quality:

The Cochrane collaboration risk of bias assessment tool was utilized to describe the potential risk of bias associated with various aspects of study design[41]. The following aspects of study design were evaluated for potential risk of bias: method of sequence generation; concealment of allocation; blinding; incomplete outcome data; selective outcome reporting; and other potential sources of bias which included whether the funding source for the study may have

had a financial conflict of interest. Each item was rated as being potentially at low-risk of bias ("Yes"), high-risk of bias ("No") or unclear. All items were rated in duplicate by two members of the research team.

Assessment of Feasibility of Interventions:

Given that there are several barriers which have been identified to the provision of non-pharmacological interventions for NPS in LTC and variation in the availability of services[42-45] and limited time available for nursing staff to implement interventions[46, 47] we assessed the feasibility of interventions for NPS included in our review. We described aspects of the interventions that would possibly affect the feasibility of implementing interventions in LTC settings categorized according to three domains: requirements for specialized staff to implement the intervention; direct financial costs to LTC home for supplies needed for interventions; and, requirements for staff time for either training or for implementation of the intervention. Each study was rated on these three categories as having either "High", "Medium", "Low" or unclear feasibility based on the information provided in the studies. Studies rated as being "High" for a particular item of study feasibility were considered to be easier to implement in typical LTC settings when compared to interventions rated as "Medium" or "Low". For staff time or training interventions were rated as being of "High" feasibility if they required less than 1 hour for training and less than 15 minutes daily for staff to implement, a "Medium" level of feasibility was assigned if 1 – 4 hours of training were required or 15 – 60 minutes daily were required for implementation, and greater amounts of time for training or implementation received a rating of "Low" feasibility on this item. Interventions were rated as being of "High" feasibility on the specialized staff domain if the intervention could be employed using only LTC nursing staff and physicians, "Medium" feasibility was assigned if specialized staff (e.g. psychiatrists or

psychologists) were required for training purposes with the intervention being carried out by regular LTC staff; "Low" feasibility was assigned if any intervention was only carried out by specialized staff without involvement of regular LTC staff. For monetary costs we assigned scores of "High" feasibility if the interventions did not require modifications to the LTC environment or estimated costs of supplies were less than approximately $100.00 U.S. dollars per person, "Medium" feasibility was assigned to interventions requiring $100.00 - $500.00 to implement or if minor modification were required to the LTC environment; and "Low" feasibility was assigned to interventions requiring greater expenditures of money or LTC facility modifications. For the ratings of financial costs related to interventions we did not include any costs associated with paying for external organizations to train staff although if additional equipment was required these were included in the assessment of direct costs to the LTC facility.

Data Synthesis:

Information from study characteristics, assessment of study quality, and feasibility were summarized in tables. We classified interventions into the following categories: nursing staff training interventions; comprehensive mental health assessment or consultation; psychosocial activities; exercise; music therapy; and, other forms of sensory stimulation. Meta-analyses were planned within subgroups of similar interventions provided that there were studies which were qualitatively similar in terms of study design, patient population, outcome measures and duration of intervention. Summary measures in meta-analysis included standardized mean differences for continuous variables using Hedge's g statistic and odds ratios for binary outcome measures. Two-sided p values of <0.05 were utilized as the threshold for statistical significance.

RESULTS:

Study Selection:

The flow of studies through the review process is outlined in Figure 1. A total of 4,586 citations were identified through searches of electronic databases and 55 references from hand-searches of reference lists for a total of 3,919 unique citations. After screening of titles and abstracts 419 full-text articles were retrieved and reviewed for inclusion criteria with 40 studies meeting inclusion criteria[48-87].

Characteristics of Included Studies:

Of the 40 studies meeting inclusion criteria, 11 examined training LTC staff in strategies to manage NPS[48-58], and 3 studies evaluated the effects of individualized geriatric mental health assessment or consultation[59-61]. Several studies evaluated the effects of providing programming or activities including 10 studies of the effects of various individual or group-based psychosocial activities[62-71], five studies examined exercise[72-76], 3 studies evaluated the effects of music[77-79], and 8 studies evaluating other forms of sensory stimulation[80-87].

A total of 3,519 individuals were included in all the studies with the sample size of studies varied from 20 to 306 participants and a median study sample size of 80 participants. The median mean age of participants was 84 years and the majority of participants were women (78%) in studies reporting the gender distribution. Most studies included individuals with relatively advanced dementia according to cognitive scores as reported on the MMSE or other measures of cognition with average MMSE scores of between 5 – 10 in most studies. The duration of studies varied between 1 to 52 weeks with a median study duration of 12 weeks. Many of the included studies were conducted in the United States (N=15), with the Netherlands

(N=4), Canada (N=3), the United Kingdom (N=3), or other countries (N=15) contributing a smaller number of studies.

Effects of Interventions on Neuropsychiatric Symptoms of Dementia:

A variety of outcome measures were utilized in the included studies (Table 2). Most of the studies included participants with relatively mild to moderate severity of NPS according to baseline measures of NPS as reported on NPS symptom rating scores. Of the 40 included studies, 16 (40%) reported a statistically significant difference between non-pharmacological intervention and control conditions on at least one NPS outcome measure[48, 56, 58, 59, 61, 63, 68, 72, 74, 76, 77, 79, 81, 83, 84, 86] (Table 2). These included 3 studies of staff training[48, 56, 58], 2 studies of geriatric mental health consultation or assessment[59, 61], 2 studies of psychosocial interventions[63, 68], 3 studies involving exercise[72, 74, 76], 2 of music therapy[77, 79] and 3 involving other forms of sensory stimulation[81, 84, 86]. The magnitude of the effects of interventions on NPS appeared to be modest in most studies reporting a statistically significant difference with only 2 studies reporting outcomes that appeared to reflect clinically significant reductions in NPS[59, 81]. The remaining 24 studies did not report any significant difference between the intervention and control conditions or it was unclear if there was any significant effect of the intervention. Given the heterogeneity of patient populations, interventions, duration of treatment and outcomes meta-analysis was not performed.

