Comparative Effectiveness Review
Number 177

Nonpharmacologic Interventions for Agitation and Aggression in Dementia

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Effective Health Care Program

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Nonpharmacologic Interventions for Agitation and Aggression in Dementia

Structured Abstract

Objective. To assess the efficacy, comparative effectiveness, and adverse effects of nonpharmacologic interventions for agitation and aggression in individuals with dementia.

Data sources. Ovid MEDLINE®, Ovid Embase®, and the Cochrane Central Register of Controlled Trials bibliographic databases; hand searches of references of relevant studies.

Review methods. Two investigators screened abstracts and full-text articles of identified references for eligibility. Eligible studies included randomized controlled trials evaluating nonpharmacologic interventions to manage agitation/aggression in individuals with dementia in nursing home, assisted living, or community settings. We analyzed outcomes of agitation/aggression, general behavior, patient quality of life, admission to long-term care, and staff and caregiver outcomes related to patient behavior and care burden. We assessed risk of bias, extracted data, and evaluated strength of evidence for each comparison and outcome. We analyzed pooled estimates to assess efficacy and comparative effectiveness. We conducted a qualitative analysis when data could not be pooled.

Results. We identified 126 unique randomized controlled trials as of July 2015. Patient-level interventions involving music, aromatherapy with lavender, and bright light were similar to usual treatment or attention control at managing agitation/aggression in people with dementia (low-strength evidence); interventions tailored to recipients' skills, interests, or both were similar to usual care in managing agitation/aggression in people with dementia (low-strength evidence). Care delivery–level interventions (dementia care mapping and person-centered care) were similar to usual care in managing agitation/aggression in people with dementia (low-strength evidence). Evidence was insufficient to draw conclusions on the effectiveness of most caregiver-level interventions in managing agitation/aggression in people with dementia; caregiver interventions targeting caregiver skills and behavior were similar to attention control in managing agitation/aggression (low-strength evidence). However, these interventions show benefits in caregiver confidence in caregiving and caregiver distress. Adverse effects were rarely reported.

Conclusions. Although many trials have been conducted to determine effective nonpharmacologic interventions for agitation/aggression in dementia, which is a critical topic, the evidence base is weak because of the variety of comparisons, measurement issues, and other methodological limitations. When evidence was sufficient to draw conclusions about effectiveness for a group of interventions, agitation/aggression outcomes were typically similar to those of control groups. Future research is needed to guide providers and informal caregivers toward effective interventions for agitation/aggression in dementia.

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Executive Summary

Background

Dementia and Agitation and Aggression

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) categorizes individuals with acquired cognitive deficits as having major or minor neurocognitive disorders (NCDs).[1] Subtypes of NCDs include major and mild NCD due to Alzheimer's disease, frontotemporal disorder, or Lewy bodies, and vascular NCD. Historically, patients with these NCDs have been referred to as having dementia. Because "dementia" is the far more familiar term, we have used it rather than "NCD" throughout this report.

Many individuals with dementia exhibit neuropsychiatric symptoms at some point, usually in advanced disease stages.[2] While neuropsychiatric symptoms are wide ranging, they tend to cluster into five domains: depression, agitation, aggression, apathy, and psychosis.[3] Agitation and aggression are among the most challenging. Aggression is more serious than agitation because it can cause harm to the patient and others. Agitation/aggression in individuals with dementia is associated with institutionalization among community-dwelling people, social isolation, and other negative outcomes.[4] These behaviors challenge formal and informal caregivers and contribute to caregiver anger, resentment toward the patient, stress, and decreased psychological health.[5-7]

Terminology about agitation/aggression is confusing.[8] Agitation and aggression are typically grouped together as part of a spectrum, although they have different manifestations and implications. Agitation affects primarily the person with dementia (although the behaviors may be disruptive for others in his/her environment). By contrast, aggression involves at least one other person (the target of the aggression) and can represent real risks. Therefore, although it makes sense to identify and treat the underlying cause of agitation whenever possible, not all agitation needs intervention per se; sometimes, depending on its manifestation, agitation can simply be tolerated. Aggression, however, needs to be dealt with because of the possible risk to others. Despite these different treatment implications, agitation and aggression are frequently confounded in the literature. Hence, we refer to these symptoms as "agitation/aggression" for the remainder of this report.

Antipsychotic medications are often used to treat agitation/aggression in individuals with dementia. This was more common in the past but still occurs today despite current clinical guidance recommending nonpharmacologic interventions as the first choice for agitation/aggression in dementia.[9-12] Antipsychotic medications have limited efficacy and significantly increase the risk of stroke and mortality.[13-15] For some individuals with dementia, side effects of antipsychotic medications can lower quality of life.[16] Reducing unnecessary use of antipsychotics for behavioral symptoms in individuals with dementia is important. Evidence of effective nonpharmacologic approaches would strengthen the efforts to urge less use of inappropriate psychoactive drugs, but the absence of that evidence should not diminish such efforts in light of the harmful effects of these medications. By contrast, the nonpharmacologic approaches have virtually no reports of adverse effects.

Nonpharmacologic interventions aim to (1) prevent agitation/aggression, (2) respond to episodes of agitated and aggressive behaviors to reduce their severity and duration, and/or (3) reduce caregiver distress. Individuals with dementia typically reside in nursing homes or assisted

living facilities or at home in their community (community dwelling). The duration of successful interventions varies with the goal of the intervention. Some are short lasting, designed to neutralize episodes of agitation/aggression when they occur. By contrast, preventive approaches aim to reduce the frequency and severity of agitation/aggression over time.

Interventions delivered in nursing homes and assisted living facilities can be at the patient level, where a therapy is delivered directly to the patient, or the care delivery level, involving the approach, staff, and/or environment used in care delivery. Strategies often involve specific activities or enhancing communication.[17] Care delivery–level interventions include a variety of care delivery models, staff/caregiver education and training, and environmental approaches.[18] Examples include training to enhance staff knowledge and skills in managing behavioral symptoms among residents, care delivery models such as dementia care mapping, and enhancements to the environment aimed at reducing exposure to elements that induce agitation/aggression.

Interventions delivered to community-dwelling individuals with dementia can be at the patient or caregiver level. The caregiver is typically an informal family caregiver (i.e., an unpaid family member who provides care to the person with dementia). Patient-level interventions are similar to those in residential settings. Some patient-level interventions targeted to individuals in less advanced stages of dementia include activities, such as exercise classes. Caregiver-level interventions to address agitation/aggression typically provide education and skills training to enhance understanding of the disease process, specific symptoms, and how to best address agitation/aggression. Table A provides a classification scheme and examples of the types of interventions used in various settings.

Desired outcomes of nonpharmacologic interventions include a reduction in the incidence and severity of agitation and aggression. Measuring these outcomes is complex. A wide variety of instruments are available. Available instruments are (1) based on different theoretical frameworks, (2) designed to evaluate behaviors in different settings (e.g., home or nursing home), (3) intended to be administered by different individuals (e.g., caregiver, nurse, or patient), and (4) rely on a variety of mechanisms to obtain responses (e.g., interviews with people with dementia or direct observation). More than 45 specific instruments are used to evaluate behavioral symptoms in dementia. The appropriate instrument depends on disease severity and context of care (e.g., setting, severity of disease, and whether the purpose is to identify any agitation/aggression or specific behaviors).[3] Instruments that specifically measure agitation/aggression include the Agitated Behavior in Dementia Scale (ABID),[19] the Cohen-Mansfield Agitation Inventory (CMAI),[20] and the Pittsburgh Agitation Scale (PAS).[21] Additionally, some general behavioral symptom instruments include subscales specific to agitation/aggression.

Evidence synthesis on the efficacy and comparative effectiveness of nonpharmacologic interventions for addressing agitated and aggressive behaviors in people with dementia is needed. This evidence could inform decisionmakers about the best ways to reduce the frequency and severity of those behaviors. Actions inspired by the evidence synthesis could improve functioning, reduce distress, and reduce or delay nursing home admission for individuals with dementia while reducing the use of antipsychotic drugs.

Table A. Types of interventions addressing agitation/aggression in dementia

Setting	Intervention Level	Intervention Type	Goals	Examples
Nursing Homes and Assisted Living Facilities	**Patient level**	Sensory	Preventing incidents	Music therapy (listening), aromatherapy, bright light therapy, multisensory stimulation
		Structured activities	Preventing incidents	Dancing, exercise, social interaction, music therapy (playing, singing), art therapy, outdoor walks
		Complementary and alternative medicine	Preventing incidents; treating incidents	Aromatherapy, reflexology, acupuncture, acupressure, massage, Reiki
		Psychological	Preventing incidents	Validation therapy, reality orientation, reminiscence therapy, support groups
	Care delivery level	Care delivery models	Preventing incidents; treating incidents	Dementia care mapping, patient-centered care
		Staff training and education	Preventing incidents; treating incidents	Specific curriculums for communication, managing behaviors
		Environmental	Preventing incidents	Walled-in areas, wandering areas, way-finding enhancement, reduced-stimulation areas, enhanced environments
Community Dwelling	**Patient level**	Same as for nursing homes and assisted living facilities	Same as for nursing homes and assisted living facilities	Same as for nursing homes and assisted living facilities
	Caregiver level	Caregiver education	Preventing incidents; treating incidents	Specific curriculums to educate caregivers about dementia
		Caregiver education and training	Preventing incidents; treating incidents	Specific curriculums to educate caregivers about dementia and build skills to manage behaviors
		Caregiver education and training with psychosocial support	Preventing incidents; treating incidents	Specific curriculums to educate caregivers about dementia and build skills to manage behaviors with additional components such as support groups or counseling

Scope and Key Questions

This systematic review assesses the efficacy and comparative effectiveness of nonpharmacologic interventions on agitation/aggression in dementia. While the reduction of agitation/aggression is our primary outcome, other outcomes (intermediate and secondary) related to these interventions are important. Intermediate outcomes include immediate changes fostered by the intervention, such as reduction in antipsychotic medications or improvements in caregiver confidence in caregiving. If interventions are effective and agitation/aggression reduced, this reduced agitation/aggression should lead to improvements in secondary outcomes of burden of care or staff/caregiver distress.

Key Questions and Analytic Framework

Our review addresses the following Key Questions based on an analytic framework (Figure A).

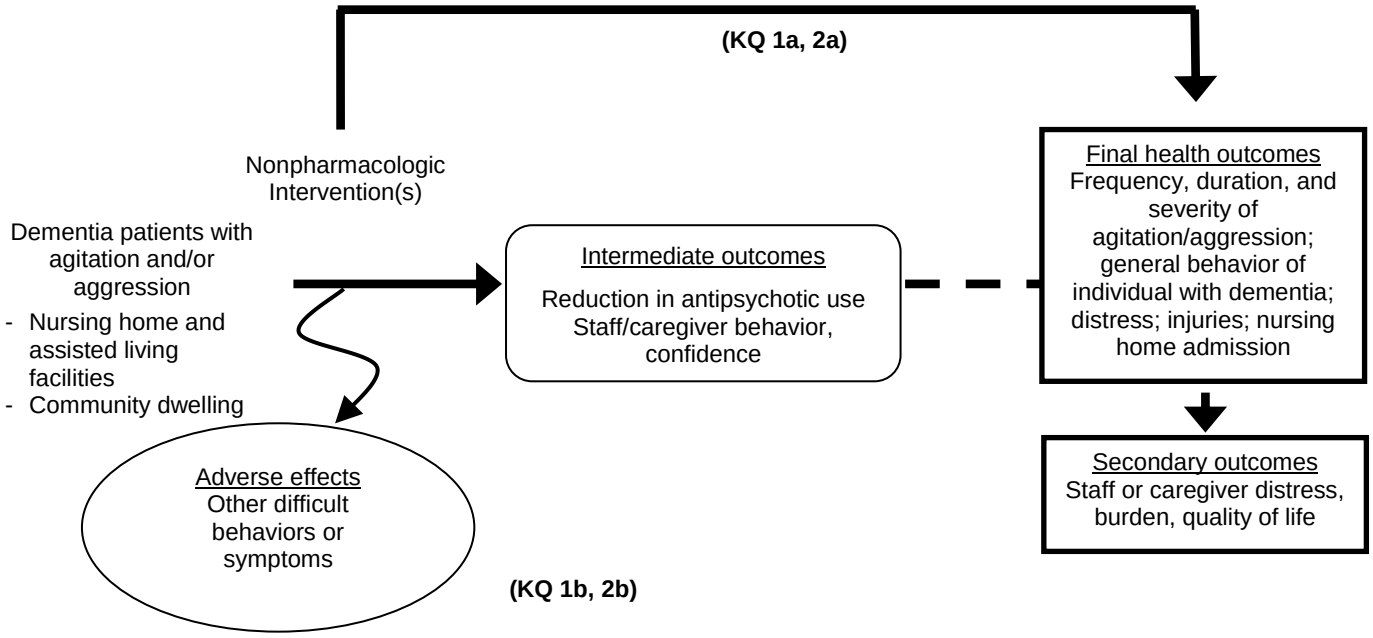
Key Question 1a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?

Key Question 1b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?

Key Question 2a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?

Key Question 2b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?

Figure A. Analytic framework for nonpharmacologic interventions to manage agitation/aggression in dementia



KQ = Key Question

PICOTS

The PICOTS (populations, interventions, comparisons, outcomes, timing, and setting) addressed in this review are described in Table B.

Table B. Populations, interventions, comparisons, outcomes, timing, and setting (PICOTS)

PICOTS Element	Description
Populations	KQ 1: Individuals with dementia residing in nursing home and assisted living settings; nursing home and assisted living facility staff KQ 2: Community-dwelling individuals with dementia; informal caregivers of individuals with dementia
Interventions	Nonpharmacologic interventions aimed at preventing or responding to agitation/aggression
Comparisons	Usual care (as specified by trial investigators) or no treatment Attention control or placebo Other nonpharmacologic interventions Pharmacologic interventions
Outcomes	**Final (Patient) Health Outcomes** KQ 1 & KQ 2: Frequency, duration, and severity of agitation/aggression; frequency, duration, and severity of aggressive behaviors; general behavior of people with dementia; distress; quality of life; injuries to residents, staff, others KQ 2: Injuries to people with dementia, caregivers; admission to nursing home **Secondary Outcomes** KQ 1: Staff distress, burden, quality of life KQ 2: Caregiver distress, burden, quality of life **Intermediate Outcomes** KQ 1: Staff behavior change, reduction in antipsychotic use KQ 2: Caregiver behavior change, reduction in antipsychotic use **Adverse Effects of Intervention(s)** Increase in other difficult behaviors (e.g., wandering) Increase in other symptoms (e.g., depression, anxiety)
Timing	Any duration of followup; relevant timing will vary with the nature of the intervention
Setting	KQ1: Nursing homes and assisted living facilities KQ2: Community dwelling (people with dementia living at home)

KQ = Key Question

Methods

Inclusion Criteria

Studies were included based on the PICOTS framework outlined previously. The study-specific inclusion criteria are described in Table C. We chose to include only randomized controlled trials (RCTs), given the necessity of an adequate comparison group to assess subjective outcomes. Selection bias in cohort studies would limit the believability of the results.

Table C. Study inclusion criteria

Category	Criteria for Inclusion
Study enrollment	Trials that enroll one of the following: • Residents of nursing homes and assisted living facilities diagnosed with dementia (any type) with agitation/aggression • Long-term care staff caring for individuals with dementia and associated agitation/aggression • Community-dwelling individuals diagnosed with dementia (any type) with agitation/aggression • Caregivers of community-dwelling individuals with dementia and associated agitation/aggression
Study objective	Nonpharmacologic intervention aiming to prevent and/or decrease agitation and aggression associated with dementia
Study design	Randomized controlled trials
Time of publication	Literature published from 1994 forward (reflects interventions used today)
Publication type	Published in peer-reviewed journals
Language of publication	English

Literature Search Strategy

We searched Ovid Medline®, Ovid Embase®, and the Cochrane Central Register of Controlled Trials (CENTRAL) to identify RCTs. Our search strategy included relevant medical subject headings and natural language terms for concepts of dementia and behavioral symptoms. These concepts were combined with filters to select RCTs. We screened bibliographic database search results for studies relevant to our PICOTS framework and study-specific criteria. Two investigators independently reviewed titles and abstracts to identify trials meeting the PICOTS framework and inclusion/exclusion criteria. Titles and abstracts that either investigator identified as potentially eligible underwent full-text screening. Two investigators determined eligibility on full-text review, consulting with a third investigator as necessary to resolve differences. We documented the exclusion status of articles undergoing full-text screening.

We searched ClinicalTrials.gov and Embase (publication type: conference abstracts, proceedings) for gray literature to assess reporting bias. Trial registration for nonpharmacologic interventions appears to be infrequent. Search results were primarily for pharmacologic interventions, making an assessment of publication bias for the intervention studied in this review limited.

Data Abstraction and Management

RCTs meeting inclusion criteria were distributed among investigators for risk-of-bias assessment. One investigator extracted data for trials of low or moderate risk of bias. Data fields extracted included author, year of publication, geographic location, intervention, and control characteristics (intervention components, timing, frequency, and duration). Trials with high risk

of bias were excluded from the analysis in an effort to report the best available evidence. Relevant data were extracted into evidence tables. While agitation/aggression is our primary outcome, we extracted data for other measures of behavior or behavioral symptoms because many trials used these more general instruments instead of instruments designed specifically to assess agitation/aggression. These data will be verified and uploaded into the Systematic Review Data Repository after the posting of the final report.[22]

Risk-of-Bias Assessment of Individual Trials

Two investigators independently assessed the risk of bias of eligible trials using instruments developed for the project based on Agency for Healthcare Research and Quality (AHRQ) guidance.[23] Risk of bias refers to the level of concerns about whether the design, conduct, and reporting of a trial threaten the ability to believe the results. We assessed several risk-of-bias domains, including selection bias (adequate randomization methods, allocation concealment); performance bias (participant and personnel blinding, intervention definition); detection bias (outcome assessor blinding, outcomes measurement, statistical analysis); attrition bias (amount, nature, and handling of incomplete data); reporting bias (selective reporting of outcomes or analyses); and other risks of bias not captured by the selected domains. Summary risk-of-bias assessments for each study were classified as low, moderate, or high based on the collective risk of bias inherent in each domain and confidence that the results were believable given the study's limitations. Investigators conferred to reconcile discrepancies in overall risk-of-bias assessments when one investigator assessed a trial as high risk of bias. In certain situations, a third party was consulted to reconcile the summary judgment.