There was limited information available on the type of NPS that responded to non-pharmacological interventions. Physically aggressive behavior did not appear to change following nursing training intervention although verbal agitation and physically non-aggressive agitated behavior did appear to be reduced as measured on subscales on the Cohen-Mansfield Agitation Inventory (CMAI)[48]. A second study of staff training also appeared to have some

effect on reductions of general levels of agitation as measured by the CMAI total score although benefits were not observed on the Neuropsychiatric Inventory (NPI) which also contains measures of hallucinations, delusions, and mood[56]. A study of validation therapy found that physically aggressive behavior measured on CMAI was reduced at 3 months and one year, whereas non-aggressive physical agitation and verbal agitation were not affected at 3 months and only physically non-aggressive behavior was significantly different at 1 year[63]. Aromatherapy was associated with significant reductions in total agitation, physically aggressive behavior, physically nonaggressive agitation and verbally nonaggressive agitation but not verbal agitation[81]. The number of physically non-aggressive behaviors on the CMAI were also reduced in one study of therapeutic touch while physically aggressive behavior and verbal agitation were unchanged[86].

Assessment of Study Quality:

The potential risk of bias associated with aspects of study design are summarized in Table 3. Only one study was rated as being at low risk of bias on all items related to study quality[71]. The majority of studies did not report study methodology in sufficient detail to make a definitive assessment of the potential risk of bias on some items and therefore were rated as being at unclear risk of bias. Three of the studies included in the review did not blind outcome raters to treatment assignment[52, 53, 82] while the remaining studies were described as double-blinded.

Feasibility of Interventions for Neuropsychiatric Symptoms of Dementia in Long-Term Care:

The potential feasibility of interventions varied according to the category of intervention employed. For studies evaluating the effects of staff training programs most studies used

specialized staff to either train LTC staff or to be directly involved in providing feedback to LTC staff , with all studies in this category receiving a rating of either low or medium feasibility in the specialized staff category (Table 4). Likewise, the requirements for LTC in terms of time commitments in either participating in the training programs or implementation resulted in scores of either low or medium feasibility for this group of interventions. Similarly, most of the remaining categories of non-pharmacological interventions also were rated as low to medium feasibility on the items for specialized staff as LTC staff were not involved in the implementation of most interventions as described in the studies. Conversely, the direct costs to the LTC facilities in terms of having to purchase equipment was minimal for most of the staff education interventions. Only one study provided economic evaluations as part of the study publication[56].

DISCUSSION:

This review identified that there are several interventions that have been investigated for treatment of NPS in LTC settings although there are only a few large, high quality studies in this area. There is some support in the literature for interventions involving training of LTC staff, geriatric mental health consultation, provision of psychosocial activities, or activities involving exercise, music or other forms of sensory stimulation. It should be noted that although some studies supported these types of interventions, there were both positive and negative trials within each of these categories of interventions. Unfortunately, given the heterogeneity of study design and outcome measures, meta-analysis was not possible and therefore the overall effects of categories of interventions could not be summarized quantitatively. Our review also found that the majority of interventions were carried out by specialized staff external to the LTC home and

as such many of these interventions should be conceptualized as efficacy trials; the effectiveness of these interventions in real-world LTC settings as implemented by LTC staff during routine care practices require further evaluation. Another important finding of our review was that there were no comparison trials of non-pharmacological and pharmacological interventions, which is a common decision faced by clinicians in LTC.

The findings of our review are in keeping with previous reviews[27-39], guidelines[25] and consensus statements[26, 88] published on the evidence for management of NPS. However, previous reviews did not distinguish between studies conducted in community or hospital settings while this review was restricted to studies conducted in LTC where the availability of resources, comorbidity of patients, and severity of cognitive impairment would differ when compared to community or hospital-based samples. Also, many previous reviews did not limit studies to those using randomized controlled designs or failed to assess the quality of studies using standard criteria which is important in understanding the potential bias and internal validity of the primary studies.

Although the present review identified some non-pharmacological interventions for NPS with evidence to support their use, one potential limitation of these interventions surround the resource requirements required for implementation in typical LTC settings. There are relatively few studies describing access to services that might be utilized for managing NPS of dementia in LTC. For example, a study of psychiatric consultation to a sample of U.S. LTC facilities found that the majority of homes had access to psychiatric consultation at a frequency of monthly or less while over a quarter of rural LTC facilities had no access to psychiatric consultation at all[44]. A survey of access to psychiatric services in Ontario, Canada also found that less than half of all facilities reported having any access to psychiatrists with rural LTC homes having less access to

psychiatrists than urban centres with the majority of LTC reporting that more services were required[42]. While two-thirds of LTC have a mental disorder only 2.3% received any mental health treatment by psychiatrists in a one month period[43]. Therefore, interventions for NPS that rely on availability of geriatric psychiatrists or other specialized services may not be feasible in many LTC settings.

Our review identified that certain interventions, such as staff training and education, generally evaluate patient outcomes over a prolonged period of time which is appropriate given the required time for staff to receive training and for changes in practitioner behavior to have an impact on resident behaviors. Interventions of this design are likely to demonstrate benefit in terms of preventing NPS from emerging in individuals who do not already have challenging behaviors or perhaps reducing symptoms in individuals with pre-existing NPS. The application of these interventions to individuals with acute presentations of behavioral symptoms is likely to be less practical given the large-scale system wide implementation of the intervention. Other interventions such as geriatric mental health consultation with individualized treatment planning may be more appropriate for individuals with more acute presentations of NPS, although the evidence in favour of these interventions is limited to a few studies[59, 61]. Other interventions such as music, sensory stimulation and psychosocial activities have generally been studied over shorter periods of time and are probably most effective in reducing NPS while participants are actively engaged in the intervention. These interventions will require ongoing implementation for sustained benefit[89, 90] although they may be more effective and easier to implement with residents with existing NPS. Interestingly, we did not identify any studies evaluating the effects of increasing the number of nursing staff in LTC. Given the demands on LTC staff to provide patient care[46, 91], administer medications[46, 47] and completing documentation and other

administrative activities[46, 91], increasing the number of nursing staff and thereby the amount of time available for psychosocial interactions may be one method of increasing staff engagement in activities that may reduce NPS. Qualitative studies of LTC nursing staff have identified that having training in management strategies for NPS, and adequate time to implement such strategies could help increase the use of non-pharmacological interventions[92].

There was limited information provided by studies regarding the types of NPS that are most likely to respond to non-pharmacological interventions. Commonly utilized conceptual frameworks for understanding NPS suggest that certain symptoms such as vocal or non-aggressive physical agitation may be related to unmet needs such as pain, other uncomfortable sensations, learned behaviors, or a reduced-threshold to stress[34, 93, 94]. There was only limited information available in the included studies on the specific types of behaviors that were most likely to respond to non-pharmacological intervention although some of the included studies reported that verbal agitation and physically non-aggressive behavior might be more responsive to some non-pharmacological interventions than physically aggressive behavior[48, 56, 86]. Further study into non-pharmacological interventions that might be effective for physically aggressive behavior or acute presentations of agitation or aggression is urgently needed. Additional information is also required to understand the roles of non-pharmacological interventions and pharmacological interventions for different patient populations or symptoms. Given that there were no direct comparison trials of pharmacological and non-pharmacological interventions there is limited information available on the relative efficacy and safety of these approaches to managing NPS.

There are some limitations to our review. One of the major limitations of this review is the limited quality of the studies which were included in our review. Similar to reviews of

pharmacological treatments for NPS, authors of studies included in our review often failed to identify primary outcomes or reported multiple outcomes which make interpretation of the results challenging[95]. Also, we limited our search to English language publications to facilitate the review process although it is possible that some publications may have been overlooked. Given the small sample sizes of many studies the reported findings may have been underpowered to detect significant benefit or harms associated with many therapies. Unfortunately, due to the heterogeneity of studies we were not able to undertake meta-analyses although the utility of conducting meta-analyses on studies of low methodological quality is questionable. Our review also excluded some studies that used quasi-experimental study designs or studies utilizing cross-over study designs which have been utilized in many LTC studies due to concern about significant placebo response and potential carryover effects which have been observed in some studies[19].

Strengths include our rigorous search strategy, detailed description of studies, assessment of study quality, and examination of the feasibility of studies. Our review focussed entirely on studies conducted within the LTC setting so the results of our review will apply to LTC whereas previous reviews have included interventions conducted in community or hospital based settings whose results may not always generalize to LTC.

Conclusion:

Currently there are only a small number of high-quality clinical trials for non-pharmacological interventions for NPS of dementia in LTC. A variety of different types of interventions including staff training, geriatric mental health assessment, and activities such as exercise and pleasant psychosocial activities have some evidence to support their use. There were no studies that were rated as consistently highly feasible when the considering the need for

specialized staff, costs, and time for required for implementation or training. Further study is required on the specific types of symptoms most likely to respond to various NPS and relative efficacy and safety of non-pharmacological treatments when compared to medications. Additional research is also required to determine the effectiveness of non-pharmacological interventions when implemented in routine clinical care outside of research settings and pragmatic approaches to managing NPS in LTC.

Conflicts of Interest: No conflicts of interest.

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Table 1: Description of Included Studies

	Intervention	Number	Mean Age	Gender (% female)	Setting	Cognitive Impairment MMSE (SD)	Dementia Diagnosis	Duration
Nursing and Staff Training Approach								
McCallion 1999 [48]	Nurse training sessions and coaching	49	84.5 (9.0)	42 (85.7)	2 LTC in USA	6.3 (6.6)	Clinical diagnosis, dementia	6 months
	Waitlist	56	83.3 (9.0)	50 (89.3)	- -	4.9 (6.0)	- -	- -
Proctor 1999 [49]	Staff training, psychosocial management	60	83.4 (5.5)	43/54 (79.6)	2 LTC and 10 residential homes in UK	- -	AGECAT	6 months
	- -	60	82.7 (9.1)	44/51 (86.3)	- -	- -	- -	- -
Wells 2000 [50]	Education sessions	20	88.9 (6.3)	17 (85.2)	4 units in LTC in Canada	6.0 (6.26)	Medical diagnosis, "dementia", AD	3, 6 months after delivery
	Usual care	20	88.3 (5.6)	16 (82.8)	- -	2.9 (4.78)	- -	- -
Burgio 2002 [51]	Training of nurses in care (formal staff management)	47	82.2 (10.1)	40 (85.1)	2 LTC, 9 nursing units in USA	6.69 (9.17)	Physician diagnosed, AD, vascular, mixed	4 weeks, 3 and 6 months
	Usual care (conventional staff management)	32	77.4 (11.7)	21 (65.6)	- -	6.59 (7.59)	- -	- -
Magai 2002 [52]	Non-verbal training group, 10 hours of training	41	84.6 (8.1)	38 (92.7)	3 LTC in USA	3.2 (4.5)	MDS, MMSE, "dementia"	12 weeks
	Behavioural placebo group (had sessions but on different topic), 10 hours of non-specific training	23	87.7 (4.2)	21 (91.3)	- -	3.0 (5.4)	- -	- -
	Waitlist, control, no training	27	86.4 (9.3)	26 (96.3)	- -	4.2 (5.3)	- -	- -

Schrijnemaekers 2002 [53]	Emotion oriented care, clinical lessons, training program, supervision meetings	77	84.3 (5.5)	70 (90)	16 LTC in Netherlands	10.8 (5.1)	MMSE < 21, moderate to severe cognition problems	12 months
	Usual care	74	85.9 (5.6)	66 (89)	- -	11.3 (5.1)	- -	- -
Finnema 2005 [54]	Emotion oriented care, nursing training	67	83.8 (5.3)	54 (81)	16 geriatric psychiatry wards, 14 LTC in Netherlands	GDS N(%) severe: 36 (54)	AD, vascular dementia, mixed DSM-IV	9 months
	Usual care	79	83.6 (5.8)	64 (81)	- -	34 (43)	- -	- -
Testad 2005 [55]	Education sessions, staff training and follow-up	55	84.9 (5.6)	37 (67)	4 LTC in Norway	CDR: 2.0 (1.0)	"dementia"	7 months
	Usual care	96	84 (6.3)	69 (72)	- -	CDR: 2.2 (0.9)	- -	- -
Chenoweth 2009 [56]	Dementia-care mapping	109	83 (7.6)	90 (83)	15 LTC in Australia	5.6 (1.3)	"dementia"	4 months and 4 months follow-up
	Person-centered care	82	84 (6.4)	74 (76)	- -	5.6 (0.7)	- -	- -
	Usual care	82	85 (6.6)	60 (73)	- -	5.3 (1.1)	- -	- -
Deudon 2009 [57]	Staff education intervention, 90 min training session + coaching	174	86.5 (7.6)	134 (77)	16 LTC in France	9.2 (6.8)	ICD, AD, vascular, mixed, DLB, Frontotemporal dementia, non-specific dementia	2 months, 3 month follow-up
	Usual care	132	86.0 (6.7)	104 (78.8)	- -	12.1 (6.0)	- -	- -
Testad 2010 [58]	Staff education and training	75	86 (9)	56 (74.7)	4 LTC in Norway	FAST: 6 (1)	Chart diagnosis, dementia	12 months