Data Synthesis

We summarized the results in detailed tables for each unique population and intervention type. We searched for but did not find established minimum important differences for measurement instruments of key outcomes. We primarily synthesized results across conceptually similar comparisons and outcomes using qualitative synthesis. When comparisons could be reasonably pooled (i.e., comparable patient/caregiver populations, interventions, and outcomes), we conducted a meta-analysis using a Knapp-Hartung random effects model in R[24] and created forest plots in Stata.[25] We calculated risk ratios, absolute risk differences, or both with the corresponding 95% confidence intervals (CIs) for binary primary outcomes. We calculated weighted mean differences and/or standardized mean differences (SMDs) with the corresponding 95% CIs for continuous outcomes. We assessed the contextual and methodological heterogeneity and variation in effect size to determine appropriateness of pooling data.[26] We assessed the magnitude of statistical heterogeneity with the I^2 statistic.[26]

Strength of the Body of Evidence

In contrast to risk of bias, the overall strength of evidence was assessed across all studies that address a pairing of outcomes and interventions. Strength of evidence was evaluated based on five domains: (1) study limitations (the pattern of risk of bias across all relevant studies); (2) directness (single direct link between intervention and outcome); (3) consistency (similarity of effect direction and size); (4) precision (degree of certainty around an estimate); and (5) reporting bias.[27] Other factors considered in assessing strength of evidence included dose-response relationship, the presence of confounders, and strength of association.

Based on these factors, the overall strength of evidence for each outcome was assessed as follows.[27]

High: Very confident that estimate of effect lies close to true effect. Few or no deficiencies in body of evidence; findings believed to be stable.

Moderate: Moderately confident that estimate of effect lies close to true effect. Some deficiencies in body of evidence; findings likely stable, but some doubt remains.

Low: Limited confidence that estimate of effect lies close to true effect; major or numerous deficiencies in body of evidence. Additional evidence necessary before concluding that findings are stable or that estimate of effect is close to true effect.

Insufficient: No evidence, unable to estimate an effect, or no confidence in estimate of effect. No evidence available or the body of evidence precludes judgment.

Applicability

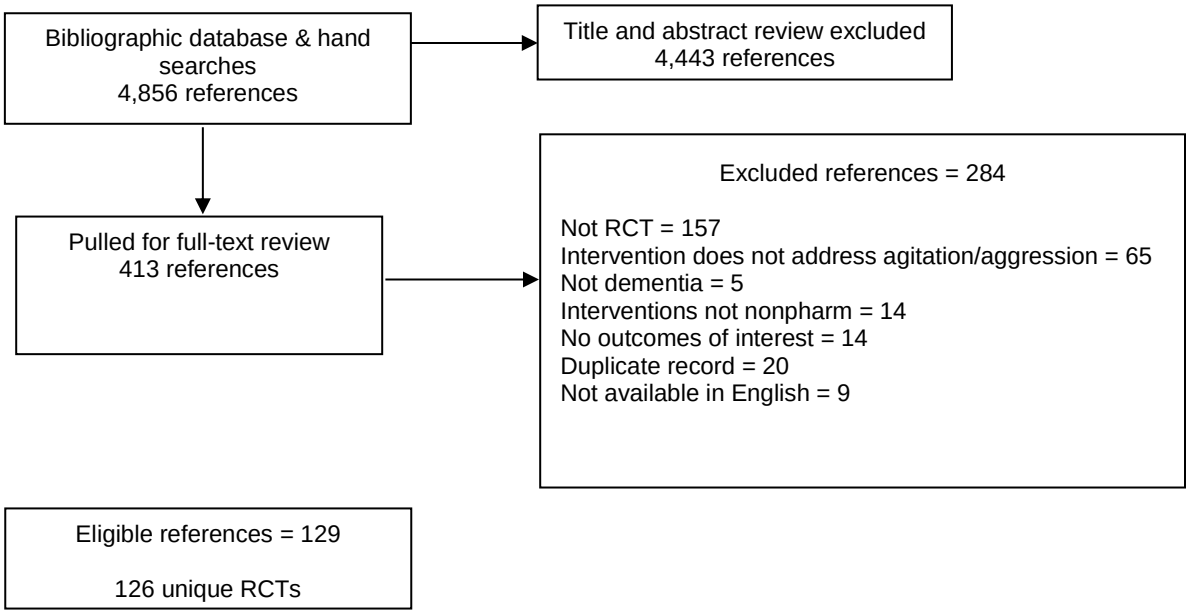
Applicability of trials was determined according to the PICOTS framework. Study characteristics affecting applicability included the population from which the trial participants were enrolled, diagnostic assessment processes, narrow eligibility criteria, and patient and intervention characteristics different from those described in population trials of behavioral symptoms in dementia.[28]

Results

Results of Literature Search

Our bibliographic database and hand searching identified 4,855 unique records, of which 410 required full-text review after title and abstract screening (Figure B). We completed full-text review to identify 129 eligible articles representing 126 unique RCTs.

Figure B. Literature flow diagram



RCT = randomized controlled trial

We divided the 129 records into four categories for analysis based on the setting in which the interventions occurred:

- Patient-level interventions delivered in nursing home and assisted living facility settings (n = 68; 67 unique RCTs)
- Care delivery–level interventions delivered in nursing home and assisted living facility settings (n = 28; 27 unique RCTs)
- Patient-level interventions delivered to community-dwelling individuals with dementia (n = 5; 5 unique RCTs)
- Caregiver-level interventions delivered to caregivers of community-dwelling individuals with dementia (n = 28; 27 unique RCTs)

Patient-Level Interventions in Nursing Homes and Assisted Living Facilities

Of the 68 eligible records that fit into this category, 27 were assessed high risk of bias and not used in analysis. Our analysis of the remaining 40 unique RCTs is organized by intervention type. Table D provides summary results and strength of evidence.

Key Points

- Low-strength evidence shows that music interventions, aromatherapy with lavender, and bright light therapy are similar to no intervention, placebo, and/or attention control in decreasing agitation/aggression among nursing home and assisted living facility residents with dementia.
- Low-strength evidence shows that interventions tailored to patient skills, interventions tailored to patient interests, and interventions tailored to both skills and interests have effects similar to each other on agitation/aggression among nursing home and assisted living facility residents with dementia.
- Evidence was insufficient for all other outcomes and comparisons.

Music Interventions

Four of the trials compared music interventions with usual care, no treatment, and attention controls.[29-32] Trials were conducted in Italy, Japan, Taiwan, and the United States. Inclusion criteria varied; most trials required that participants have behavioral symptoms as well as a diagnosis of dementia. In two trials the music interventions were delivered to groups of residents,[30,31] and in the other two the interventions were individualized.[29,32] Music intervention sessions varied in length (10 to 30 minutes), frequency (1 time, weekly, 3 times per week), and duration (1 time to 6 months). Type and number of staff involved in the intervention also varied. Trials assessing the efficacy of music interventions enrolled a total of 233 nursing home residents.[29-32] The Remington trial[32] differed notably from the three other music intervention trials in that it measured effects immediately and within 30 minutes of the intervention; the remaining trials evaluated the longer term effect of music therapy by measuring outcomes at a variety of timepoints during several weeks.

The Remington study showed a benefit for the music intervention for agitation/aggression.[32] The other three trials failed to show a statistically significant improvement over usual care, no treatment, or attention control. Pooled results from two of these trials showed similar effects with music and control. Evidence was insufficient to conclude whether music interventions reduce agitation/aggression immediately after participation. Low-strength evidence shows that music

interventions are similar to usual care, no treatment, or attention control in decreasing agitation/aggression in individuals with dementia.

Four trials enrolling a total of 218 nursing home residents with dementia and behavioral symptoms compared music interventions with other therapies.[29,32-34] None showed a difference between music interventions and any other interactive intervention (including other music interventions, interactive reading, recreational activities, and hand massage) on agitation/aggression. Low-strength evidence suggests that music interventions are similar to interactive comparisons at decreasing agitation/aggression in dementia. Two of these trials also reported a general behavior outcome with conflicting results, resulting in insufficient evidence to draw conclusions about efficacy. Music interventions and interactive comparisons had similar effects on general behavior outcomes. Evidence was insufficient to assess the comparative effectiveness of music interventions versus other interactive interventions on general behavior.

Aromatherapy

Aromatherapy interventions involve inhalation or topical application of scented essential oils, such as lavender. Efficacy trials often used placebo aromas or sprays, such as sunflower oil. We identified six trials with acceptable risk of bias that assessed the efficacy of aromatherapy in nursing home residents with agitation/aggression.[35-40] The trials enrolled a total of 215 nursing home residents and were conducted in nursing homes in Australia, Japan, Hong Kong, and the United Kingdom. Four trials studied lavender[36-39] and two studied Melissa oil.[35,40] Treatments ranged in frequency and method of delivery. Aromatherapy was delivered via drops on clothing, diffused in the air, or applied as lotion. Frequency of aromatherapy ranged from two to three times a day for durations of 3 to 6 weeks.

Only in one trial (n = 72) did aromatherapy improve agitation/aggression compared with placebo.[35] This trial used a different scent (Melissa) than most other trials (lavender). The Melissa scent as lotion was also applied to the patient by a staff member, whereas the other trials delivered aromatherapy without touch, except for one trial arm that combined hand massage with aromatherapy. Low-strength evidence shows that aromatherapy with lavender is similar to placebo in managing agitation/aggression in dementia. Evidence regarding the effectiveness of Melissa in managing agitation/aggression in dementia is insufficient to draw conclusions. Evidence for all other outcomes and harms was insufficient.

Bright Light Therapy

Light therapy interventions included some variant of bright light therapy. Four trials that studied the efficacy of light therapy had acceptable risk of bias.[41-44] Interventions involved exposure to bright light, defined variably as 2,500 lux, greater than 2,500 lux, and 10,000 lux. Comparison groups received exposure to standard light (100 to 250 lux), dim red light, or no treatment. Bright light therapy sessions were typically 1 to 2 hours per day at varying times of day. Treatment durations ranged from 10 days to 10 weeks.

Bright light efficacy trials enrolled a total of 225 nursing home residents. Two trials provided data on agitation/aggression, measured with the CMAI, sufficient for pooling. The pooled standardized mean difference in agitation/aggression for these two trials was 0.09 (95% CI, -0.32 to 0.50). Low-strength evidence shows that bright light therapy is similar to standard light in managing agitation/aggression in dementia. Evidence was insufficient for other outcomes and harms.

Therapeutic Touch (or Noncontact Therapeutic Touch)

Therapeutic touch refers to transfers of energy without necessarily using physical touch. Typically, a practitioner sits next to the patient and places his or her hands on or near the patient to transfer energy. Two trials with acceptable risk of bias examined therapeutic touch.[45,46] These trials enrolled a total of 108 nursing home residents. Treatments were delivered once a day in 30- to 40-minute sessions for 5 days in one trial and twice daily for 5- to 7-minute sessions for 3 days in the other. Interventions were delivered by trained professionals. Comparison groups received simulated therapeutic touch. Only one trial reported agitation/aggression, and it found no differences between intervention and inactive control. Both trials reported general behavior measures, with evidence of a positive effect in one and mixed results in the other. Evidence was insufficient to draw conclusions regarding the effectiveness of therapeutic touch for agitation/aggression or general behavior in dementia. Evidence for all other outcomes and adverse effects was insufficient.

Massage

We identified three trials testing the efficacy of massage for agitation/aggression in dementia. In two of three trial arms, Remington compared hand massage with no treatment.[32] Rodriguez-Mansilla and colleagues compared massage of back and lower limbs by physiotherapists for 20 minutes every day, with no treatment in two of three arms.[47] Moyle and colleagues compared foot massage with attention control.[48]

Remington reported an agitation/aggression outcome;[32] Rodriguez-Mansilla and colleagues and Moyle and colleagues reported general behavior.[47,48] Studies had methodological limitations and inconsistent findings, and estimates were imprecise. Therefore, evidence is insufficient to draw conclusions about the effect of massage on agitation/aggression or general behavior among nursing home residents with dementia.

Tailored Versus Nontailored Interventions

We identified four trials with acceptable risk of bias that compared tailored interventions with nontailored interventions.[49-52] The interventions varied in the resident characteristics used for tailoring. One tailored the intervention based on patient preferences and abilities,[49] one on the Montessori model,[50] another on unmet needs,[51] and the fourth on balancing arousal throughout the day according to the patients' response to different activities.[52]

Only the trial tailoring interventions to unmet needs found a decrease in the level of agitation/aggression with tailored activities compared with nontailored activities.[51] Another trial showed an increase in aggression with the intervention.[49] All trials had methodological limitations and imprecise estimates. These issues, combined with the inconsistency, provided insufficient evidence to draw conclusions regarding the effectiveness of tailored activities compared with nontailored activities.

Different Tailored Activity Interventions

Two trials enrolling 158 nursing home residents compared interventions tailored with different resident characteristics. The first tested the Needs-Driven, Dementia-Compromised Behavior model. This model posits that activities for an individual with behavioral symptoms must fit his or her physical and cognitive functional abilities and personality.[53,54] It was tested in two different trials with multiple arms: groups that received activities appropriate to their abilities but opposite to their personalities; a group that received activities appropriate to their

personalities but opposite to their abilities; and a group that received activities appropriate to both. Evidence was insufficient to draw conclusions about the comparative effectiveness of interventions tailored to different patient characteristics.

Unique Comparisons

The efficacy and/or comparative effectiveness of several other nonpharmacologic interventions was studied in single trials. These interventions included ear acupuncture, acupressure, structured activities, reminiscence, exercise, pleasant experiences, multisensory stimulation, activities of daily living, simulated presence, humor therapy, family visit enhancement, and electrostimulation and are described in our full report, available on the AHRQ Effective Health Care Web site.[55] All trials were relatively small and had methodological limitations. Most comparisons had similar effects between treatment and control. Evidence was insufficient to conclude whether any intervention offered a benefit in managing agitation/aggression in dementia or in affecting all other outcomes or adverse effects over comparisons.

Table D. Patient-level interventions in nursing home and assisted living facility residents with dementia

Intervention-Comparison	Total Number of Trials (Number of Participants)	Strength of Evidence - Summary of Results
Agitation/Aggression		
Music vs. no treatment/attention control (for sustained reduction in agitation/aggression)	4 (233)	Low – agitation/aggression not improved
Music vs. no treatment/attention control (for immediate reduction in agitation/aggression)	1 (34)	Insufficient – no conclusions drawn
Music vs. comparison intervention (for sustained reduction in agitation/aggression)	4 (218)	Low – agitation/aggression not improved
Aroma therapy with lavender vs. no treatment/attention control	3 (245)	Low – agitation/aggression not improved
Aroma therapy with Melissa vs. no treatment/ attention control	1 (72)	Insufficient – no conclusions drawn
Aroma therapy with Melissa vs. comparison intervention	1 (77)	Insufficient – no conclusions drawn
Light therapy vs. no treatment/attention control	4 (225)	Low – agitation/aggression not improved
Therapeutic touch vs. no treatment/attention control	1 (51)	Insufficient – no conclusions drawn
Massage vs. no treatment/attention control	1 (34)	Insufficient – no conclusions drawn
Massage vs. comparison intervention	1 (55)	Insufficient – no conclusions drawn
Tailored activities vs. nontailored activities	4 (334)	Insufficient – no conclusions drawn
Tailored activities vs. different tailored activities	2 (158)	Low – agitation/aggression not improved
General Behavior		
Music vs. no treatment/attention control (for sustained reduction in agitation/aggression)	2 (99)	Insufficient – no conclusions drawn
Music vs. comparison intervention (for sustained reduction in agitation/aggression)	1 (26)	Insufficient – no conclusions drawn
Aroma therapy with lavender vs. no treatment/attention control	2 (98)	Insufficient – no conclusions drawn
Aroma therapy with Melissa vs. comparison intervention	1 (77)	Insufficient – no conclusions drawn
Light therapy vs. no treatment/attention control	3 (133)	Low – general behavior not improved
Therapeutic touch vs. no treatment/attention control	2 (108)	Insufficient – no conclusions drawn
Massage vs. no treatment/attention control	1 (71)	Insufficient – no conclusions drawn
Tailored activities vs. nontailored activities	1 (87)	Insufficient – no conclusions drawn

Intervention-Comparison	Total Number of Trials (Number of Participants)	Strength of Evidence - Summary of Results
Exercise vs. no treatment/attention control	1 (134)	Insufficient – no conclusions drawn
Exercise vs. interactive control	1 (170)	Insufficient – no conclusions drawn

Care Delivery–Level Interventions in Nursing Homes and Assisted Living Facilities

Twenty-seven unique RCTs assessed care delivery–level interventions for agitation/ aggression in residents of nursing homes or assisted living facilities. The 19 trials with acceptable risk of bias examined a wide variety of care delivery–level interventions, including dementia care mapping, patient-centered care, emotion-oriented care, various staff trainings, and environmental changes to assist way-finding. We grouped trials by intervention type and comparison. Trials differed in the unit of randomization (i.e., at the level of nursing home, staff, or residents). In many of the studies the intervention was compared with "usual care," but the nature of this care was poorly specified. In some instances, the intervention was added to this usual care; in others it was offered as an alternative. It was frequently not even clear if psychoactive medications were being given concurrently. Table E provides a summary of the results by intervention type and comparison.