	Usual care	70	86 (11.25)	51 (72.9)	- -	FAST: 6 (3.25)	- -	- -
Comprehensive Assessment								
Rovner 1996 [59]	Activity program, psychotropic drug management, educational rounds	42	82.0 (8.0)	36 (86)	LTC in USA	9.1 (7.4)	DSM-III-R, "dementia"	6 months
	Standard care	39	81.2 (7.2)	26 (67)	- -	8.9 (6.1)	- -	- -
Brodaty 2003 [60]	Case management	28	82.9 (8.09)	62 (72)	LTC in Australia	AMTS: 3.29 (2.32)	AMTS, DMS-IV, "dementia"	12 weeks
	Consultation with specialist	27	82.9 (8.09)	- -	- -	- -	- -	- -
	Standard care	31	82.9 (8.09)	- -	- -	- -	- -	- -
Cohen-Mansfield 2007 [61]	Systematic non-pharmacological therapy	89	88.0 (6.4)	75 (84.3)	LTC in USA	7.26 (6.0)	AD, vascular, Parkinsons disease dementia	10 days
	Routine care/educational sessions	78	85.0 (8.6)	59 (75.6)	- -	6.88 (6.5)	- -	10 days
Psychosocial Interventions/Activities								
Mitchell 1996 [62]	Individualized special instruction, 30 mins/day, + 5 days	15	78.6	18 (60)	LTC in USA	CDRS: 2-3	NINCDS-ADRDA, AD, multi-infarct dementia, Organic Brain Syndrome, "dementia"	7 days
	Waiting list	15	78.6	- -	- -	- -	- -	- -
Toseland 1997 [63]	Validation therapy, 4 30 min sessions/week	31	87.79 (5.95)	27 (86)	Skilled care LTC in USA	SPMSQ: 7.43 (2.10)	MDS, "dementia"	1 year
	Social contact, 4 30 min sessions/week	29	87.29 (6.12)	20 (69)	- -	SPMSQ: 7.46 (7.79)	- -	- -
	Usual care	28	87.78 (7.56)	19 (68)	- -	SPMSQ: 7.15 (3.01)	- -	- -

McCallion 1999 [64]	Family visit communication program, 8 weeks then follow up, 4 1½ hr group sessions and 3 1 hr family conferences	32	86.4 (6.6)	30 (93.8)	5 Skilled care LTC in USA	5.81 (6.29)	MDS and chart, "dementia"	6 months
	Usual care	34	85.5 (6.7)	22 (64.8)	- -	7.97 (7.05)	- -	- -
Beck 2002 [65]	ADL with nursing staff, 45-60 mins/day	28	82.29 (8.9)	22 (78.6)	7 LTC in USA	11.44 (7.69)	Unclear, "dementia"	12 weeks
	Psychosocial activity (25 standardized modules), 15-30 mins daily	29	82.18 (7.64)	24 (82.1)	- -	10.65 (6.76)	- -	- -
	Combined ADL and psychosocial acitivity, 90 mins/day	22	82.82 (9.81)	18 (81.8)	- -	7.91 (5.41)	- -	- -
	Routine/normal care	19	86.47 (6.37)	17 (89.5)	- -	11.47 (6.43)	- -	- -
	One-on-one interaction with nursing staff, 30 mins/day	29	86.45 (6.92)	22 (75.9)	- -	11.11 (6.39)	- -	- -
Opie 2002 [66]	Early intervention group	48	84.4 (6.9)	35 (73)	LTC in Australia	6.46 (7.37)		1 month
	Late intervention group (usual care)	51	83.7 (7.2)	37 (73)	- -	6.33 (6.72)		- -
Politis 2004 [67]	Geriatric network kit, 30 mins, 3x/week	18	84.4 (4.5)	15 (83.3)	LTC in USA	8.7 (5.9)	DSM-IV, AD	4 weeks
	Spend time together talk, patient decides	18	83.5 (4.9)	15 (83.3)	- -	10.2 (5.3)	- -	- -
Lichtenberg 2005 [68]	One-on-one pleasant event 3x/week, 20-30 mins, 3 months	9	84.8 (4.9)	8 (90)	2 LTC in USA	14.5 (1.2)	AD (60%)	6 months
	Usual care	11	85.0 (5.1)	10 (90)	- -	14 (0.8)	- -	- -

Deponte 2006 [69]	Validation Therapy	30	86.8	- -	LTC in Italy	11.0 (+/- 7)	"Dementia"	3 months
	Sensorial Reminiscence	- -	- -	- -	- -	12.4 (+/- 4.5)	- -	- -
	No treatment	- -	- -	- -	- -	12.3 (+/- 4.3)	- -	- -
Tappen 2009 [70]	Therapeutic conversation (3x/week)	15	83.8 (7.45)	14 (93)	LTC home in USA	10.60 (6.99)	NINCDS-ADRDA, AD	16 weeks
	Usual care	15	90.26 (5.95)	13 (87)	- -	12.26 (7.43)	- -	- -
Wang 2009 [71]	Reminiscence Therapy	38	79.32 (6.35)	18 (47.4)	Care facility in Taiwan	CDR: 1.43 (0.59)	Mild-moderate dementia	8 weeks
	Usual care	39	78.76 (7.60)	19 (48.7)	- -	CDR: 1.18 (0.59)	- -	- -
Exercise								
Alessi 1999 [72]	Day time physical activity and nighttime intervention	15	88.6 (10.4)	13 (86.7)	LTC in USA	13.6 (8.5)	? all with dementia	14 weeks and 5 nights
	Nighttime intervention alone	14	88.3 (5.7)	13 (92.9)	- -	13.1 (8.1)	- -	- -
Hopman-Rock 1999 [73]	PAP, exercise group, 2x/week	45	83.8 (5.8)	41 (91)	11 LTC in Netherlands	CST-14: 5.1 (3.3)	"dementia"	6 months
	Control usual care (usual activities)	47	84.2 (5.6)	46 (98)	- -	CST-14: 6.1 (3.2)	- -	6 months
Landi 2004 [74]	Exercise/physical activity	15	80.9 (8.5)	8 (53)	LTC in Italy	CDS: 2.6 (1.3)	AD – CPS score unclear	4 weeks
	Usual care	15	80.9 (8.5)	7 (47)	- -	CDS: 2.4 (2.0)	AD – "medium cognitive impairment"	- -
Rolland 2007 [75]	Exercise program (1 hr, 2x/week)	67	82.8 (7.8)	48 (71.7)	5 LTC in France	9.7 (6.8)	Diagnosis of dementia on MMSE <25, NINDA-ADRDA, AD	12 months