Key Point

- Low-strength evidence shows that dementia care mapping and person-centered care are similar to usual care in decreasing agitation/aggression among residents with dementia.

Dementia Care Mapping

Dementia care mapping is a systematic approach to identifying and strategically responding to presumed causes of agitation/aggression and distress. The process consists of observing care, the environment, and factors associated with resident well-being as identified by behavioral indicators, and then identifying positive and negative aspects of care delivery. Feedback is given to nursing home staff and used to inform action plans. Three trials with acceptable risk of bias evaluated the effectiveness of dementia care mapping in nursing homes using cluster randomized designs.[56-58] These trials enrolled a total of 643 nursing home residents.

All trials assessed agitation/aggression. Only Chenoweth and colleagues reported an effect in favor of dementia care mapping on the primary measure of agitation/aggression.[56] Rokstad and colleagues reported mixed results, with a significant improvement for dementia care mapping with one instrument but not another. Both statistically significant results were small and unlikely to be clinically meaningful.[56,57] Pooled results showed similar effects on agitation/aggression with dementia care mapping and usual care (SMD, -0.12; 95% CI, -0.66 to 0.42; $I^2 = 53$). Low-strength evidence showed that dementia care mapping is similar to usual care in managing agitation/aggression in dementia. Evidence for all other outcomes and adverse effects was insufficient.

Person-Centered Care

Person-centered care aims to foster personhood (e.g., positive relationships with others) as dementia progresses. It involves observations and feedback but requires less effort to identify underlying causes of behaviors than dementia care mapping. Three trials evaluated person-

centered care using cluster randomized designs.[56,57,59] Trials enrolled a total of 775 nursing home residents.

All trials assessed agitation/aggression. Only Chenoweth and colleagues reported a statistically significant effect of person-centered care for agitation/aggression. However, because the effect size was unlikely to be clinically meaningful, the statistical difference should not be interpreted as evidence of effectiveness. Rokstad and colleagues reported a statistically significant reduction in agitation/aggression for person-centered care assessed with one instrument but not another. Pooled results of these three trials showed similar effects with person-centered care and usual care on agitation/aggression in dementia (SMD, -0.15; 95% CI, -0.67 to 0.38; $I^2 = 56$). Low-strength evidence shows that person-centered care and usual care have similar effects on agitation/aggression in dementia. Evidence was insufficient for all other outcomes and for adverse effects. Evidence for general behavior and intermediate outcomes was insufficient.

Protocols To Reduce Use of Antipsychotics

Three trials tested staff training and clinical protocols to reduce the use of antipsychotics.[59-61] Trials enrolled a total of 1,263 nursing home residents.

Fossey and colleagues reported a null effect for the intervention.[59] In contrast, Rapp and colleagues and Zwijsen and colleagues showed that interventions reduced agitation/aggression.[60,61] Zwijsen and colleagues did not report data sufficient to pool with the other trials.[61] Pooled results from Fossey and colleagues and Rapp and colleagues showed similar effects with protocols or usual care on agitation/aggression as measured by the CMAI (mean difference, -4.5; 95% CI, -38.84 to 29.93; $I^2 = 32$).[59,60] Evidence was insufficient to draw conclusions regarding the effect of protocols to reduce the use of antipsychotics among residents with dementia. Antipsychotic dose was no different with protocols or usual care (SMD, -0.28; 95% CI, -3.50 to 2.94). Evidence was insufficient to draw conclusions regarding the efficacy of interventions on other outcomes or adverse effects.

Emotion-Oriented Care

Emotion-oriented care consists of understanding the resident's perception of the environment and the role of verbal and nonverbal communication in the caregiver-patient relationship. Two trials evaluated emotion-oriented care using cluster randomized designs.[62,63] Trials enrolled a total of 297 nursing home residents.

Neither trial showed an effect for emotion-oriented care on agitation/aggression.[62,63] Evidence was insufficient to assess the efficacy of emotion-oriented care for managing agitation/aggression in dementia.

Unique Comparisons

Twelve trials examined unique interventions, including staff education and training for dementia; staff training versus psychosocial management of behavioral symptoms; staff training regarding resident awareness; educating occupational therapists to identify patient preferences; a protocol to enhance resident comfort; staff training on nonverbal sensitivity; a nursing assistant communication skills program; an intervention to improve interactions between care staff, the environment, and residents; advanced illness care teams, and a way-finding intervention. These studies are described in more detail in our full report, available on the AHRQ Effective Health Care Web site.[55] These trials typically had small sample sizes and methodological problems; thus, evidence was insufficient for all comparisons and outcomes.

Table E. Care delivery–level interventions in nursing home and assisted living facility residents with dementia

Intervention-Comparison	Total Number of Trials (Number of Participants)	Strength of Evidence – Summary of Results
Agitation/Aggression		
Dementia care mapping vs. usual care	3 (643)	Low – agitation/aggression not improved
Person-centered care vs. usual care	3 (813)	Low – agitation/aggression not improved
Protocols to reduce neuroleptic use vs. usual care	3 (1,263)	Insufficient – no conclusions drawn
Emotion-oriented care vs. usual care	2 (297)	Insufficient – no conclusions drawn
General Behavior		
Dementia care mapping vs. usual care	3 (643)	Insufficient – no conclusions drawn
Person-centered care vs. usual care	2 (467)	Insufficient – no conclusions drawn
Protocols to reduce neuroleptic use vs. usual care	1 (659)	Insufficient – no conclusions drawn
Intermediate Outcomes		
Dementia care mapping vs. usual care	1 (180)	Insufficient – no conclusions drawn (staff behavior)
	2 (339)	Insufficient – no conclusions drawn (staff distress)
	1 (158)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
Person-centered care vs. usual care	2 (505)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
	1 (159)	Insufficient – no conclusions drawn (staff distress)
Protocols to reduce neuroleptic use vs. usual care	3 (1,263)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
	1 (659)	Insufficient – no conclusions drawn (staff behavior)
Emotion-oriented care vs. usual care	1 (151)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
Secondary Outcomes		
Dementia care mapping vs. usual care	1 (159)	Insufficient – no conclusions drawn (injuries)
	1 (180)	Insufficient – no conclusions drawn (staff distress/burden/quality of life)
Person-centered care vs. usual care	1 (159)	Insufficient – no conclusions drawn (injuries)
Emotion-oriented care vs. usual care	1 (146)	Insufficient – no conclusions drawn (staff distress/burden/quality of life)

Patient-Level Interventions for Community-Dwelling Individuals With Dementia

We identified five unique RCTs of patient-level interventions for agitation/aggression in community-dwelling individuals with dementia.[64-68] Three were assessed as high risk of bias and were not included in the analysis.[65,67,68] Table F provides a summary of the results by intervention type and comparison.

Key Point

- Evidence on patient-level interventions for agitation/aggression in community-dwelling individuals with dementia is extremely limited.

Multisensory Stimulation Versus Interactive Control

Baker and colleagues randomized 50 community-dwelling individuals with dementia to a multisensory stimulation intervention (n = 25) or an interactive control group (n = 25).[66] Hattori and colleagues randomized 43 community-dwelling individuals with dementia to an art therapy

intervention (n = 22) or interactive control group (n = 21).[64] Because the data were so limited, evidence was insufficient to draw conclusions for any outcomes and adverse effects regarding the effectiveness and harms of patient-level interventions on community-dwelling people with dementia.

Table F. Patient-level interventions for agitation/aggression in community-dwelling individuals with dementia

Outcome Intervention-Comparison	Total Number of Trials (Number of Participants)	Strength of Evidence – Summary of Results
Agitation/Aggression		
Multisensory stimulation vs. other interactive activity	1 (50)	Insufficient – no conclusions drawn
General Behavior		
Multisensory stimulation vs. other interactive activity	1 (50)	Insufficient – no conclusions drawn
Art therapy vs. other interactive activity	1 (43)	Insufficient – no conclusions drawn
Caregiver Burden		
Art therapy vs. other interactive activity	1 (43)	Insufficient – no conclusions drawn

Caregiver-Level Interventions for Community-Dwelling Individuals With Dementia

We identified 28 articles reporting on 27 unique RCTs of caregiver-level interventions for agitation/aggression in community-dwelling people with dementia, and we grouped trials using previously proposed taxonomy.[69] Seven of these trials were high risk of bias and excluded from analysis, resulting in analysis of 20 unique RCTs with an acceptable risk of bias.[47-70,76-90] We first identified the primary functional domain addressed by the intervention. Because we included trials that addressed agitation/aggression, this domain was either knowledge or skills for interventions eligible for our review. Because most interventions were multicomponent, we also identified the secondary functional domain addressed by the intervention (i.e., knowledge, skills, behavior, or affect). This was not always clear, and we classified domains as primary and secondary based on the amount of time spent in the domain. While further description using the proposed taxonomy could have addressed delivery characteristics, such as whether the intervention is delivered in person, in a group, or remotely (Internet, telephone); the type of professional conducting the intervention; and whether the intervention is modifiable to the particular situation, we did not attempt to stratify intervention types beyond the functional domains addressed because our data were limited to 20 RCTs. We discuss the interventions by the primary and secondary functional domains addressed.

We conducted a qualitative analysis by comparison because interventions and outcomes were heterogeneous and pooling was not appropriate. Several types of comparisons were used in these trials and they varied widely in intensity. The least intensive comparator was no treatment, wait-list, or usual care (assuming this is something both groups were likely receiving anyway, making it essentially no treatment). Other trials provided a very limited amount of information, such as pamphlets or lists of community resources. We labeled these information controls. Other trials had more intensive controls, with some degree of attention in the form of education without the proposed active ingredient or telephone contact. For trials in which the attention seemed more involved than minimal provision of information but involved less contact than the actual intervention, we labeled these attention controls. When the attention or comparison involved a

similar amount of contact time as the intervention but lacked the proposed active ingredient, we labeled them sham interventions. Table G provides the evidence summary for caregiver-level interventions.

Key Points

- Evidence for most comparisons was insufficient to conclude whether caregiver-level interventions were effective in managing agitation/aggression in community-dwelling individuals with dementia. This was mainly because of heterogeneous comparisons and small sample sizes. Trials often showed no difference between intervention and comparison, but differences were typically too imprecise to conclude a lack of efficacy.
- Evidence was sufficient to draw conclusions for only five comparison-outcome pairs:
  - Low-strength evidence shows that interventions targeting caregiver skills and knowledge were similar to no treatment in managing care recipient general behavior.
  - Low-strength evidence shows that interventions targeting caregiver skills and behavior were similar to no treatment in managing caregiver burden.
  - Low-strength evidence shows that interventions targeting caregiver skills and behavior were similar to attention control in managing care recipient agitation/ aggression.
  - Moderate-strength evidence shows that interventions targeting caregiver skills and behavior were better than attention control in managing caregiver distress.
  - Moderate-strength evidence shows that interventions targeting caregiver skills and behavior were better than attention control in improving caregiver confidence in caregiving.

Interventions Targeting Caregiver Knowledge and Skills

Guerra and colleagues and Ostwald and colleagues compared interventions that primarily addressed knowledge and secondarily addressed skills versus no treatment.[70,89] These small trials provided insufficient evidence to draw conclusions about the effectiveness of caregiver interventions addressing knowledge and skills managing agitation/aggression in community-dwelling individuals with dementia.

Interventions Targeting Caregiver Knowledge and Affect

Chien and Lee compared an intervention addressing caregiving knowledge and affect with attention control.[71] However, methodological limitations and lack of precision for all outcomes render this evidence insufficient to draw conclusions regarding these comparisons.

Interventions Targeting Caregiver Skills and Knowledge

Six trials studied interventions that targeted caregiver skills and knowledge. Five of these compared the intervention with no treatment (wait-list, information, usual care).[72-77] Low-strength evidence shows that these interventions are similar to no treatment in managing general behavior. One trial compared the intervention with an antipsychotic medication. These trials provided insufficient evidence to draw conclusions for any other outcome. Few trials measured similar outcomes, and when they did, methodological limitations and imprecision were apparent. Often trials did not show statistical differences in outcomes, but precision was not sufficient to conclude a lack of effectiveness.

Interventions Targeting Caregiver Skills and Behavior

We identified nine trials that primarily targeted caregiver skills and secondarily behavior.[78-86] Trials studying skills-behavior interventions used several types of comparisons. Two trials compared interventions with no treatment. Evidence on behavior was insufficient, but low-strength evidence shows that skills-behavior interventions were similar to no treatment in managing caregiver burden. Evidence was insufficient for all other outcomes.

Five trials compared interventions targeting caregiver skills-behaviors with attention controls. Low-strength evidence shows that these interventions are similar to attention control in managing care recipient agitation/aggression. However, moderate-strength evidence shows that these interventions are better than attention control in improving caregivers' caregiving abilities and managing caregiver distress. Evidence on other outcomes was insufficient. Two trials compared interventions targeting caregiver skills-behaviors with sham treatments. These data provide insufficient evidence to draw conclusions for any outcome.

Interventions Targeting Caregiver Skills and Affect

Two eligible trials studied interventions primarily targeting caregiver skills and secondarily affect.[87,88] Two trials compared interventions targeting caregiver skills and affect with no treatment. This evidence was insufficient to draw conclusions for any outcomes, given methodological limitations, imprecision, and inconsistent or unknown consistency with regard to specific outcomes.

Table G. Caregiver-level interventions: evidence summary

Intervention Versus Comparison	Outcome	Evidence Summary
Knowledge-skills vs. no treatment, wait-list, or information control Guerra, 2011[70] Ostwald, 1999[89]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior k = 2; n = 140	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL k = 1; n = 56	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 2; n = 140	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL k = 1; n = 56	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver behavior k = 1; n = 84	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
Knowledge-affect vs. attention control Chien, 2008[71]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior k = 1; n = 88	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 1; n = 88	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress/QoL k = 1; n = 88	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver behavior	Insufficient – no data

Intervention Versus Comparison	Outcome	Evidence Summary
Skills-knowledge vs. wait-list, usual care, or information control De Rotrou, 2011[73] Klodnicka, 2011[72] Gallagher-Thompson, 2010[74] Ulstein, 2007[75] Gitlin, 2003[76]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior k = 5; n = 657	Skills-knowledge interventions similar to no treatment on care recipient general behavior (low-strength evidence, moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 2; n = 337	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL	Insufficient – no data
	Caregiver behavior k = 1; n = 190	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
Skills-knowledge vs. haloperidol Teri, 2000[77]	Care recipient agitation/aggression k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Care recipient general behavior k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver behavior	Insufficient – no data
Skills-knowledge vs. placebo Teri, 2000[77]	Care recipient agitation/aggression k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient general behavior k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL k = 1; n = 75	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver behavior	Insufficient – no data
Skills-behavior vs. wait-list or information control Gitlin, 2008[82] Gonzalez, 2014[78] Marriott, 2000[86]	Care recipient agitation/aggression k = 1; n = 56	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient general behavior k = 2; n = 144	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 2; n = 158	Skills-behavior interventions similar to no treatment on caregiver burden (low-strength evidence, moderate risk of bias, indirect)
	Caregiver distress/QoL k = 1; n = 56	Insufficient – no conclusions drawn (moderate risk of bias, unknown consistency)
	Caregiver behavior k = 1; n = 56	Insufficient – no conclusions drawn (moderate risk of bias, unknown consistency)

Intervention Versus Comparison	Outcome	Evidence Summary
Skills-behavior vs. attention control Gitlin, 2010[81] Huang, 2013[79] Gitlin, 2010[80] Gerdner, 2002[83] Marriot, 2000[86]	Care recipient agitation/aggression k = 3; n = 575	Skills-behavior interventions similar to attention control on care recipient agitation/aggression (low-strength evidence, moderate risk of bias, imprecise)
	Care recipient general behavior k = 1; n = 102	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL k = 1; n = 209	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 2; n = 448	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress k = 3; n = 685	Skills-behavior interventions improve caregiver distress more than attention control (moderate-strength evidence, moderate risk of bias)
	Caregiver behavior k = 1; n = 239	Skills-behavior interventions improve caregiver confidence more than attention control (moderate-strength evidence, moderate risk of bias)
Skills-behavior vs. sham treatment Gormley, 2001[85] Bourgeois, 2002[84]	Patient agitation/aggression k = 2; n = 125	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient general behavior k = 2; n = 125	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient taking psychotropic medication k = 1; n = 62	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden k = 1; n = 62	Insufficient – no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress/QoL	Insufficient – no data
	Caregiver behavior	Insufficient – no data
Skills-affect Belle, 2006[87] Mittelman, 2004[88]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior k = 2; n = 924	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission k = 1; n = 518	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Caregiver burden k = 1; n = 518	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Caregiver distress/QoL k = 1; n = 406	Insufficient – no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Caregiver behavior	Insufficient – no data

k = total trials; n = total dyads; QoL = quality of life

Discussion

Reducing off-label use of antipsychotic drugs for individuals with dementia is a priority. Adverse effects of these medications have been demonstrated in a previous systematic review.[90] The Centers for Medicare & Medicaid Services has launched an active campaign to reduce the use of psychoactive medications in individuals with dementia.[9, 91] Strong evidence that nonpharmacologic treatments can effectively reduce agitation/aggression and improve patient quality of life would ideally support practice change. However, even without such evidence, efforts to reduce the use of antipsychotic medications in people with dementia should continue, given the risks and limited efficacy of these drugs.