	Routine care	67	83.1 (7.0)	53 (79.1)	- -	7.9 (6.4)	- -	- -
Williams 2007 [76]	Comprehensive exercise, individually 5days/week	30	88 (6.32)	76 (85)	5 LTC in USA	8.50 (7.61)	AD, NINCDS-ADRDA	16 weeks
	Supervised walking	31	- -	- -	- -	12.71 (7.47)	- -	- -
	Social conversation	29	- -	- -	- -	9.82 (7.31)	- -	- -
Music Therapy								
Sung 2006 [77]	Group music with movement, 30 mins, 2x/week	18	76.8 (9.1)	7 (38.9)	Residential care facility in Taiwan	GDS: 3-6	DSM-IV, "dementia"	4 weeks
	Usual care	18	78.4 (7.9)	3 (27.8)	- -	- -	- -	- -
Svansdottir 2006 [78]	Music therapy, 30 min, 3x/week, 6 weeks	20	71-87	- -	2 LTC, 2 psychogeriatric wards in Iceland	GDS: 5-7	ICD-10 AD	6 weeks
	Routine care	18	71-87	- -	- -	- -	- -	- -
Raglio 2008 [79]	MT	30	84.4 +/- 5.5	M (5)	- -	11.1 (+/- 5.5)	AD, vascular, mixed	14 weeks
	Educational support	29	85.8 +/- 5.4	M (4)	- -	10.7 (+/- 5.7)	- -	16 weeks
Sensory Stimulation								
Scherder 1998 [80]	Tactile stimulation massage (30 mins/day, 5 days/week)	16	85.7	- -	- -	CST: 10.4	NINCDS, CDS	6 weeks
	Sham electrical stimulation	- -	- -	- -	- -	- -	- -	- -
Ballard 2002 [81]	Aromatherapy with Melissa oil, applied twice daily	36	77.2 (7.6)	20 (56)	8 LTC in UK	CDR Stage 3	Severe dementia, CDR Stage 3	4 weeks

	Placebo sunflower oil	36	79.6 (8.5)	23 (64)	- -	- -	- -	- -
Ancoli-Israel 2003 [82]	2500 lux x 10 days (white light)	92	82.3 (7.6)	63 (68.5)	LTC in USA	5.7	NINCDS	10 days
	Dim red light 300 lux	- -	- -	- -	- -	- -	- -	- -
Van Weert 2005 [83]	Snoezelen	62	84.0 (8.6)	49 (79)	12 wards in 6 LTC in Netherlands	BIP: 14.5 (3.1)	DSM-III-R	18 months
	Usual Care	63	82.6 (8.2)	52 (82.5)	- -	BIP: 13.4 (4.0)	- -	- -
Woods 2005 [84]	Therapeutic touch, 5-7 mins, 2x/day	19	78.9 (3.78)	15 (79)	3 LTC SCU, Canada	6.11 (8.5)	DSM-IV, AD, vascular, mixed	9 days
	Routine care	19	81.16 (5.32)	16 (84)	- -	6.39 (7.15)	- -	- -
	"Minimized therapeutic touch" (placebo), 5-7 mins, 2x/day	19	82.37 (5.93)	15 (79)	- -	5.06 (6.22)	- -	- -
Scherder 2006 [85]	Cranial electrostimulation, 30m/day, 5 days/week	11	83.73	11 (100)	"institute" in Netherlands	18	NINCDS-ADRDA, Probable AD	6 weeks
	Control, "no current applied"	10	84.50	8 (80)	- -	20	- -	- -
Hawranik 2008 [86]	Therapeutic touch, once/day, 5 days	17	83.3 (8.32)	10 (58.8)	LTC in Canada	6.6 (7.30)	AD	5 days
	Usual care	18	80.9 (7.41)	12 (66.7)	- -	2.9 (4.31)	- -	- -
	Placebo-stimulated therapeutic touch, once/day, 5 days	16	84.2 (6.20)	14 (87.5)	- -	7.1 (7.54)	- -	- -
Burns 2009 [87]	Bright light for 2 weeks	22	84.5 (1.7)	16 (73)	LTC in UK	6.9 (5.3)	AD, vascular, DLB, mixed	8 weeks
	Standard light	26	82.5 (1.5)	16 (62)	- -	5.1 (5.6)	- -	- -

AD = Alzheimer's Disease; ADL = activities of daily living; AGECAT = Automatic Geriatric Examination for Computer-Assisted Taxonomy; AMTS = Abbreviated Mental Test Scale; BIP = Behavioural Observation Scale for Intramural Psychogeriatry; CDR = Clinical Dementia Rating; CPS = cognitive performance scale; DAT = Diagnosis Dementia of the Alzheimer Type; DLB = dementia with Lewy bodies; DSM = Diagnostic and Statistical Manual of Mental Disorders; GDS = Global Deterioration Scale; ICD = international classification of diseases; LTC = long-term care; MDS = minimum dataset; MMSE = Mini-Mental State Examination; NINCDS –ADRDA = National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; PAP = Psychomotor Activation Programme; SCU - Special Care Unit; SD = standard deviation

Table 2: Effects of Non-Pharmacological Interventions on Neuropsychiatric Symptoms of Dementia

	Intervention	Outcome	Baseline Mean (SD)	Primary Endpoint Post Treatment	Difference	Outcome*
Nursing and Staff Training Approach						
McCallion 1999 [48]	Nurse Training Waitlist	CMAI – physically aggressive agitation	15.2 (9.8) 13.3 (7.5)	12.21 (8.31) 12.0 (6.2)	No effects found for aggressive behaviour subscale	I = C
	Nurse Training Waitlist	CMAI – physically non-aggressive agitation	12.49 (6.3) 11.1 (5.5)	11.38 (6.0) 10.4 (6.3)	Physically non-aggressive behaviour declined from baseline to 3 months	I > C
	Nurse Training Waitlist	CMAI – verbal agitation	16.2 (11.4) 10.4 (6.2)	12.8 (8.4) 12.1 (6.9)	Verbal aggression decreased at 3 and 6 months	I > C
	Nurse Training Waitlist	CMAI - total	43.87 34.78	36.47 34.45		?
Proctor 1999 [49]	Staff Training Control	Crighton Scale	12.1 29.5	13.7 25.05	-0.7 (-3.0 – 1.6) - 4.46	I = C
Wells 2000 [50]	Education Sessions Usual care	PAS	0.35 (0.33) 0.29 (0.38)	0.17 (0.24) 0.33 (0.38)		I = C F=4.43, p=.19
	Education Sessions Usual care	MIBM Agitation	4.50 (1.06) 4.55 (1.23)	5.02 (1.21) 4.11 (1.48)		? F=4.06, p=.021
Burgio 2002 [51]	Nurse Training Usual care	CMAI	42.2 (18.6) 34.9 (13.6)		Unclear No difference between groups	I = C F=5.12, p<.05
Magai 2002 [52]	Non-verbal training group	Symptomatology (CDS + CMAI + BEHAVE-AD)	83.7 (51.2)	65.5 (37.7)	Change in CMAI/BEHAVE-AD not significant	I = C F=1.15, p>.5

	Behavioural placebo group Waitlist		25.2 (5.2) 40.6 (7.8)	39.2 (15.2) 61.6 (31.1)		
Schrijnemaekers 2002 [53]	Emotion oriented care Usual care	GIP			No difference between groups over time After 6 months, significantly different GIP = less deterioration on anxious behaviour.	I = C
	Emotion oriented care Usual care	CMAI			Control had less deterioration on physical non-aggressive behaviour	
Finnema 2005 [54]	Emotion oriented care Usual care	CMAI physical aggression	2.11 (3.1) 1.44 (2.8)	2.15 (3.0) 1.38 (2.5)	+ 0.04 - 0.06	I = C p=0.5
Testad 2005 [55]	Education sessions Usual care	BARS	16.8 (10-42) 17.3 (10-40)	21.2 (10-37) 17.4 (10-44)	BARS increase in experimental group Intervention had statistically significantly higher BARS score than control at follow-up	I < C p>.05
Chenoweth 2009 [56]	Dementia-care mapping Person-centered care Usual care	CMAI	46.1 (6.5) 47.5 (9.1) 50.3 (6.8)	45.1 (6.6) 41.7 (9.2) 58.7 (6.9)	No difference at 4 months, DCM and PCC better than usual care at 8 months	I > C
	Dementia-care mapping Person-centered care Usual care	NPI	12.7 (5.1) 21.3 (6.8) 16.9 (5.3)	16.8 (5.1) 14.5 (6.9) 20.2 (5.4)		I = C
Deudon 2009 [57]	Staff Training Usual care	CMAI	53.08 (18.1) 48.21 (15.9)	47.01 (16.0) 47.54 (18.1)	-6.52 (16.8) -0.83 (17.6),	I = C p=.05

Testad 2010 [58]	Staff training Usual care	CMAI	42.3 (13.9) 35.7	39.3 (12.1) 36.1 (8.5)	- 3.0, + 0.4	I > C p=.034
Comprehensive Assessment						
Rovner 1996 [59]	Activity program Standard care	Behaviour present	42/42 (100%) 39/39 (100%)	12/42 (28.6) 20/39 (51.3)	71.4% 48.7%	I > C p=.037
Brodaty, 2003[60]	Case management Consultation with specialist Standard Care	NPI			26% reduction in NPI 5.1% reduction in NPI 5.6% reduction in NPI	I = C
	Case Management Consultation with specialist Standard Care	BEHAVE-AD			19.4% reduction in BEHAVE-AD score 6.9% reduction in BEHAVE-AD score 2.9% reduction in BEHAVE-AD score	
Cohen-Mansfield 2007 [61]	Systematic non-pharmacological therapy Routine Care	ABMI	5.17 (3.75) 5.05 (3.36)	3.23 (3.16) 4.10 (3.47)	- 1.94 - 0.95	I > C F=10.22, p=.002
Psychosocial Interventions/Activities						
Mitchell 1996 [62]	Individualized special instruction Waiting list	ABC	48 40	52 48	Both groups deteriorated	I = C
Toseland	Validation therapy	CMAI			Reduction in physical aggressive behaviour at 3	I > C

1997 [63]	Social contact Usual care				months, At 1 year no difference in non-aggressive or verbal	p=.001 I = C
McCallion 1999 [64]	Family visit communication program Usual care	CMAI total	37.4 32.8	36.2 33.7	"Only physically non-aggressive behaviours improved with treatment"	I = C
Beck 2002 [65]	Activities of daily living with personal nursing assistant Psychosocial activity Combined activities of daily living and psychosocial activity Routine care Placebo	DBS	172.51 (191.47) 348.02 (467.50) 287.66 (373.73) 408.71 (427.24) 325.96 (337.14)	164.56 (154.95) 383.24 (367.54) 286.21 (365.78) 281.97 (410.85) 336.80 (366.55)	No significant difference between groups	I = C
Opie 2002 [66]	Early intervention group Late intervention group (usual care)	CMAI BAGS			No change in counts of behaviour between groups during intervention Restlessness and all behaviour decreased treatment group at 4 week follow-up No significant difference between groups over time	I = C
Politis 2004 [67]	Geriatric network kit Spend time together talk	NPI	16.2 (21.2) 21.2 (16.4)	10.0 (10.3) 9.8 (11.5)	- 6.2 - 0.2	I = C
Lichtenberg	One-on-one pleasant event	BEHAVE-AD	15.5 (9.8)	8.0 (3.8)	- 7.5	I > C