Evidence about the risks associated with antipsychotic use in older adults is mounting. Overmedication with antipsychotics robs individuals of experiencing life because of sedation. For people with dementia, psychoactive medications can cause harm and even death. Even in clinical circumstances in which psychoactive drugs are appropriate, they must be used sparingly for specific documented behaviors at the lowest effective dose. Ideally, nonpharmacologic approaches, which have few, if any, adverse effects, would be substituted as antipsychotic medication is reduced, creating a win-win situation. Caregivers who are confident about the efficacy of nonpharmacologic options may be more willing to reduce and forgo medications.

Key Findings and Strength of Evidence

Unfortunately, despite the urgent need for evidence demonstrating that nonpharmacologic interventions can be effective in reducing the most challenging behaviors common in people with dementia, the current evidence is disappointing. While we identified a large number of trials that tested interventions for improving behavioral symptoms in dementia, fewer specifically measured agitation/aggression. Few groups of studies had sufficient similarity in interventions, comparisons, and outcomes to allow appropriate data pooling. When pooling was not appropriate, we attempted a qualitative synthesis of similar comparisons and outcomes. Despite these attempts, our analysis still consists of several unique comparisons, often from small studies with methodological limitations, resulting in evidence insufficient to draw conclusions about efficacy or comparative effectiveness. In some cases, low-strength evidence showed that interventions were not effective in reducing agitation/aggression.

For example, among patient-focused interventions in nursing home and assisted living settings, music, aromatherapy with lavender, and bright light therapy had similar effects on agitation/aggression as inactive control (placebo, attention control, usual care). Further, among interventions implemented at the care delivery level in nursing home and assisted living settings, dementia care mapping and patient-centered care had similar effects on agitation/aggression as usual care. Evidence was insufficient to draw conclusions on the effectiveness of most caregiver-level interventions in managing agitation/aggression in people with dementia. Caregiver interventions targeting caregiver skills and behavior were similar to attention control in managing agitation/aggression (low-strength evidence). However, these interventions show benefits in caregiver confidence in caregiving and caregiver distress.

Limitations of Current Literature

Our review reflects the limitations of the available literature. Research on the nonpharmacologic management of agitation/aggression in dementia is not well coordinated and has major problems. These problems can be divided between broad conceptual issues and methodological limitations of the trials.

Conceptual Issues

Conducting research and systematic reviews on this topic is challenging for several reasons. Our approach of combining the two behaviors (agitation and aggression) was a pragmatic way to handle the lack of distinction in the research we were synthesizing. However, as noted earlier, the manifestations and implications of agitation and aggression are very different and likely should be approached differently. In some cases, agitation can simply be tolerated and may not need interventions per se. By contrast, aggression needs to be dealt with because of risk to others.

Trials often combined agitation/aggression as an outcome, but they are not synonymous. Although aggression is a form of agitation, it differs from agitation and anxiety in a caregiving context. Agitation/aggression was rarely described other than in reports of instrument scores. Further, agitation/aggression was reported in a variety of ways. Some instruments combined them; others separated them. However, when the behaviors were separately assessed with certain elements of an instrument, we could not always determine whether that instrument was designed to yield valid and reliable subsets of questions. Scales to measure agitation include elements such as restlessness or aimless pacing, repetitive requests and "verbalizations," and so forth.

Agitation may be prompted by loss of memory, or it may reflect anxiety. When it reflects anxiety, then its underlying cause must be ascertained (e.g., pain or discomfort or some specific stimulus). Agitated verbal or physical behavior may be annoying and even frustrating to caregivers but is not necessarily a problem requiring treatment. By contrast, verbal and especially physical aggression often requires treatment. At minimum, aggression may arouse fear or disturb the calm of other patients in group settings; at worst, it may cause injury to caregivers or other patients. Aggression is also likely to harm its perpetrator in the form of increased restrictions or temporary or permanent removal to another setting, resulting in increased confusion. For these reasons, aggression is likely to be treated more assertively than various forms of agitation. Ironically, the epidemiology of agitation/aggression is not well understood, from the distribution of agitated behavior to how often various behaviors occur separately or together in the same patient and whether any discernible progression can be observed.

Changes in aggression and agitation will vary with the goal of the intervention. Interventions designed to respond to a behavior are different from those designed to prevent the occurrence or reduce the intensity of future behaviors. In the former case, a successful intervention ends an episode but its duration of effect is likely to be short. By contrast, a more preventive approach aims to have a longer lasting effect, marked by fewer or less severe future events. Although we attempted to classify interventions on the basis of the intent (i.e., responsive or preventive), we found that many studies failed to make the distinction clear. Future research should address this distinction more overtly in presenting the conceptual model for the effectiveness of the intervention being tested.

Understanding that we might not find studies that reported agitation/aggression per se, we included studies that assessed behavioral symptoms with more general instruments. These instruments, such as the Neuropsychiatric Inventory (NPI) or the Multi-dimensional Observation Scale for Elderly Patients (MOSES), contain items across a wide variety of behavioral symptoms. Changes in overall scores on these instruments are neither easily interpreted nor directly related to agitation/aggression. The intent of the research using these broad behavioral instruments to measure outcomes is not clear.

Several different instruments were used to assess agitation/aggression. Certain instruments are best suited to certain settings and people with dementia. Whether each study selected the most appropriate instrument was unclear, and we found little research aiming to identify changes in these instrument scores associated with clinically meaningful difference. When we did find evidence of an established minimal important difference, that minimal important difference was rarely used in subsequent research. Additionally, although the CMAI is a widely used instrument in nursing home and assisted living settings and has been determined to be valid and reliable, many studies reported only subscales of the CMAI. Whether these subscales are valid, reliable, or sensitive to change was unclear. We found few references documenting established minimal important differences for any of the instruments used to assess agitation/aggression, general behavior, or intermediate and

secondary outcomes. Without an understanding of what constitutes a clinically meaningful change, interpretation of statistically significant differences and assessment of precision were challenging.

Methodological Limitations

Individual studies assessed as having a low or moderate risk of bias still presented several methodological problems. Trials were mostly small; they varied widely in intervention types and intensity, outcomes addressed and instruments used to measure those outcomes, analysis techniques, and reporting; and few trials had low risk of bias. Many trials were underpowered. Underpowered studies that cannot be pooled add little value to the field and should not be conducted. Calculation of sample sizes necessary for appropriately powered RCTs should incorporate the high attrition rate commonly found in this population of older adults with health problems. Sample size calculations should also take into consideration that individuals with dementia may change living status (e.g., move from the community to a facility) and face a higher risk of death than other individuals of similar age. Withdrawals and dropouts created considerable loss of participants from already small sample sizes in some studies. Although attrition was predictably high in the studies we reviewed, it was not always adequately described, and intention-to-treat analysis was rarely conducted.

Details regarding the population, setting, and methodology were often inadequately described. Few studies provided details on dementia type or severity/stage of illness. Interventions were not always well defined, a common problem in nonpharmacologic research.[92] An established and widely used taxonomy to describe interventions is lacking. Clear delineation of interventions (what was done by whom and how often) is needed. Reference to a treatment manual or protocol was rarely provided. Trials did not always document how the staff was trained to implement the intervention or how fidelity to the treatment protocol was assessed. Control conditions were also often poorly described. Sample selection and method of randomization were not reported. Blinding of participants and providers was rarely conducted. Few studies described and accounted for simultaneous treatments, especially psychoactive medications. This was especially a problem in older studies. When use of psychoactive medications was reported, trials rarely eliminated their use; at most, medications were held constant during the study or medication changes were recorded as an outcome. Outcome assessors were often aware of the intervention status of participants or of the research question, potentially biasing the findings. Many studies used multiple outcomes and analyzed multiple comparisons, but most failed to make statistical adjustments for the multiple comparisons.

Trials comparing interventions with "usual care" rarely defined usual care. Individuals with dementia, especially in group residential settings, were typically exposed to a wide variety of activities and therapies designed to improve functioning and quality of life. In some instances, interventions were added to this usual care; in others, they were alternatives. It was frequently not clear if psychoactive medications were concurrently given.

Similarly, physical environments and rules of conduct in residential settings were seldom described, yet they could have powerful effects on reducing or ameliorating agitation/aggression. Most of the nursing home studies took place in multiple facilities, either with facilities or units randomized or with both intervention and control groups in each study site. In these cases, we know little about how settings varied. Studies did not account for potential differences in trial settings in statistical analyses, but even if they had, sample size would have made facility differences in effects hard to find.

Intervention purpose was not always clear. The expected effectiveness of interventions likely varies with the nature and purpose. Interventions designed to respond to a behavior are different

from those designed to prevent the occurrence or intensity of such behaviors. In the former case, a successful intervention ends an episode, but its duration of effect will be short. By contrast, a more preventive approach should have a longer lasting effect, marked by fewer or less severe events over a period of time. Although we attempted to classify interventions on the basis of the intent (i.e., responsive or preventive), many studies failed to make the distinction clear. Future research should address this distinction more overtly in presenting a conceptual model for the effectiveness of the intervention being tested.

These two goals, prevention or response, imply different strategies. Preventing or minimizing events can rely on environmental manipulation such as music or light, or activities that create a diversion or draw on strengths of remote memories; it may involve individually based approaches to identify triggers for a given person and subsequently avoid them. (This is essentially the basis for dementia care mapping and for the general stance that agitation/aggression is communication that caregivers need to try to decipher and respond to.) Conversely, managing events once they arise may involve distraction, calming behavior by staff, or moving individuals to a calming environment.

In light of this distinction, preventive strategies should be enacted over long time periods in order to reduce the frequency and/or intensity of events. Likewise, treatments designed to prevent agitation/aggression should produce long-lasting effects, and thus longer term followup is appropriate. Some of these treatments require staff to change their approach to dealing with individuals with dementia. Sustaining any behavior changes that follow may require additional caregiver or staff support beyond that involved in the initial intervention. Other techniques aim to stop or diminish episodes of agitation/aggression when they arise. Unlike preventive strategies, reactive strategies are in the moment and need to work immediately; however, their effect may not last beyond the episode. Therefore, the measures of success for preventive and reactive approaches should differ. However, we found substantial confusion in distinguishing strategies and measures.

We might expect to see interventions tested for effectiveness before being used as the basis for training, but such was not the case. Instead, the line between training studies and interventions proved hard to draw. Several interventions required that staff be trained to behave differently, but the training was sparsely described. Some studies used a combination of outside experts and trained staff to implement interventions.

Changing the behavior of caregiving staff is challenging, especially in nursing homes, where training and oversight are modest at best. Nursing home staffs are notoriously overworked and may not be eager to take on new tasks, especially ones that require them to radically alter their typical behavior and routines. Although all nursing homes are required to have in-service educators and to conduct training at intervals, staff training tends to be perfunctory and brief, with sparse oversight and encouragement. Maintaining a new behavior requires regular feedback to engender a sense that it is working. Staff training is even more difficult when the staffing is unstable or staff feel great pressure to complete other assigned tasks. The more that interventions require clinical judgment, the more difficult they are to implement, especially within nursing home hierarchies.

In regard to assisted living and other group residential settings and in-home care services, training requirements are even fewer, dependent largely on State rules. Furthermore, the appropriate staff to conduct interventions in such settings is harder to define. Some studies used external staff to establish the effectiveness of the behavior; and the effects of these interventions tend to have short half-lives because implementation disappears when the study ends. Relying on internal staff to administer the intervention increases chances of longer term success, but doing

so is far more complicated. As mentioned, staff must then be trained and supervised. Ultimately, the more an intervention depends on staff, the harder it is to separate it in research from a training study.

In summary, the evidence for nonpharmacologic treatment of agitation/aggression in individuals with dementia is weak and obfuscated by inconsistent and confusing terminology. Our findings are consistent with many prior reviews but are more pessimistic than others, which showed benefit for certain interventions. A recent systematic review of music therapy for a broad range of behavioral and psychological symptoms found a small effect for anxiety and behavior (broadly defined).[93] That review included a broader range of symptoms and study designs than ours and did not specifically address agitation/aggression. A recent review that specifically addressed agitation concluded that music therapy following protocol failed to produce a sustained benefit.[94] The same review found no evidence of efficacy for aromatherapy or light therapy.[94] Livingston and colleagues concluded that the available evidence showed that dementia care mapping and person-centered care showed efficacy.[94] They included a broader range of study designs than we did, failed to conduct a meta-analysis, and may have concluded efficacy when changes from baseline were present in the absence of differences from a control group. Brodaty and Arasaratnam concluded that caregiver interventions improved behavioral outcomes in community-dwelling individuals with dementia.[95] However, this study included a broad range of psychological and behavioral symptoms, and the strongest effects were from studies focusing on depression.

Applicability

Our conclusions are likely relevant to the broad population of individuals with dementia, but they provide little insight into what interventions might reduce agitation/aggression in this population. The populations described appear to be similar to the overall population with dementia within each setting, at least by age and sex. The ethnic composition is less representative. Few details were provided regarding other patient characteristics, such as dementia type, stage, and severity. When dementia type was described, Alzheimer's disease was typically the most prevalent, consistent with national estimates. Assessing the applicability of results of trials conducted in nursing homes and assisted living facilities is difficult, however. These facilities vary greatly in size, environments, and staffing models. Few trials described these characteristics, so applicability is unclear.

Many trials were conducted in countries outside of the United States. Nursing home populations and the facilities themselves may differ significantly from one country to another. Therefore applicability to the U.S. population may vary depending on how similar nursing homes and their populations are to those of the United States.

Future Research Needs

Managing agitation/aggression in dementia with nonpharmacologic interventions is a critically important topic. Many trials have been conducted, but the evidence is limited and offers little insight about promising practices. Many research gaps remain (Table H). Studying the nonpharmacologic management of agitation/aggression in dementia needs to become more systematic.

A more coordinated effort to the conduct of future research on this topic might more efficiently address the conceptual and methodological issues impairing the current state of the science. Conceptual issues limit what researchers are able to do with available resources.

Future trials should use consistent and validated instruments specifically designed to accurately measure agitation/aggression. A recent systematic review of instruments available to measure neuropsychiatric symptoms in dementia identified and classified seven instruments as specifically measuring agitation and four specifically measuring aggression.[3] Specific components of these instruments suggest a cloudy distinction between the behaviors in the identified instruments. For instance, the Agitated Behavior in Dementia Scale (ABID), CMAI, and Disruptive Behavior Rating Scales (DBRS) are classified as instruments measuring agitation, but individual components ask about physical and verbal aggression, thereby treating aggression as a component of agitation. Psychometric properties of these instruments suggested that reliability (1 or more types) and validity (1 or more types) had been established for most instruments but these properties were better for some instruments than others. Researchers should select instruments most appropriate to the population, setting, intervention, and purpose of the study. Selected instruments should be sensitive to changes associated with treatment. Unfortunately, a few of these instruments did not provide indication of sensitivity to detect change, such as Brief Agitation Rating Scale (BARS) and CMAI.[3] In addition, more work needs to be done on establishing minimal important differences for the major outcomes.

Future research should separate the intervention effects on agitation and aggression separately. Decisionmakers are likely to consider agitated behaviors more tolerable than aggressive behaviors, especially physically aggressive behaviors that may result in injuries. Therefore, assessing effects of treatment with regard to agitation and aggression separately would provide a more actionable evidence base. However, descriptions of these behaviors in the literature and instruments measuring them currently commingle them, making separation impossible at the review stage. A few studies attempt to analyze results using individual components of selected instruments. Because the instruments are not typically designed or tested for reliability and validity at this level, it is unclear that their use in this way is appropriate. A clearer map of specific types of agitation/aggression and links to specific interventions may prove more valuable than addressing the general dementia population with broadly defined behavioral symptoms. Trials should be designed to adequately address treatment goals within appropriate timelines. A roadmap that uncouples agitation and aggression and links each to treatment goals may be helpful. More attention to the role of environment would help elucidate the effectiveness of interventions. If the pathway is via changing staff (or informal caregiver) behavior, evidence of that intermediate effect would be helpful.

A clearer taxonomy to describe components and characteristics of interventions is needed. Few trials provided sufficient information; few interventions described components with similar terminology; interventions varied widely in intensity and other delivery characteristics when other information was provided.

Future comparative effectiveness research should rely on RCTs. Given the variation in intervention fidelity and complexity in RCT reports, and the great difficulties of addressing selection bias even in RCTs, we believe that observational studies would be difficult to interpret. Simultaneous treatments, such as psychoactive treatments, must be accounted for. Nonetheless, this line of research will continue to be difficult. The incidence of problems is unpredictable and nursing home environments are unstable.

Future research should take a more systematic approach. Variations in treatment should be tested sequentially and under more defined conditions. This type of research could move the field forward. Interventions need to be more precisely described, with attention to what is done (how much, how often), under what circumstances, and by whom. Fidelity needs to be assessed and reported. Likewise the nature of “usual care” needs to be explicated and any concurrent

treatment delineated. An order of procedure that would be clinically acceptable might start with adding a candidate treatment. That approach, if it produced a substantial effect, could then be tested instead of existing drug therapy.

Further, physical environment was rarely addressed (e.g., private or shared rooms; freedom or restrictions of movement; policies for dining, bathing, and care routines that may generate resistance). Few studies examined such environmental and practice shifts (other than the training to generate more effective staff), and the environments for these studies were rarely described.

Future RCTs should be adequately powered, and power calculations should incorporate the expected high attrition rate when calculating necessary sample sizes. Given that many studies showed little or no effect for most interventions, accumulating more studies with small sample sizes is unlikely to change the results. Future trials should adequately describe the intervention and control condition, blind outcomes assessors, and use instruments appropriate to the intervention. They should also appropriately correct for multiple comparisons and account for simultaneous treatments, such as psychoactive medications.