2005 [68]	Usual care		12.4 (7.2)	7.0 (4.1)	- 5.4	F=8.4, p=.01
Deponte 2006 [69]	Validation Therapy Sensorial Reminiscence No treatment	NPI	18.9 (14.9) 17.6 (15.4) 10.6 (10.3)	14.9 (13.3) 9.9 (9.1) 10.8 (9.0)	- 4 - 7.7 + 0.2	?
Tappen 2009 [70]	Therapeutic conversation Usual care	AD-RD (hostile)	14.86 (4.2) 15.5 (7.9)	15.7 (5.8) 17.0 (3.7)		I = C F=0.37, p=.5
	Therapeutic conversation Usual care	DMAS	23.66 (14.73) 21.33 (15.67)	21.26 (12.80) 28.13 (12.21)	- 2.4 + 6.8	F=3.59, p=.06
Wang, 2009[71]	Reminiscence Therapy Control	CAPE-BRS	13.97 (4.48) 13.90 (5.18)	12.87 (5.96) 14.37 (5.69)	- 1.1 +0.47	I = C
Exercise						
Alessi 1999 [72]	Day time physical activity and nighttime intervention Nighttime intervention alone	# observations	9.4 (15.4) 5.9 (9.7)	7.3 (14.0) 14.7 (19.7)		I > C F=7.86, p=.009
Hopman-Rock 1999 [73]	Exercise Group Control usual care	BIP - restlessness	4.1 (2.8) 5.0 (3.1)	4.2 (2.7) 4.6 (3.3)		I = C F=1.38, p=.88
Landi 2004 [74]	Exercise/physical activity Usual Care	Physical Abuse	4/15 - 26% 5/15 - 32%	2/15 - 13% 5/15 - 32%	Significant reduction in behaviour problems	I > C
	Exercise/physical activity Usual Care	Verbal Abuse	7/15 - 43% 6/15 - 39%	3/15 - 22% 5/15 - 32%	Not reported	?

Rolland 2007 [75]	Exercise program Routine care	NPI	10.7 (6.9) 11.4 (7.7)	8.3 (8.9) 8.9 (10.4)	- 2.5 - 2.2	I = C p=.78
Williams 2007 [76]	Comprehensive exercise Supervised walking Social conversation	Lawton OAS 2 week positive		+ 11.11 - 3.38 + 9.65		I > C
	Comprehensive exercise Supervised walking Social conversation	Lawton OAS 2 week negative		- 4.81 + 9.14 - 5.65	Comprehensive exercise group better than other groups at 2 weeks on negative affect	P=.006
Music Therapy						
Sung 2006 [77]	Group music with movement Usual care	Modified CMAI, measured during the intervention	5.11 (2.45) 4.72 (1.81)	3.44 (1.29) 4.50 (1.65)	+ 1.67 - 0.22	I > C
Svansdottir 2006 [78]	Music therapy Routine care	Total BEHAVE-AD	5.5 5.4	4.4 4.7	- 1.1 - 0.7	I = C p=0.3
Raglio 2008 [79]	Music Therapy Educational support	NPI	27 29.5	14.64 25.05	- 12.36 - 4.46	I > C
Sensory Stimulation						
Scherder 1998 [80]	Tactile stimulation massage Sham electrical stimulation	BOP Behaviour inventory	1.25 2.38	0.63 1.88	- 0.62, -0.5	I = C F = 1.64, p = .22

Ballard 2002 [81]	Aromatherapy Placebo	CMAI total score	68.3 (15.3) 60.6 (16.6)	45.2 (10.4) 53.3 (17.6)		I > C Z=2.7, p=.005
	Aromatherapy Placebo	Response rate 30% improvement		21/36 (60%) 5/36 (14%)		χ^2=16.3, p<.001
Ancoli-Israel 2003 [82]	White Light Dim Red Light	CMAI			"No significant change in CMAI or ABRS"	I = C
Van Weert 2005 [83]	Snoezelen Usual Care	CMAI	14.51 (SE) 12.34 (SE)	12.12 (SE) 13.83 (SE)	- 2.39 + 1.49	I > C
Woods 2005 [84]	Therapeutic touch Routine care	ABRS	1.55 (1.03) 1.53 (0.99)	1.03 (0.67) 1.48 (1.12)	- 0.52 - 0.05	I > C
Scherder 2006 [85]	Cranial electrostimulation Control	BOP "aggressiveness"	1.04 (1.42) 1.70 (1.49)	1.14 (1.52) 1.76 (1.32)	+ 0.1 + 0.06	I = C F=0.01, p=.93
Hawranik 2008 [86]	Therapeutic touch Usual care Placebo-stimulated therapeutic touch	CMAI # behaviours			No significant difference across the three groups in the incidence of physically aggressive and verbally agitated behaviours Less physically non-aggressive behaviours in TT vs. UC	I = C I > C
Burns 2009 [87]	Bright Light Standard light	CMAI	62.0 (18.4) 57.5 (13.8)	49.5 (13.8) 49.5 (10.4)	- 12.5 - 8	I = C

* I = intervention, C = comparison group; I = C = no statistically significant difference between groups; I > C intervention superior to comparison group, ? = unclear if intervention and control group differed significantly

ABC = Aberrant Behavior Checklist; ABMI = Agitation Behaviour Mapping Instrument; AD-RD = Alzheimer's Disease and Related Disorders Mood Scale; BARS = Brief Agitation Rating Scale, BEHAVE = AD - Behavioural Pathology in Alzheimer's Disease Rating Scale; BOP = Beoordelingsschaal voor Oudere Patienten; CAPE-BRS = Clifton Assessment Procedures for the Elderly – Behavioral Rating Scale; CDS = Cornell scale for depression in dementia; CMAI = Cohen-Mansfield Agitation Inventory; DBS = Disruptive Behavioural Scale; DCM = Dementia-Care Mapping; DMAS = dementia mood assessment scale; GIP = Gedragsobservatieschaal voor de Intramurale Psychogeriatrie; GDS = Global Deterioration Scale; MIBM = Modified Interaction Behaviour Measure; NPI = Neuropsychiatric Inventory; OAS = observed affect scale; PAG = Physically Aggressive Behaviour; PAS = Pittsburgh Agitation Scale; PCC = Person-Centered Care; PNB = Physically Non-Aggressive Behaviour; VA = Verbal Agitation