Table H. Future research needs

Issue or Key Question	Results of Literature Review	Types of Studies Needed To Answer Question	Future Research Needs
General methodological issues	Agitation and aggression not consistently described, defined, or treated as separate behaviors	Consensus conference	Consensus among experts to arrive at standard definitions of specific behavioral symptoms
	Improvement and agreement needed on instruments to measure agitation/aggression	Consensus conference	Consensus among experts to identify or develop instruments with adequate psychometric properties to measure agitation/aggression and guidance on which measures to use in selected settings and populations
	Few groups of studies with sufficient similarity in interventions, comparisons, and outcomes to allow appropriate data pooling	Consensus conference	Standardization of promising practices; study of those practices in RCTs; development of guidance to assist researchers in selecting the appropriate instruments to measure agitation/aggression
	No established minimum important differences for commonly used instruments measuring agitation/ aggression outcomes	Original research	Studies to determine thresholds for commonly used instruments that indicate clinically meaningful changes, which could be used in comparative effectiveness research
	Wide heterogeneity in interventions, comparisons, outcomes, and analysis techniques	Consensus conference	Consensus among experts about which interventions might be most appropriate and effective in which populations and settings; prioritization of interventions with specific characteristics that could lead to a more homogeneous set of trials that could provide sufficient evidence to draw conclusions
	Agitation/aggression not specifically studied; behaviors broadly addressed in many trials	RCTs	Trials that address agitation or aggression specifically, enrolling people with dementia with similar symptoms to better study the potential of interventions to manage these specific behaviors
	Objectives of interventions not well specified	RCTs	Interventions designed to prevent or respond to agitation/aggression; trials designed according to objective
	Small underpowered studies	RCTs	Funding/conducting RCTs with power adequate to answer the research question; avoidance of underpowered studies, which do not strengthen available evidence; power calculations incorporating the expected high rate of attrition common in this population

Issue or Key Question	Results of Literature Review	Types of Studies Needed To Answer Question	Future Research Needs
KQ 1a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?	Study of populations in nursing home settings with a wide variety of agitation/aggression behaviors that might respond differently to specific treatments	RCTs	Populations for intervention trials made up of persons with dementia with similar symptoms; larger trials to provide more valuable information and strengthen the evidence base
	Few trials studying particular environmental interventions	RCTs	Trials that assess environmental changes
KQ 1b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?	Harms rarely reported; most interventions unlikely to have serious harms	RCTs	Recording and reporting harms or lack thereof for each treatment group
KQ 2a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?	Tailored interventions that did not demonstrate an effect on behaviors; few trials specifically targeting agitation/aggression	RCTs	Population for intervention trials made up of people with dementia with similar symptoms to determine if certain behavioral symptoms do not respond to nonpharmacologic treatment
	Lack of clarity about whether benefits to caregivers of tailored education and training (improved confidence in managing behaviors) are maintained after the intervention ends	RCTs	Long-term followup to determine if caregiver benefits are maintained after intervention ends; testing to determine if booster sessions or long-term psychosocial interventions help maintain intervention benefits
KQ 2b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?	Harms rarely reported; most interventions unlikely to have serious harms	RCTs	Recording and reporting harms or lack thereof for each treatment group

KQ = Key Question; RCT = randomized controlled trial

Conclusions

Research on nonpharmacologic treatment of agitation/aggression seems to have developed in a piecemeal fashion without overarching coordination. Our review found insufficient evidence to draw conclusions regarding most of the interventions that have been studied to address

agitation/aggression in individuals with dementia. The strongest evidence for interventions in treating agitation/aggression showed null effects. Despite the urgent need for alternatives to medication for the treatment of problem behaviors, the current state of the literature provides little information useful to changing practice. Nonetheless, efforts to find alternatives to psychoactive medication treatment should continue.

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Introduction

Background and Objectives

The most recent edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) categorizes individuals with acquired cognitive deficits as having major or mild neurocognitive disorders (NCD).[1] Subtypes of NCDs include major and mild NCD due to Alzheimer's disease, due to frontotemporal disorder, due to Lewy bodies, and vascular NCD. Historically, patients with these NCDs have been referred to as having dementia. Because dementia is the far more familiar term, we have used it rather than NCD throughout this report.

Up to 90 percent of those with dementia exhibit behavioral or psychological symptoms at some point, more often in advanced stages of the disease.[2] Symptoms tend to occur in clusters and can include depression, psychosis, aggression, agitation, anxiety, and wandering.[2-4] Behavioral and psychological symptoms cause considerable patient distress and are associated with accelerated functional and cognitive decline. Dementia-related symptoms challenge both formal and informal caregivers and are associated with increases in caregiver anger, resentment toward the patient, stress, and decreased psychological health.[5-7] Not surprisingly, dementia-related symptoms are the leading predictors of institutionalization.[8] However, staff in nursing homes and assisted living facilities are also challenged by behavioral and psychological symptoms, which affect an estimated 80 percent of nursing home and assisted living facility residents with dementia.

Among dementia-related symptoms, agitation and aggression are especially distressing to patients, family caregivers, and nursing home and assisted living facility staff. Agitation and aggression are costly to manage and are associated with institutionalization among community-dwelling patients, social isolation, and other negative outcomes.[8] The terms agitation and aggression are used to describe many types of behaviors and many adjectives are used to describe agitated and aggressive behaviors (e.g., disruptive, problem, difficult, and challenging). Agitation is defined as "excessive motor activity with a feeling of inner tension and characterized by a cluster of related symptoms including anxiety and irritability, motor restlessness and abnormal vocalization, often associated with behaviors such as pacing, wandering, aggression, shouting, and nighttime disturbance."[9] Aggression is commonly described to be a subtype of agitation[10] consisting of overt harmful actions (physical or verbal) that are clearly not accidental.[9]

Ultimately, terms describing agitation and aggression in the literature are confusing and inconsistent.[11] Agitation and aggression are typically grouped together as part of a spectrum, although they have different manifestations and implications. Agitation affects primarily the person with dementia (although the behaviors may be disruptive for others in his/her environment). By contrast, aggression directly involves at least one other person (the target of the aggression) and can represent a real risk to that person. As a result, one might argue that although it makes sense to identify and treat the underlying cause of agitation whenever possible, some manifestations of agitation may not need intervention per se; they can simply be tolerated. By contrast, aggression needs to be dealt with because of the possible risk to others. We refer to these symptoms or behaviors as agitation/aggression.

Historically, drugs have been used to manage behavioral symptoms in patients with dementia, particularly for agitation/aggression. Pharmacotherapy for behavioral symptoms is based on a biological/genetic framework for the etiology of the condition. However, drug

therapies generally, and antipsychotic medications specifically, have limited efficacy and increased risk for adverse effects, including mortality.[12-14] Drug treatments for dementia are also associated with reduced quality of life.[15] Evidence of effective nonpharmacological approaches would strengthen the efforts to urge less use of inappropriate psychoactive drugs, but the absence of that evidence should not diminish such efforts in light of the harmful effects of these medications. By contrast, the nonpharmacological approaches have virtually no reports of adverse effects.

Clinical guidelines recommend nonpharmacologic interventions as the first choice for agitation/aggression in patients with dementia.[16-19] However, nonpharmacologic interventions are under-used in clinical practice. In part this is because clinicians lack knowledge regarding their efficacy and possible risks, but caregivers are also reluctant to forsake drugs until they are confident in managing agitation/aggression without them. To reduce inappropriate use of antipsychotics and other psychotropic drugs for behavioral symptoms in patients with dementia will require evidence for the effectiveness and harms of nonpharmacologic treatments. Clinicians and caregivers will also need education on the use of these approaches.

Nonpharmacologic interventions aim to (1) prevent agitation/aggression behaviors, (2) respond to episodes of agitation/aggression to reduce their severity and duration, and/or (3) reduce caregiver distress. Individuals with dementia may reside in nursing homes or assisted living facilities or in their own homes or with family members (community-dwelling).

Interventions delivered in nursing homes and assisted living facilities can be at the patient level, where a therapy is delivered directly to the patient, or care delivery level, involving the approach, staff, and/or environment used in care delivery. Examples of patient-level interventions used in residential settings include sensory-based approaches such as aroma, bright light, or touch, as well as activity-based approaches involving music, art, or horticulture.[20] Care-delivery level interventions include a variety of care-delivery models, staff/caregiver education and training, and environmental approaches.[21] Examples include trainings to enhance staff knowledge and skills in managing behavioral symptoms among residents, care-delivery models such as patient-centered care or dementia care mapping, and enhancements to the environment aimed at reducing exposure to agitation/aggression triggers.

Interventions delivered to community-dwelling individuals with dementia can be at the patient or caregiver level. The caregiver is typically an informal family caregiver. Patient-level interventions would be similar to those in residential settings. However, patient-level interventions may also include activities, such as exercise classes, that are accessible to individuals in less advanced stages of dementia. Caregiver-level interventions to address agitation/aggression address the family caregiver approach to caregiving. These interventions provide education and skills training to enhance understanding of the disease process, specific symptoms, and how to best address agitation/aggression. Table 1 provides a description and examples of the types of interventions used in various settings.

The expected effectiveness of interventions will vary with their nature and purpose. Interventions designed to respond to a behavior are different from those designed to prevent the occurrence or intensity of such behaviors. In the former case, a successful intervention ends an episode, but the duration of effect is likely to be short. By contrast, a more preventive approach aims to have a longer lasting effect, marked by fewer events over a period of time. Although we attempted to classify interventions on the basis of the intent (i.e., responsive or preventive), we found that many studies failed to make the distinction clear.

Measuring behavioral outcomes is a complex process for which a wide variety of instruments are available. These instruments (1) are based on different theoretical frameworks, (2) are designed to evaluate behaviors in different settings (e.g., in-home, hospital, or long-term care), (3) are administered by different individuals (e.g., caregiver, nurse, or patient), and (4) use different mechanisms to obtain responses (e.g., interviews with patients or direct observation). More than 45 instruments are used to evaluate behavioral symptoms in dementia, with no gold standard.[22] The appropriate instrument depends on disease severity and context of care (e.g., setting, severity of disease, and whether the purpose is to identify any behavior or to identify specific behaviors). Instruments for evaluating behavioral symptoms fall into two broad categories: *general* and *specific*.[22] Table 2 describes commonly used instruments.

Several instruments measure agitation/aggression specifically. These include the Agitated Behavior in Dementia Scale (ABID),[23] the Cohen-Mansfield Agitation Inventory (CMAI),[24] and the Pittsburgh Agitation Scale (PAS).[25] Also, some general behavioral symptom instruments include subscales specific to agitation/aggression.

General measures evaluate a host of behaviors across multiple domains (e.g., agitation, depression, and wandering). Most studies that report results from general behavioral symptom measures report overall summary scores. Examples of general behavioral measurement instruments include the Neuropsychiatric Inventory (NPI and its variants NPI-C, NPI-Q). The NPI is one of the most commonly used instruments to measure behavior. The Revised Memory and Behavior Problem Checklist and the CERAD Behavior Rating Scale for Dementia are other examples of instruments measuring general behavioral symptoms in individuals with dementia.

Our understanding and measurement of agitation/aggression in individuals with dementia has changed over time. Agitation/aggression are now more often considered distinct behaviors. For example, an early version of the NPI combined agitation/aggression into a single domain. In contrast, the Neuropsychiatric Inventory Clinician (NPI-C), a second-generation survey designed to incorporate input from clinicians, separates the behaviors into two distinct domains.[4] The context in which agitation/aggression occur is considered paramount to determining appropriate interventions. Clinical algorithms have been developed to help identify the presence and causes of symptoms in order to effectively manage behaviors.[26-28] However, instruments often document the occurrence of behavioral symptoms without identifying their source or cause. Ideally, algorithms are used alongside specific instruments to provide appropriate context for the occurrence of behaviors.

Evidence synthesis on the efficacy and comparative effectiveness of nonpharmacologic interventions specifically for agitation/aggression in patients with dementia could reduce the frequency and severity of those behaviors and improve functioning, reduce distress, and reduce or delay residential long-term care. These interventions may also reduce the use of antipsychotic drugs. Results from this review will inform practice regarding the appropriate and effective management of agitation/aggression in individuals with dementia.

To address these gaps in the literature, we conducted a systematic review based on an analytical framework (Figure 1) to address the Key Questions (KQs):

Table 1. Types of interventions addressing agitation/aggression in dementia

Setting	Intervention Level	Intervention Type	Goals	Examples
Nursing Homes and Assisted Living Facilities	**Patient level**	Sensory	Preventing incidents	Music therapy (listening), aromatherapy, bright light therapy, multisensory stimulation.
		Structured Activities	Preventing incidents	Dancing, exercise, social interaction, music therapy (playing, singing), art therapy, outdoor walks
		Complementary and Alternative Medicine	Preventing incidents; treating incidents	Aromatherapy, reflexology, acupuncture, acupressure, massage, Reiki
		Psychological	Preventing incidents	Validation therapy, reality orientation, reminiscence therapy, support groups
	Care Delivery Level	Care Delivery Models	Preventing incidents; treating incidents	Dementia care mapping; patient centered care
		Staff Training and Education	Preventing incidents; treating incidents	Specific curriculums for communication, managing behaviors
		Environmental	Preventing incidents	Walled in areas, wandering areas, wayfinding enhancement, reduced stimulation areas, enhanced environments
Community Dwelling	**Patient level**	Same as patient-level above		Same as patient-level above
	Caregiver level	Caregiver education	Preventing incidents; treating incidents	Specific curricula to educate caregivers about dementia.
		Caregiver education and training	Preventing incidents; treating incidents	Specific curricula to education caregivers about dementia and build skills to manage behaviors.
		Caregiver education and training with psychosocial support	Preventing incidents; treating incidents	Specific curricula to educate caregivers about dementia and build skills to manage behaviors with additional components such as support groups or counseling.

Table 2. Instruments measuring intermediate, primary, and secondary outcomes

Outcome Category	Outcome	Instrument	Measurement/Instrument Properties	MIDs Reported in Literature
Intermediate Outcomes	Caregiver Behavior Change	Caregiving Mastery Index, a subscale of the Caregiving Appraisal Measure	12 items assessing caregiving mastery Range 12-60; higher scores indicate greater mastery[29]	None identified
Primary Outcomes	Patient Agitation/ Aggression	Agitated Behavior in Dementia Scale (ABID)	16 items assessing the frequency of agitation/aggression (verbally and physically threatening or aggressive; harmful to self; inappropriate screaming or crying out; destroying property; refusing to accept appropriate care; leaving/trying to leave; socially inappropriate behaviors; inappropriate sexual behavior; restlessness; worrying/fearful; easily agitated; nighttime waking; incorrect, distressing beliefs; sensing distressing people that are not truly present) over the past 2 weeks (each week rated separately and added together for each item) and caregiver distress and reaction once in the last 2 weeks; to be used in noninstitutionalized patients Range 0 to 48 (care recipient); higher scores indicate greater agitation Range 0 to 64 (caregiver); higher scores indicate greater reaction[30]	None identified
		Brief Agitation Rating Scale (BARS)	10 items assessing the frequency of agitated behavior (based on CMAI) over the past two weeks. Range 10 to 70; higher scores indicate greater agitation.[22]	None identified
		Cohen-Mansfield Agitation Inventory (CMAI)	Number of items varies by form (29 items for standard form, 14 items for the short form, 37 items for the community form); assesses the frequency of agitation/aggression over the past 2 weeks. Range 0-203; higher scores indicate greater agitation[31-33]	≥45 indicates clinically significant agitation requiring treatment[34] 30% change in overall score[35]
		Disruptive Behavior Rating Scales (DBRS)	21 items assessing the frequency and severity of disruptive behavior across four dimensions (physical aggression, verbal aggression, agitation, wandering) assessed daily for 1 week; range 0 to 105; higher scores indicate greater agitation.[22]	None identified
		Pittsburgh Agitation Scale (PAS)	4 items assessing aberrant vocalization, motor agitation, aggressiveness, and resistance to care over period of 1 to 8 hours; Range 0 to 4 per item (scores are not totaled); higher scores indicate greater agitation[22,25]	None identified
	General Behavior	Behaviour Rating Scale (BMD)	Designed for carers to assess behavior and mood at home.[36]	None identified
		Neuropsychiatric inventory (NPI, and its variants NPI-C, NPI-Q)	12-91 items, varying by domain screening responses; assesses aberrant motor behavior, agitation, anxiety, apathy, appetite and eating behaviors, caregiver distress, delusions,	8 points[38]

Outcome Category	Outcome	Instrument	Measurement/Instrument Properties	MIDs Reported in Literature
			disinhibition, dysphoria, euphoria, hallucinations, irritability, nighttime behavior issues. Range depends on screening responses for each domain and responses for frequency and severity; higher scores indicate greater behavioral problems[37]	
		Revised Memory and Behavior Problem Checklist (RMBPC)	24 items; assesses caregiver reactions, depression problems, disruptive behaviors, and memory-related problems Range 0-96 for patient behaviors and 0-96 for caregiver reactions; higher scores indicate greater frequency of behavior problems and greater caregiver distress[39]	None identified
		Memory and Behavior Problem Checklist (MBPC)	Previous version of RMBPC[40]	None identified
		CERAD Behavior Rating Scale for Dementia (BRSD)	51 items in original version, 46 items in revised version, 17 items in short form; assesses affect, aggression, agitation/irritability, apathy, defective self-regulation, depressive features, vegetative features, psychotic features Range unclear; higher scores indicate greater behavioral problems[41]	None identified
		MOUSEPAD	59 items assessing psych symptoms and behavioral disturbances (delusions, hallucinations, misidentifications, reduplications, walking, eating, sleeping, sexual behavior, aggression) Range 0-3 per item that assesses severity after yes/no response; higher scores indicate greater behavioral problems[42]	None identified
		Behavior and Mood Disturbance (BMD)	34 items assessing behavioral and mood disturbances (apathy, depression, disinterest, irritability, pacing, wandering, withdrawn behaviors) Range 0-136 (0-4 per item); includes Apathetic-Withdrawn subscale, Active-Disturbed subscale, and Mood-Disturbance subscale; higher scores indicate greater behavioral problems[43]	None identified
		Rehabilitation Evaluation Hall and Baker tool (REHAB)	23 items assessing deviant behavior (physical and verbal aggression) and general behavior (community skills, disturbed speech, self-care, social activity) Range 0-126 for the general behavior subscale and 0-21 for the deviant behavior subscale; higher scores indicate greater behavioral problems[44,45]	None identified
		Behavioral Pathology in Alzheimer's disease (BEHAVE-AD)	25 items assessing activity disturbances, affective disturbances, aggressiveness, anxieties and phobias, diurnal rhythm disturbances, hallucinations, paranoid, and delusional ideation Range 0-75 plus a 4-point global assessment; higher scores indicate greater behavioral problems[46]	None identified

Outcome Category	Outcome	Instrument	Measurement/Instrument Properties	MIDs Reported in Literature
		Multi-dimensional observation scale for elderly patients (MOSES)	40 items assessing depressed/anxious mood, disoriented behavior, irritable behavior, self-care functioning, and withdrawn behavior Range 0-4 or 0-5 per item, total range varies by subscale; higher scores indicate greater behavioral problems[47]	None identified
Secondary Outcomes	Caregiver Distress	Perceived Change Index	13 items assessing affect, managing caregiving challenges, and somatic symptoms Range 13-65; higher scores indicate worsening in well-being[48]	None identified
	Caregiver Burden	Zarit Burden Interview (Brief version)	12 assessing caregiver burden Scores 0-4 per item, total range 0 to 48; higher scores indicate greater burden[49]	None identified
		Zarit Burden Interview	29 items assessing caregiver burden Scoring is 0-4 per item, total range 0 to 116; higher scores indicate greater burden[50]	None identified

ABID = Agitated Behavior in Dementia; BARS = Brief Agitation Rating Scale; BEHAVE-AD = Behavioral Pathology in Alzheimer's disease; BMD = Behavior and Mood Disturbance; BRSD = Behavior Rating Scale for Dementia; CMAI = Cohen-Mansfield Agitation Inventory; DBRS = Disruptive Behavior Rating Scale; MBPC = Memory and Behavior Problem Checklist; MID = minimally important difference; MOSES = Multi-dimensional Observation Scale for Elderly Patients; NPI = Neuropsychiatric Inventory; PAS = Pittsburgh Agitation Scale; REHAB = Rehabilitation Evaluation Hall and Baker; RMBPC = Revised Memory and Behavior Problem Checklist

Key Questions

Key Question 1a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?

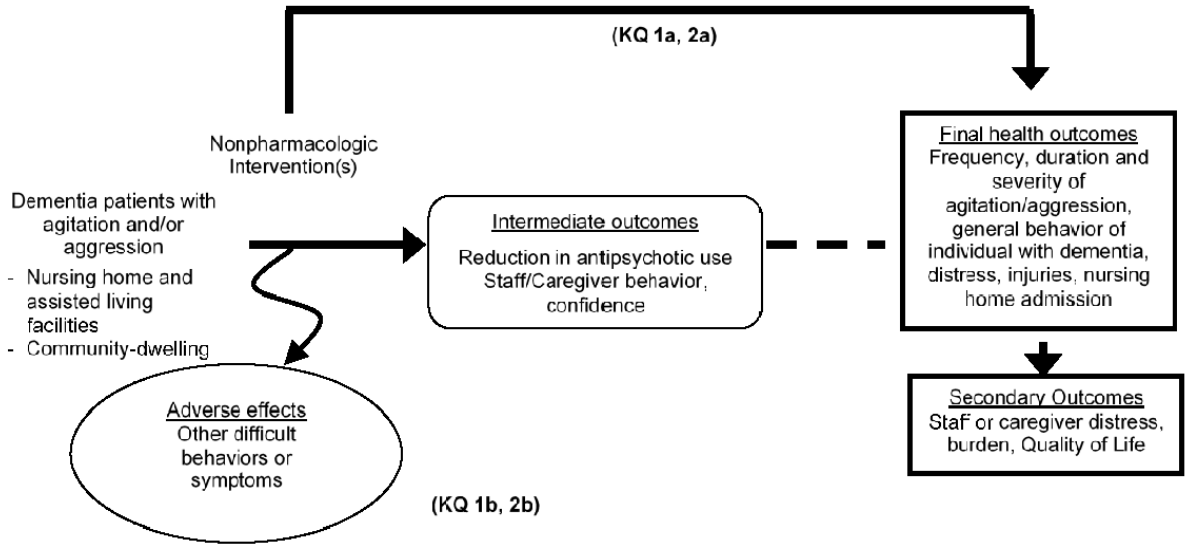
Key Question 1b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia who reside in nursing home and assisted living settings?

Key Question 2a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?

Key Question 2b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?

Analytical Framework

Figure 1. Analytic framework for nonpharmacologic interventions to manage agitation/aggression in dementia



KQ = Key Question

Populations, Interventions, Comparisons, Outcomes, Timing, and Setting (PICOTS)

The PICOTS (populations, interventions, comparisons, outcomes, timing, and setting) addressed in this review are described in Table 3.

Table 3. Populations, interventions, comparisons, outcomes, timing, and setting (PICOTS)

PICOTS Element	Description
Populations	KQ1: Individuals with dementia residing in nursing home and assisted living settings; nursing home and assisted living facility staff KQ2: Community-dwelling individuals with dementia; informal caregivers of individuals with dementia
Interventions	Nonpharmacologic interventions aimed at preventing or responding to agitation/aggression
Comparisons	Usual care (as specified by trial investigators) or no treatment Attention control or placebo Other nonpharmacologic interventions Pharmacologic interventions
Outcomes	**Final (Patient) Health Outcomes** KQ1 & KQ2: Frequency, duration, and severity of agitation/aggression; frequency, duration and severity of aggressive behaviors; general behavior of person with dementia; distress; quality of life; injuries to patients, staff, others KQ2: Injuries to patients, caregivers; admission to nursing home **Secondary Outcomes** KQ1: Staff distress, burden, quality of life KQ2: Caregiver distress, burden, quality of life **Intermediate Outcomes** KQ1: Staff behavior change, reduction in antipsychotic use KQ2: Caregiver behavior change, reduction in antipsychotic use **Adverse Effects of Intervention(s)** Increase in other difficult behaviors (i.e., wandering) Increase in other symptoms (i.e., depression, anxiety)
Timing	Any duration of followup. Relevant timing will vary with the nature of the intervention
Setting	KQ1: Nursing homes and assisted living facilities KQ2: Community-dwelling (patients living at home)

KQ = Key Question

Methods

Criteria for Inclusion/Exclusion of Studies in the Review

Studies were included based on the PICOTS framework outlined above; the study-specific inclusion criteria are described in Table 4.

Table 4. Study inclusion criteria

Category	Criteria for Inclusion
Study Enrollment	Studies that enroll one of the following: • Residents of nursing home, assisted living, individuals diagnosed with dementia (any type) with agitation/aggression • Long-term care staff caring for individuals with dementia and associated agitation/aggression • Community-dwelling individuals diagnosed with dementia (any type) with agitation/aggression • Caregivers of community-dwelling individuals with dementia and associated agitation/aggression
Study Objective	Nonpharmacologic intervention aiming to prevent and/or decrease agitation/aggression associated with dementia
Study Design	Randomized controlled trials
Time of Publication	Literature published from 1994 forward (reflects interventions used today)
Publication Type	Published in peer reviewed journals
Language of Publication	English

Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions

We searched Ovid Medline®, Ovid Embase®, and the Cochrane Central Register of Controlled Trials (CENTRAL) to identify randomized controlled trials (RCTs). Our search strategy included relevant medical subject headings and natural language terms for concepts of dementia and behavioral symptoms (Appendix A). These concepts were combined with filters to select RCTs. We screened bibliographic database search results for studies relevant to our PICOTS framework and study-specific criteria. Titles and abstracts were reviewed by two independent investigators to identify studies meeting PICOTS framework and inclusion/ exclusion criteria. Titles and abstracts identified as potentially eligible by either investigator underwent full-text screening. Two investigators decided eligibility based on full-text review, consulting with a third investigator as necessary to resolve differences. We documented the exclusion status of articles undergoing full-text screening (Appendix B).

We searched ClinicalTrials.gov using “dementia” as the condition. Search results were scanned to identify studies, outcomes, and analyses not reported in the published literature. These results also informed our assessment of publication and reporting bias and inform future research needs. However, search results for this topic were not typically on target. Trial registration of behavioral intervention and/or in psychiatric, psychological, or dementia research does not appear to be common.

Data Abstraction and Data Management

RCTs meeting inclusion criteria were distributed among investigators for data extraction. Data fields extracted included author, year of publication, setting, subject inclusion and

exclusion criteria, intervention, and control characteristics (intervention components, timing, frequency, and duration). We extracted additional data from studies assessed as low or moderate risk of bias (assessment method described below). Relevant data were extracted into evidence tables. These data will be uploaded into the Systematic Review Data Repository after completion of final report.[51]

Assessment of Methodological Risk of Bias of Individual Studies

Two investigators independently assessed risk of bias of eligible studies using instruments developed for the project based on AHRQ guidance.[52] Risk of bias refers to the level of concerns about whether the design, conduct, and reporting of a trial threatens the ability to believe the results. We assessed several risk of bias domains including selection bias (adequate randomization methods, allocation concealment); performance bias (participant and personnel blinding, intervention definition); detection bias (outcome assessor blinding, outcomes measurement, statistical analysis); attrition bias (amount, nature, and handling of incomplete data); reporting bias (selective outcome or analysis reporting); and other risks of bias not captured by the selected domains. Summary risk of bias assessments for each trial were classified as low, moderate, or high based on the collective risk of bias inherent in each domain and confidence that the results were believable given the study's limitations. Investigators conferred to reconcile discrepancies in overall risk of bias assessments when only one investigator assessed a trial as high risk of bias. In certain situations, a third party was consulted to reconcile the summary judgment.

Data Synthesis

We summarized the results in detailed tables for each unique population and intervention type. We did not identify established minimum important differences for key outcomes measurement instruments. We primarily synthesized results across conceptually similar comparisons and outcomes using qualitative synthesis. When comparisons could be reasonably pooled (i.e., comparable interventions and outcomes), we conducted a meta-analysis of the data using a Knapp-Hartung random effects model in R[53] and constructed Forest plots with Stata.[54] We calculated risk ratios (RR) and/or absolute risk differences (ARD) with the corresponding 95 percent confidence intervals (CI) for binary primary outcomes. Weighted mean differences (WMD) and/or standardized mean differences (SMD) with the corresponding 95 percent CIs were calculated for continuous outcomes. We assessed the clinical and methodological heterogeneity and variation in effect size to determine appropriateness of pooling data.[55] We assessed the magnitude of statistical heterogeneity with the I^2 statistic.[55]

Grading the Strength of Evidence for Major Comparisons and Outcomes

In contrast to risk of bias, overall strength of evidence was assessed across all studies that address a pairing of outcomes and intervention. Strength of evidence was evaluated based on five domains: (1) study limitations (the pattern of risk of bias across all relevant studies); (2) directness (single, direct link between intervention and outcome); (3) consistency (similarity of effect direction and size); (4) precision (degree of certainty around an estimate), and (5) reporting bias.[56] Based on study design and risk of bias of the individual studies within the

comparison, study limitations were rated as low, medium, or high. Consistency was rated consistent, inconsistent, or unknown/not applicable (e.g., single study) based on whether intervention effects were similar in direction and magnitude, and the statistical significance of all studies. Directness was rated direct or indirect based on whether the outcome was a final patient-centered outcome or an intermediate or secondary outcome. Precision was rated precise or imprecise based on the degree of certainty surrounding each effect estimate or qualitative finding. Imprecise estimates include clinically distinct conclusions within the confidence interval. Reporting bias was evaluated by the potential for publication bias by comparing studies identified and considered potentially eligible from grey literature searches to identified published studies. Other factors considered in assessing strength of evidence included dose-response relationship, the presence of confounders, and strength of association.

Based on these factors, the overall strength of evidence for each outcome was assessed:[56]

High: Very confident that estimate of effect lies close to true effect. Few or no deficiencies in body of evidence, findings believed to be stable.

Moderate: Moderately confident that estimate of effect lies close to true effect. Some deficiencies in body of evidence; findings likely stable, but some doubt remains.

Low: Limited confidence that estimate of effect lies close to true effect; major or numerous deficiencies in body of evidence. Additional evidence is necessary before concluding that findings are stable or that estimate of effect is close to true effect.

Insufficient: No evidence, unable to estimate an effect, or no confidence in estimate of effect. No evidence is available or the body of evidence precludes judgment.

Assessing Applicability

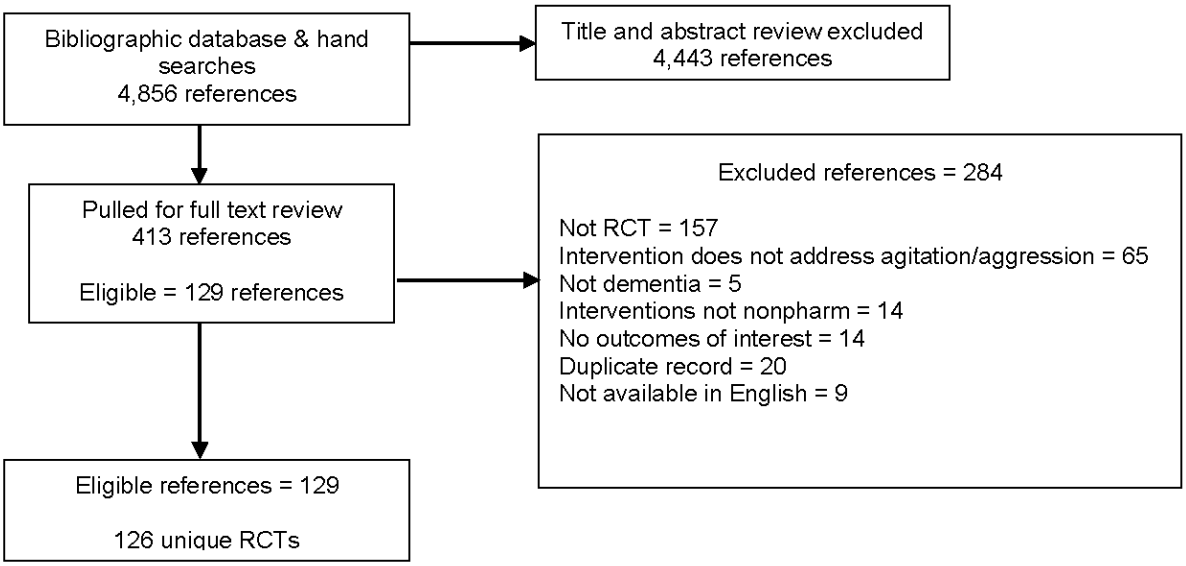
Applicability of studies was determined according to the PICOTS framework. Study characteristics affecting applicability included the population from which the study participants are enrolled, diagnostic assessment processes, narrow eligibility criteria, and patient and intervention characteristics different than those described by population studies behavioral symptoms in dementia.[57]

Results

Literature Search and Screening

Our bibliographic database and hand searching identified 4,855 unique records, of which 410 required full-text review after title and abstract screening (Figure 2). We completed full-text review to identify 129 eligible articles representing 126 unique RCTs.

Figure 2. Literature flow diagram



RCT=Randomized Controlled Trial

We divided the 129 records into four categories for analysis based upon the setting in which the interventions occurred:

1. Patient-level interventions delivered in nursing home and assisted living facility settings (n=68; 67 unique RCTs)
2. Care-delivery level interventions delivered in nursing home and assisted living facility settings (n=28; 27 unique RCTs)
3. Patient-level interventions delivered to community-dwelling individuals with dementia (n=5; 5 unique RCTs)
4. Caregiver-level interventions delivered to caregivers of community-dwelling individuals with dementia (n=28; 27 unique RCTs)

We extracted basic study characteristics into evidence tables. These data will be transformed into the appropriate format, checked for accuracy, and then uploaded to the Systematic Review Data Repository after the final version of this report is posted. Supporting documentation for each category of interventions including risk of bias assessments of individual studies, descriptions of high-risk-of-bias trials, and strength of evidence assessments of unique interventions, comparisons, and outcomes appear in Appendix C for patient-level nursing home and assisted living facility interventions, Appendix D for care delivery-level nursing home and assisted living facility interventions, Appendix E for patient-level community interventions, and Appendix F for caregiver-level community interventions.

Patient-Level Nonpharmacologic Interventions for Agitation/ Aggression in Individuals With Dementia in Nursing Homes and Assisted Living Facilities

Key Points

- Low strength evidence shows that music interventions, aromatherapy with lavender, and bright light therapy are similar to no intervention, placebo, and/or attention control in decreasing agitation/aggression among nursing home and assisted living facility residents with dementia.
- Low strength evidence shows that interventions tailored to patient skills, interventions tailored to patient interests, and interventions delivered to both skills and interests have similar effects on agitation/aggression among nursing home and assisted living facility residents with dementia.
- Evidence was insufficient for all other outcomes and comparisons.