Table 3: Risk of Bias Assessment

	Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Outcome Reporting	Other - Funding Source
Nursing and Staff Training Approach						
McCallion 1999 [48]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Proctor 1999 [49]	Yes	Unclear	Yes	Yes	Yes	Yes
Wells 2000 [50]	Unclear	Unclear	Unclear	No	Yes	Yes
Burgio 2002 [51]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Magai 2002 [52]	Unclear	Unclear	No	Yes	Yes	Yes
Schrijnemaekers 2002 [53]	Unclear	Unclear	No	Unclear	Unclear	Yes
Finnema 2005 [54]	Unclear	Unclear	Unclear	No	Yes	Yes
Testad 2005 [55]	Unclear	Unclear	Yes	Yes	Yes	Yes
Chenoweth 2009 [56]	Yes	Unclear	Yes	Yes	Yes	Yes
Deudon 2009 [57]	Unclear	Unclear	Yes	Yes	Yes	Yes
Testad 2010 [58]	Unclear	Unclear	Yes	Unclear	Yes	Yes
Comprehensive Assessment						
Rovner 1996 [59]	Yes	Unclear	Yes	Yes	Yes	Yes
Brodaty 2003 [60]	Yes	Unclear	Yes	Yes	Yes	Yes
Cohen-Mansfield 2007 [61]	No	No	Unclear	Yes	Yes	Yes
Psychosocial Interventions/Activities						
Mitchell 1996 [62]	Unclear	Unclear	Yes	Yes	No	Yes

Toseland 1997 [63]	Unclear	Unclear	Yes	No	Yes	Yes
McCallion 1999 [64]	Unclear	Unclear	Yes	Yes	Yes	Yes
Beck 2002 [65]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Opie 2002[66]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Politis 2004 [67]	Yes	Unclear	Yes	Yes	Yes	Yes
Lichtenberg 2005 [68]	Unclear	No	Yes	Yes	Yes	Yes
Deponte 2006 [69]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Tappen 2009 [70]	Unclear	Unclear	Yes	Yes	Yes	Yes
Wang 2009 [71]	Yes	Yes	Yes	Yes	Yes	Yes
Exercise						
Alessi 1999 [72]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Hopman-Rock 1999 [73]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Landi 2004 [74]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes
Rolland 2007 [75]	Yes	Unclear	Yes	Yes	Yes	Yes
Williams 2007[76]	Unclear	Unclear	Yes	Yes	Yes	Yes
Music Therapy						
Sung 2006 [77]	Yes	Unclear	Unclear	Yes	Yes	Yes
Svansdottir 2006 [78]	Unclear	Unclear	Yes	Unclear	Yes	Yes
Raglio 2008 [79]	No	No	Yes	Unclear	Yes	Yes
Sensory Stimulation						
Scherder 1998 [80]	Unclear	Unclear	Yes	Yes	Yes	Yes
Ballard 2002 [81]	Yes	Unclear	Yes	Yes	Yes	Yes

Ancoli-Israel 2003 [82]	Unclear	Unclear	No	Unclear	Yes	Yes
Van Weert 2005 [83]	Yes	No	No	No	Yes	Unclear
Woods 2005 [84]	Yes	Unclear	Yes	Yes	Yes	Yes
Scherder 2006 [85]	Yes	Unclear	Yes	Yes	Yes	Yes
Hawranik 2008 [86]	Unclear	Unclear	Unclear	Yes	Yes	Yes
Burns 2009 [87]	Yes	Unclear	Yes	Yes	Yes	Yes

Table 4: Assessment of Feasibility of Interventions

	Specified Staff	Cost	Time/Training
Nursing and Staff Training Approach			
McCallion 1999 [48]	Low	High	Low
Proctor 1999 [49]	Low	High	Medium
Wells 2000 [50]	Medium	High	Low
Burgio 2002 [51]	Low	High	Low
Magai 2002 [52]	Medium	High	Low
Schrijnemaekers 2002 [53]	Medium	High	Low
Finnema 2005 [54]	Medium	High	Low
Testad 2005 [55]	Medium	High	Medium
Chenoweth 2009 [56]	Low	Low	Low
Deudon 2009 [57]	Low	High	Medium
Testad 2010 [58]	Medium	High	Low
Comprehensive Assessment			
Rovner 1996 [59]	Low	Low	High
Brodaty 2003 [60]	Low	High	High
Cohen-Mansfield 2007 [61]	Low	Low	Low
Psychosocial Interventions/Activities			
Mitchell 1996 [62]	Low	High	High
Toseland 1997 [63]	Low	High	High
McCallion 1999 [64]	Low	High	High
Beck 2002 [65]	Low	High	High
Opie 2002[66]	Low	Medium	Low
Politis 2004 [67]	Low	Medium	High
Lichtenberg 2005 [68]	Low	High	Low
Deponte 2006 [69]	Low	Low	High
Tappen 2009 [70]	Low	High	High
Wang 2009 [71]	Medium	Unclear	High

Exercise			
Alessi 1999 [72]	Low	High	Medium
Hopman-Rock 1999 [73]	Low	High	Low
Landi 2004 [74]	Unclear	Unclear	Unclear
Rolland 2007 [75]	Low	Low	High
Williams 2007[76]	Low	High	High
Music Therapy			
Sung 2006 [77]	Low	High	High
Svansdottir 2006 [78]	Low	High	High
Raglio 2008 [79]	Low	Low	High
Sensory Stimulation			
Scherder 1998 [80]	Low	Low	Medium
Ballard 2002 [81]	High	Medium	High
Ancoli-Israel 2003 [82]	Low	Medium	High
Van Weert 2005 [83]	Low	Medium	Low
Woods 2005 [84]	Low	High	High
Scherder 2006 [85]	Low	Low	High
Hawranik 2008 [86]	Low	High	High
Burns 2009 [87]	Medium	Medium	Low

Figure 1: Flow of Studies Through Review Process