Overview

We identified 67 eligible trials that assessed patient-level nonpharmacologic interventions for agitation/aggression in residents of nursing homes and assisted living facilities. Of these, 27 were assessed as having a high risk of bias. These studies are described in Appendix C. Our analysis of the remaining 40 trials is provided below by intervention type (Tables 5 and 6). Trials with acceptable risk of bias examined a wide variety of interventions including therapies delivered directly to patients (e.g., music therapy, aroma therapy, bright light therapy), structured group activities (e.g., exercise), and activities specifically tailored to the individual. We grouped studies by intervention type and comparison. All studies were trials but they differed in the unit of randomization (i.e., at nursing home level, staff, or residents). In many of the studies the intervention was compared with "usual care" but the nature of this care was poorly specified. In some instances the intervention was added to usual care; in others it was offered as an alternative. It was frequently not even clear if psychoactive medications were being given concurrently. Table 5 provides a summary of the results by intervention type and comparison. Table 6 provides results for trials analyzed.

Music

Eligible Trials

We identified six trials with acceptable risk of bias that assessed the efficacy or comparative effectiveness of music interventions on agitation/aggression in nursing homes and/or assisted living facilities.[58-63]

Four of the trials compared music interventions with usual care, no treatment, and attention controls.[58-61] One trial was conducted in Japan, one in Taiwan, one in the United States, and one in Italy. Inclusion criteria varied; most trials required participants to have behavioral symptoms as well as a diagnosis of dementia. Two trials studied music interventions delivered to groups of residents[59,60] and two to individuals.[58,61] Music intervention sessions varied in length (10 to 30 minutes), frequency (one time, weekly, three times per week) and duration (one time to 6 months). Type and number of staff involved in the intervention also varied.

Sakamoto et al. randomized 39 dementia residents to a music listening intervention (n = 13), an interactive music intervention (n = 13), or a no-music control (n = 13).[58] Residents were recruited from four nursing homes in Kobe City, Japan. Inclusion criteria included a diagnosis of dementia according to DSM IV criteria and a severity in the Dementia Rating Scale of 3 or more. Those with hearing disorders, heart disease, hypertension, or diabetes were excluded because of the autonomic nervous system measures being used. Those with a history of playing a musical instrument were also excluded. The mean age of residents randomized to music listening was 79.7 years and most were female (76%). Similar characteristics were observed for the interactive music group (mean age 80.42 years and 85% female) and no-music control (mean age 81.5 years and 85% female). In the music listening intervention, participants listened to CDs; in the interactive music intervention, a music therapist led the group and encouraged them to clap, sing, and/or dance while listening. The comparison group had a staff member sit with the resident for the same amount of time in his or her room with no music. Interventions were delivered for 30 minutes once a week for 10 weeks. Patient agitation/aggression was measured using the Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) aggressiveness subscale after the tenth intervention and 3 weeks postintervention. Mean BEHAVE-AD scores were similar for the three groups after the tenth intervention and 3 weeks postintervention. General behavior was measured using the Behavioral and Social Symptoms of Dementia (BPSD) scale and the BEHAVE-AD scale; mean scores were similar for the three groups after the tenth intervention and 3 weeks postintervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Lin et al. randomized 100 individuals with dementia in three Taiwan nursing homes to music therapy (n = 49) or a usual care control (n = 51).[59] Residents needed to be diagnosed with dementia and to speak Mandarin or Taiwanese. The mean age of residents randomized to the intervention group was 81.46 years and 53 percent were female. Demographic characteristics of residents in the usual care group were similar (mean age 82.15 years and 53% were female). The intervention group received 30-minute sessions twice a week for a total of 12 sessions over 6 weeks. Sessions were led by the study investigators who received training in music therapy. Sessions focused on various musical activities. Examples of musical activities included rhythmical music and slow-tempo instrumental activities, therapeutic singing, and listening to specially selected music. Residents in usual care did not receive music therapy and they continued to engage in normal daily activities. Agitation/aggression was measured using the validated Chinese version of the Cohen-Mansfield Agitation Inventory administered after the sixth and twelfth sessions and at 1 month postintervention. Unadjusted overall mean scores were similar between intervention and control at each time point. The authors also separately analyzed the four behaviors making up the Cohen-Mansfield Agitation Inventory. Unadjusted means were similar between groups at each time point. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Raglio et al. randomized 60 individuals with dementia residing in five nursing homes near Milan, Italy, to a group music intervention (n = 30) or usual care (n = 30).[60] Usual care was not specifically described. Participation required a dementia diagnosis and moderate or high behavioral symptoms. The mean age of residents randomized to the experimental group was 85.4 years and 97 percent were female. The mean age of residents randomized to the control group was 84.6 years and 87 percent were female. The music intervention consisted of three 30-minute music therapy sessions per week for 1 month, alternating with a 1-month washout period for a total of 36 musical therapy sessions over 6 months. Three residents participated in a music

session at a time. During music sessions, residents and a music therapist interact and express emotions and behaviors through musical instruments. All residents in the intervention and control group received standard care (e.g., educational and entertainment activities). Agitation/aggression was measured with the NPI agitation subscale at baseline, the end of the intervention, and 1 month after the last washout period. Group differences were not tested and standard deviations were not provided. Postintervention general behavior measured with the global NPI (reported graphically only) was lower in the intervention group ($F_{1,51}$=4.84, $p<0.05$); statistical testing of postintervention scores was not provided. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Remington et al. randomized 68 dementia nursing home residents to four arms: calming music (n = 17), hand massage (n = 17), calming music plus hand massage (n = 17), or no treatment (n = 17).[61] Residents with dementia who were identified as having agitation/aggression were invited to participate in the study. Mean age of all study participants was 82.4 years and most were female (87%). The comparison of interest for assessing the efficacy of music interventions is that of the 34 residents randomized to music or no treatment. Residents were randomized to treatment immediately prior to receiving the intervention. If the resident did not show signs of agitation (CMAI score = 0) then assignment to treatment was delayed. The music intervention consisted of 10 minutes of calming music (a new age arrangement of Pachelbel's Canon in D) played on a CD player one time. The music was played in patient rooms or family lounge areas at a level slightly higher than background noise, but was low enough to allow for conversation. Agitation/aggression was measured using the CMAI immediately after and at 10, 20, and 60 minutes after the intervention; agitation/aggression decreased more with calming music than with no treatment. At postintervention (60 minutes) residents in the control group exhibited more agitation/aggression than residents in the treatment groups ($p <0.05$). No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Vink et al. randomized 94 individuals with dementia and behavioral symptoms from six Dutch nursing homes to music (n = 47) or a recreational activity (n = 47).[63] The mean age of residents randomized to music therapy was 82.42 years and 67 percent were female. In the recreational activity group, the mean age of residents was 81.76 years and 74 percent were female. The music intervention was delivered by trained music therapists to groups of five residents at a time. The semi-weekly 40-minute music therapies followed a structured protocol in which participation was encouraged. The comparison group received the same amount of group recreational activities facilitated by occupational therapists. Examples of recreational activities include handwork, playing shuffleboard, and playing puzzle games. Agitation/aggression was measured using the modified CMAI 1 hour before sessions, and 1, 2, and 4 hours after sessions. Agitation/aggression postintervention did not differ between residents in the music and recreational activity group. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Cooke et al. conducted a crossover trial in 47 nursing home residents, comparing a live music intervention (n = 24) with an interactive reading intervention (n = 23).[62] The study was conducted in two facilities in Australia. Residents with dementia were required to have a history of agitation/aggression in the past month. Overall mean age of study residents was not reported and most participants were female (70%). The music intervention was led by performing musicians and supplemented by a 10-minute rest period of supplemental recorded music. The musicians selected music based on participant preferences. Residents received 40-minute sessions three times a week for 8 weeks for a total of 24 sessions. Singing, clapping, dancing, or

even playing an instrument was encouraged. The comparator was a reading group intervention that included jokes, puzzles, and quizzes. This group was also encouraged to interact with the activities. After the first cycle of interventions, participants crossed over to the other intervention. Agitation/aggression was measured with the Cohen-Mansfield Agitation Inventory short-form and the Rating Anxiety in Dementia scale and was reported at baseline, after the first intervention cycle, and at the end. Agitation/aggression was similar in music and reading groups after the first intervention cycle, before crossover. General behavior was also similar between groups. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence Assessment

One trial showed a benefit for agitation/aggression with music compared with no treatment; this trial examined a simple one-time 10-minute recorded calming music in the resident's room and found an improvement in agitation/aggression immediately after and for 10 and 20 minutes after the intervention.[61] All other trials showed similar results to control groups. The trial with positive findings differed from the trials with null findings. The three trials with null findings approached music therapy as having a prolonged and sustained effect on agitation/aggression because they measured outcomes at a variety of time points throughout the long-term trial. We could pool results for only two of the three trials, showing no difference in agitation/aggression between intervention and control postintervention (standardized mean difference -0.18; 95% CI: -2.41 to 2.05) (Figure 3). Low strength evidence shows that music interventions are similar to control in decreasing agitation/aggression in dementia over a period of time.

The trial showing a positive relationship between calming music and agitation/aggression treated the intervention as having an immediate effect by measuring the outcome just after the intervention and again within 30 minutes after the intervention.[61] This evidence is insufficient to draw conclusions regarding the efficacy of music to immediately decrease agitation/aggression among individuals with dementia.

Neither of the trials that compared music interventions with other interventions showed differences between groups on agitation/aggression. Low strength evidence suggests that music interventions are not more or less effective at decreasing agitation/aggression in dementia compared with interactive comparison interventions. Two trials (n = 125) also reported a general behavior outcomes with conflicting results and evidence insufficient to draw conclusions.[58,60]

Aromatherapy

Eligible Trials

Aromatherapy interventions include inhalation or application of scented essential oils. Efficacy studies often used placebo aromas or sprays such as sunflower oil. We identified six trials with acceptable risk of bias that assessed the efficacy of aromatherapy in nursing home residents with agitation/aggression.[35,64-68] Four trials studied lavender[64-67] and two studied Melissa oil.[35,68] Trials were conducted in nursing homes in Australia, Japan, Hong Kong, and the United Kingdom.

Yang et al. randomized 186 residents with severe agitation to aroma-acupressure (n=56), aromatherapy (n=73), or usual care (n=57).[67] Mean age of residents was 84 years and 26 percent were female. Participants were diagnosed with Alzheimer's disease (91%), vascular dementia (6%), or other forms of dementia (2%). Participants in the aroma-acupressure group received 15 minutes of treatment at five acupressure points with lavender oil for 5 days a week over 1 month.

Participants in the aromatherapy group received treatment with lavender oil for the same amount of time. Usual care was not defined. One primary outcome was assessed (agitation/aggression measured by CMAI) at baseline, postintervention, and 3-week postintervention. CMAI scores were similar at initial postintervention for all groups. At 3-week postintervention, CMAI scores were significantly lower. No secondary and intermediate outcomes were reported. No adverse events were reported.

Fu et al. randomized 67 nursing home residents with dementia and a history of agitation/aggression or aggression from three nursing home and assisted living facilities in Australia to lavender aromatherapy with massage (n = 22), lavender aromatherapy without massage (n = 23), or placebo aromatherapy (water sprays) (n = 22).[64] Mean age of residents in the study was 84 years and more than half the participants were female (59%). Aromatherapy treatments were given twice a day, 7 days a week, for 6 weeks. Hand massage was done for 5 minutes (2.5 minutes per hand) twice a day for 10 days. Agitation/aggression measured with the Cohen-Mansfield Agitation Inventory-Short Form was similar across the three groups. Overall scores were not reported; item specific means were analyzed at several time points. Postintervention means were similar across the three groups at all time points. No intermediate or secondary outcomes were reported.

Burns et al. randomized 114 residents with probable or possible Alzheimer's disease to active aromatherapy (Melissa) with placebo psychotropic (n=38), placebo aromatherapy with donepezil (n=37), or both placebos (n=39).[68] Participants' mean age was 85 and 60 percent were female. Active and placebo aromatherapy was administered twice daily for 1-2 minutes, and active and placebo psychotropic were administered daily for 3 months. Two scales assessed primary outcomes (agitation/anxiety measured by PAS, general behavior measured by NPI) at baseline and postintervention (3 months). Median change from baseline was similar for both outcomes postintervention. One scale assessed secondary outcomes (patient distress measured by Blau QoL) at baseline and postintervention. Aromatherapy resulted in higher postintervention mean QoL (quality of life) than donepezil. Intermediate outcomes were not reported. Adverse events were not reported.

Fujii et al. randomized 28 dementia residents with behavioral symptoms of one nursing home facility in Japan to lavender aromatherapy (n = 14) or no treatment (n = 14).[65] The mean age of participants was 78 years and most were female (68%). Two drops of lavender oil were applied to residents' clothing three times a day approximately 1 hour after meals for 4 weeks. At the end of the intervention (4 weeks), general behavior measured with the NPI was similar with intervention and control. No intermediate or secondary outcomes were reported.

Lin et al. randomized 70 nursing home residents to lavender aromatherapy (n = 35) or sunflower inhalation (n = 35).[66] Residents with dementia and significant agitation/aggression were invited to participate in the study. The mean age of all study participants was 78.29 years and 59 percent were female. Half of the study participants were first assigned to aromatherapy for 3 weeks and then switched to control group for another 3 weeks; the other half did the opposite, with a 2-week washout period between treatments. Results are only presented for the time period before the second intervention cycle. Aromatherapy was delivered by diffusing lavender oil for at least 1 hour near the patient's pillow each night. Postintervention agitation/aggression measured with the Chinese version of the Cohen-Mansfield Agitation Inventory and general behavior measured with the Chinese version of the Neuropsychiatric Inventory were similar with intervention and control at the end of the intervention. Psychotropic medication use

postintervention did not change or differ between groups. No other intermediate or secondary outcomes were reported.

Ballard et al. randomized 72 nursing home residents in the United Kingdom to 4 weeks of aromatherapy with essential oils (Melissa) (n = 36) or placebo (sunflower oil) (n = 36).[35] Residents with dementia and with clinically significant agitation/aggression were invited to participate in the study. The mean age of residents randomized to the intervention group was 77.2 years and 56 percent were female. The mean age of residents randomized to placebo was 79.6 years and 64 percent were female. Aromatherapy was delivered in a lotion applied by staff to patients' faces and arms twice a day. At 4 weeks from baseline residents in the Melissa oil group were significantly more likely than residents in the placebo group to experience a 30 percent reduction in CMAI scores (60% vs. 14%; χ^2=16.3; p<.0001). The change in the proportion of patients prescribed additional psychotropic drugs was similar with intervention and control. No significant side effects were observed; one patient in the treatment group experienced 2 days of diarrhea.

Evidence Synthesis and Strength of Evidence

Only one of six trials showed that aromatherapy improved agitation/aggression compared with inactive controls.[35] The trial that showed an aromatherapy effect used the Melissa scent applied to the patient in lotion form by a staff member. Delivery methods in the other trials did not appear to involve touch. However, the other trial using the Melissa scent did not show an effect on behavior. Methodological limitations of the eligible studies and imprecise estimates provide insufficient evidence for the effectiveness of aromatherapy for agitation/aggression in dementia. Low strength evidence suggests that aromatherapy with lavender is not effective in managing agitation/aggression in individuals with dementia. Evidence was insufficient to draw conclusions about the efficacy of Melissa in reducing agitation/aggression in dementia due to conflicting findings in two trials.

Bright Light

Eligible Trials

Light therapy interventions included some variant of bright light therapy (BLT). Patients were exposed to full spectrum versus active control light (red dim light) or standard light. BLT sessions were typically 1 to 2 hours per day at varying times of the day. We identified four trials that studied the efficacy of light therapy with acceptable risk of bias.[69-72] Treatment lasted an average of 2 weeks.

Burns et al. randomized 48 residents in two nursing homes to bright light (n = 22) or standard light (n = 26).[70] Both homes specialized in dementia and behavioral disturbances and all participants had dementia, sleep disorders, and a history of agitation/aggression. The mean age of residents randomized to bright light therapy was 84.5 years and 73 percent were female. Characteristics of residents in the standard light group were similar (mean age of 82.5 years and 62% were female). Residents were exposed to treatment during the second and third weeks. Residents in the BLT group were exposed to full spectrum BLT 10,000 lux. Residents in the standard light group were exposed to standard light at 100 lux. In both groups, exposure was for 2 hours daily between 10 a.m. and noon for 2 weeks. During each light therapy (bright light and standard light) a nurse was present and engaged residents in conversation. Agitation/aggression measured with the CMAI and general behavior measured with the Crichton Royal Behavior

Rating Scale and MOUSEPAD were similar with BLT and standard light at 4 and 8 weeks. No intermediate or secondary outcomes were reported.

Dowling et al. randomized 70 residents with severe dementia, sleep disorders, and rest-activity disruptions (i.e., agitation/aggression) in two nursing homes in the United States to morning bright light (n = 29), afternoon bright light (n = 24), or usual indoor light (n = 17).[71] The mean age of randomized participants was 84 years and 81 percent were female. In the morning bright light group, BLT was administered from 9:30 to 10:30 a.m., and in the afternoon bright light group BLT was administered from 3:30 to 4:30 p.m. In both bright light groups, BLT (>2,500 lux) was administered daily (Monday-Friday) for 10 weeks. Residents in the control group received usual indoor light (150 to 200 lux) and participated in regularly scheduled activities. Outcomes were measured at the end of the baseline week and after the last week of intervention. Agitation/aggression measured with the NPI-NH agitation subscale increased more with morning light group than standard light ($t_{1,55}$ =-2.25, p=0.015) largely because scores in the standard light group decreased. General behavior measured with the NPI-NH overall scores was similar for intervention and control. The authors mention that this subscale change with bright light is likely not clinically meaningful despite its statistical significance. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Ancoli-Israel et al. randomized 92 residents with dementia from five U.S. nursing homes to morning bright light (n = 30), morning dim red light (n = 31), or evening bright light (n = 31).[69] The mean age of study participants was 82.3 years and 68 percent were female. For residents randomized to morning and evening bright light, an Apollo Bright-Light box was placed one meter from the patient for a resulting exposure of 2,500 lux. An eye-level photometer was used to ensure correct light exposure. The inactive control, dim red light, was administered with a red light box resulting in exposure equivalent to typical room light levels (<300 lux). In all groups, residents were exposed to light for 2 hours daily for 10 days. Morning bright light and morning dim red light were administered from 5:30 to 11:30 a.m. Evening bright light was administered from 9:30 to 11:30 p.m. During the administration of light therapy residents could engage in any activity as long as they remained facing the light. Outcomes were assessed and analyzed separately by morning and evening staff. Agitation/aggression measured with the CMAI was similar between the groups and for morning and evening staff assessments. Agitation/aggression was also assessed separately with the Physical and Verbal Agitation ratings from the Agitated Behavior Rating Scale (ABRS). Means were similar between groups. No group differences were reported for morning or evening assessments. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Lyketsos et al. randomized 15 nursing home residents with dementia and agitation/aggression to bright light or dim light.[72] Mean age of study participants was 80.8 years and 93 percent were female. Bright light (10,000 lux full spectrum lamp at 3 feet from patient) was administered daily for 1 hour for 4 weeks followed by 1 week of no treatment prior to being crossed over to the other intervention. During the administration of light therapy residents could engage in any activity as long as they faced the light. Residents in the control group were exposed to a dim, digital, low frequency light. Outcomes were assessed at 2 and 4 weeks after treatment assignment, combined and reported at the patient-intervention level after both groups received both interventions. Agitation/aggression measured with BEHAVE-AD aggression subscale and general behavior measured with BEHAVE-AD global rating was similar with bright light and dim light. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Four trials assessed the efficacy of BLT to manage agitation/aggression among dementia residents in nursing homes and assisted living facilities.[69-72] The four trials measured agitation/aggression with different scales and time points. Of the eight postintervention outcomes reported, only one showed a statistically significant difference between groups. The authors admit that this small change in the instrument is likely not clinically meaningful. Only two trials provided sufficient data for pooling (Figure 4). Bright light therapy had an effect similar to standard light in improving agitation/aggression in individuals with dementia (standardized mean difference=0.09; 95% CI: -0.32 to 0.50). Low strength evidence suggests that bright light therapy is not effective in managing agitation/aggression among nursing home and assisted living facility residents with dementia.

Therapeutic Touch

Eligible Trials

Therapeutic touch refers to transfers of energy without necessarily using actual physical touch. Typically, a practitioner sits next to the patient and places his or her hands on or near the patient to transfer energy. We identified two studies with acceptable risk of bias on therapeutic touch. These include Woods et al.[73] and Hawranik et al.[74]

Hawranik randomized 51 residents with dementia and agitation/aggression from the personal care and special needs unit of a nursing home to therapeutic touch (n = 17), simulated therapeutic touch (n = 16), and usual care (n = 18).[74] The mean age of all study participants was 82.8 years and 71 percent were female. Therapeutic touch is based on ancient healing practices and involves practitioners touching the patient or passing hands several inches from the patient. Therapeutic touch was conducted by trained practitioners. Volunteers were recruited to administer the simulated therapeutic touch (i.e., passing hands several inches from the patient). Therapeutic touch and simulated therapeutic touch were each given in 30 to 40 minute sessions once/day for 5 days. At baseline there were no differences in physically aggressive or verbally agitated behaviors between groups as measured by CMAI subscales. From baseline to the end of 5 days of intervention, there were significant differences between the three-treatment groups (therapeutic touch, simulated therapeutic touch, and usual care) ($\chi^2 = 5.98$, $p<0.05$). These differences are explained by an increased rate (2.3 times 95% CI 0.66 to 7.81) of physically nonaggressive behaviors (a subscale of the CMAI) in usual care compared with therapeutic touch. However, there were no differences between groups in the CMAI subscales of physically aggressive, physically nonaggressive, or verbally agitated behaviors at 24 hours after the final intervention, 1 week postintervention, or 2 weeks postintervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Woods randomized 57 residents with dementia and behavioral symptoms in the special care units of three Canadian nursing homes to therapeutic touch (n = 19), placebo therapeutic touch (n = 19), or usual care (n = 19).[73] The mean age of study participants was 81.04 years and 81 percent were female. Therapeutic touch consisted of a trained therapist providing contact on the neck and shoulders. Residents in the placebo therapeutic touch group received a simulated therapeutic touch (i.e., the treatment resembled therapeutic touch). Therapeutic touch and placebo therapeutic touch were given twice daily (between 10:00 and 11:30 a.m. and between 3:00 and 4:40 p.m.) for 5 to 7 minutes per session for 3 days. Behavioral observation was completed every 20 minutes from 8 a.m. to 6 p.m. for 3 days pre-intervention and for 3 days

postintervention by trained observers blinded to group assignment. Mean behavioral symptoms of dementia appear similar across groups postintervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Two trials assessed the efficacy of therapeutic touch to manage agitation/aggression among dementia residents in nursing homes.[73,74] The two studies measured agitation/aggression with different scales. One of the studies reported a statistically significant difference between groups.[73] This difference was small and is unlikely to be clinically meaningful. Evidence was insufficient to draw conclusions regarding the effectiveness of therapeutic touch for agitation/aggression in dementia.

Massage

Eligible Trials

We identified three trials testing the efficacy of massage for agitation/aggression in dementia. In two of three trial arms, Remington et al. compared hand massage with no treatment.[61] Rodriguez-Mansilla et al. compared back and lower limbs massage by physiotherapists for 20 minutes every day with no treatment in two of three arms.[75] Moyle compared foot massage with attention control.[76]

Moyle et al. randomized 55 residents with moderate- to late-stage dementia to either a foot massage condition (n=26) or attention control (n=29).[76] The mean age of participants was 86 years and 64 percent were female. Participants in the intervention received a 10-minute foot massage 5 days a week for 3 weeks; controls received quiet presence for the same amount of time as massage. One scale assessed primary outcomes (agitation/aggression measured by CMAI) at baseline, 3-week postintervention (after completion of first treatment), and 9-week postintervention (after completion of crossover treatment). Postintervention scores were similar between groups. Secondary and intermediate outcomes were not reported. Adverse effects were not reported.

Rodriguez-Mansilla et al. randomized 120 residents with dementia in three Spanish nursing homes to massage (n = 40), ear acupuncture (n = 40), or control (n = 40). The mean age of residents across all three groups was similar (massage = 85.8 years, ear acupuncture = 85.4 years, and control = 81.9 years), and most residents in the study were female (77%). The massage therapy arm is compared with the no treatment arm for efficacy of massage. The massage therapy group received a relaxing 20-minute massage of the back and lower limbs by a physiotherapist 5 days per week over 3 months. A qualified acupuncturist provided ear acupuncture. The acupuncturist applied Shenmen Muscle relaxant located in the peripheral inferior concha, close to the spleen and liver with adhesive herbal seeds of Wangbuliuxing (Semen Vaccariae Segetalis). The seeds were placed with adhesive tape and replaced with new seeds every 15 days for 3 months. The control group received no experimental therapy. General behavior was measured with an investigator-designed instrument asking staff about the number of behavioral alterations. General behavior improved more in the intervention versus control group postintervention and was maintained at 2-months postintervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Remington et al. randomized 68 nursing home residents to four arms: calming music, hand massage, calming music plus hand massage, or no treatment.[61] Details of this study are provided

in the music intervention versus control section. The three interactive arms are relevant to the comparative effectiveness of massage interventions for agitation/aggression. The music intervention consisted of 10 minutes of calming music played on a CD player one time. The hand massage intervention consisted of 10 minutes of hand massage, 5 minutes per hand. The hand massage/calming music group received both interventions simultaneously. Agitation/aggression was measured with CMAI immediately and at 10 and 20 minutes after the intervention; agitation/aggression reduced similarly in each of the interactive arms. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Three trials assessed the efficacy of massage to reduce agitation/aggression in dementia in nursing home residents.[61,75,76] Remington et al. reported an agitation/aggression outcome;[61] Rodriguez-Mansilla et al. and Moyle et al. reported general behavior.[75,76] Studies had methodological limitations, inconsistent findings, and estimates were imprecise. Therefore, evidence is insufficient to draw conclusions about the effect of massage on agitation/aggression or general behavior among nursing home residents with dementia.

Comparisons Between Tailored and Nontailored Interventions

Eligible Trials

We identified four trials with acceptable risk of bias that compared tailored interventions with nontailored interventions.[77-80] The interventions varied on the resident characteristics used for tailoring. One tailored the intervention based on patient preferences and abilities,[77] one on the Montessori model,[78] another on the unmet needs,[79] and the fourth on balancing arousal throughout the day according to the patients' response to different activities.[80]

Van Haitsma et al. randomized 180 dementia residents with moderate to severe dementia to a positive psychology intervention (n=44), attention control comparison (n=43), or usual care (n=93).[77] The mean age of residents was 89 years and 82 percent were female. Residents in the intervention received a one-to-one activity that was tailored to their preferences and abilities, such as exercise, music, reminiscence, snacks, and so forth. Residents in the attention control received one-to-one time doing a standard activity, such as reading a magazine or conversing. Usual care was not defined. The intervention was performed by certified nursing assistants in 10-minute sessions, three times weekly over 3 weeks. One scale measured primary outcomes (agitation/aggression and general behavior measured with nonverbal behavior observations) at baseline and postintervention (3 weeks). At postintervention, aggression was significantly lower in usual care compared with intervention or attention control, but intervention and attention control were no different. Adverse effects were not reported.

Van der Ploeg et al. conducted a crossover trial in which 44 dementia residents with agitation/aggression in nine Australian nursing home and/or assisted living facilities were randomized to personalized one-on-one activities according to the Montessori model (n = 15) or nonpersonalized activity (n = 29).[78] The mean age of study participants was 78.1 years and 68 percent were female. A single target behavior was selected for each resident based on nurse CMAI ratings of the residents' behavior. Residents randomized to Montessori participated in structured one-on-one activities. Up to 10 activities were selected by trained activity facilitators based on the residents' former interests and hobbies. Examples of activities include singing along to music and arranging flowers. The control condition received nonpersonalized activity. Both

groups were exposed to the activity for 30 minutes twice weekly resulting in a total of four sessions over 2 weeks. After 2 weeks, study participants crossed over. Nursing homes committed not to modify psychoactive drugs during the 4-week study period. Agitation/aggression occurred at similar rates during and after the intervention in the intervention and control groups. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Cohen-Mansfield et al. randomized 125 dementia residents with agitation/aggression in nine Maryland nursing homes to a tailored intervention (n = 89) or placebo control (n = 36). The mean age of study participants was 85.7 years and 74 percent were female. The intervention is referred to as the TREA (Treatment Route for Exploring Agitation) intervention.[79] TREA includes making a baseline assessment from multiple sources, hypothesizing unmet needs, and developing an intervention designed to meet resident needs based on interests, preferences, and past identity. A trained research assistant conducted observations and recommended interventions to staff. The control group received general staff training on resident behavior. Agitation/aggression was measured with the Agitation Behavior Mapping Instrument and was analyzed using a two-way repeated-measures analysis of covariance. This showed that agitation/aggression decreased more with intervention [8.76 (5.61) to 2.08 (2.68)] than control [7.16 (7.61) to 7.92 (9.09)]. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Kovach et al. randomized 78 dementia residents with agitation/aggression from 13 Midwest nursing homes to a tailored intervention (n = 36) or control (n = 42). The mean age of study participants was 87 years and 91 percent were female. The tailored intervention sought to decrease agitation/aggression by manipulating resident daily activities to achieve an optimum balance between states of high and low arousal.[80] Research assistants designed the new activity plan during the first assessment and the second planning stage, and the plan was implemented by regular staff for 7 days. Agitation/aggression was measured using a visual analog scale rated from 0–100 by trained observers. Difference in change in scores was similar with intervention or control (Pretest to Posttest * group: $F_{1,69}$=4.26; p=0.43). The difference in the change between groups was not tested. Mean scores postintervention were similar between intervention and usual care, but the intervention group had higher baseline scores. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Four trials studied tailored activities for agitation/aggression in dementia.[77-80] Only one trial showed reduced agitation/aggression with tailored activities compared with nontailored activities[79] and one showed higher aggression with intervention compared with usual care.[77] These studies had methodologic limitations and imprecise estimates. In addition to the inconsistency, this rendered the evidence insufficient to draw conclusions regarding the effectiveness of tailored activities compared with nontailored activities.

Comparisons Between Different Tailored Activity Interventions

Eligible Trials

Two trials compared interventions tailored to different resident characteristics.[81,82] Both of these trials were conducted by Kolanowski, et al. Studies tested the Needs-Driven, Dementia-Compromised Behavior model, which posits that activities for individuals with BPSD must fit the physical and cognitive functional abilities and personality of the resident.

Kolanowski, et al (2005) conducted a crossover RCT and randomized 33 dementia residents with agitation/aggression to activity based interventions based on skill level only, style of interest only, or skill level and style of interest. The mean age of study participants was 82.3 years and 77 percent were female. Residents randomized to skill level only received activities appropriate to their abilities but opposite to their personalities. Residents randomized to style of interest only received activities appropriate to their abilities but opposite to their personalities. Finally, residents randomized to skill level and style of interest received activities that were appropriate to both. Within each arm, activities were implemented for up to 20 minutes for 12 consecutive days. Agitation/aggression was measured with the CMAI. Postintervention outcomes were reported at the patient-intervention level. Postintervention CMAI was similar among all groups.[82] No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Kolanowski, et al (2011) evaluated the Needs-Driven, Dementia-Compromised Behavior model in 128 residents from nine community nursing homes.[81] Participants were randomly assigned to activities tailored to functional level (n = 32), activities adjusted to personality style of interest (n = 33), to both (n = 31), or to interactive control (n = 32), who received activities opposite both their skill level and personality style. The mean age of study participants was 86 and 77 percent were female. The activities were provided twice daily for 3 weeks. Agitation/aggression measured with CMAI decreased in all four groups; mean changes and postintervention means were similar across groups. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Two studies assessed the effect of interventions tailored to different resident characteristics.[81,82] Low strength evidence shows that interventions tailored to different patient characteristics have a similar effect on managing agitation/aggression in dementia.

Exercise

Eligible Trials

Two trials compared exercise.[83,84] Telenius et al. randomized 170 residents with mild to moderate dementia to high-intensity exercise (n=87) or attention control (n=83).[83] Participants' mean age was 87 and 74 percent were female. Participants in the intervention group performed intense lower body and balance exercises in small groups twice weekly for 3 months. Participants in the attention control performed leisure activities (reading, conversation, music listening) for an equivalent amount of time. One scale assessed primary outcomes (general behavior measured by NPI-Q) at baseline and postintervention (3 months). Change from baseline agitation was significantly lower in the exercise group at postintervention. One scale assessed secondary outcomes (patient distress, QoL measured by QUALID) at baseline and postintervention (3 months). Change from baseline QoL was not significantly different between groups. Intermediate outcomes and adverse effects were not reported.

Rolland et al. randomized 134 residents with mild to severe dementia to a group exercise program (n = 67) or usual care (n = 67).[84] The mean age of residents in the group exercise program was 82.8 years and 72 percent were female. The mean age of residents in usual care was 83.1 years and 79 percent were female. Residents in group exercise were placed in groups of three to seven by functional abilities so that their exercises could be tailored to their ability (e.g., walking, strength, balance, and flexibility). Sessions were delivered by a physical therapist

for 1 hour twice a week for 12 months. Residents in usual care received routine medical care. Agitation/aggression were assessed at 6 and 12 months using the NPI agitation subscale. At 6 and 12 months there was no difference in agitation/aggression between residents in the group exercise program and usual care. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

Two trials with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.[83,84]

Multicomponent Intervention

Eligible Trial

Hutson et al. randomized 39 residents with a dementia diagnosis or moderate to severe cognitive impairment to a multicomponent intervention (n=21) or usual care (n=18).[85] Participants' mean age was 87 and 74 percent were female. Participants in the intervention group received multisensory stimulation (music, food to smell and taste, looking at items to reminiscence, light exercise, massages) in 14 45-minute sessions over 7-8 weeks. Usual care was not defined. One scale measured primary outcomes (general behavior measured by NPI-Q) at baseline and postintervention. Differences between means at postintervention were not reported. One scale measured secondary outcomes (patient distress, QoL measured by QoL-AD) at baseline and postintervention. Differences between means at postintervention were not reported. Intermediate outcomes and adverse effects were not reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Multisensory Stimulation Room

Eligible Trial

Maseda et al. randomized 32 residents (diagnoses not reported) to a multisensory stimulation room (n=10), individualized activities (n=10), or usual care (n=10).[86] Participants' mean age was 87 years and 90 percent were female. Participants in the intervention group were exposed to a multisensory room (vibrating water bed, mirror, music, aroma therapy, etc.) in twice-weekly 30-minute sessions for 4 months. Participants in the activities group attended individualized activities based on patient preference (cards, quizzes, photo-viewing) for an equivalent amount of time. Usual care was defined as cognitive stimulation and ADL training. Two scales assessed primary outcomes (agitation/aggression measured by CMAI, general behavior measured by NPI-NH) at baseline, postintervention (4 months), and 2-months postintervention. Results were reported graphically. Secondary and intermediate outcomes were not reported. Adverse effects were not reported.

Evidence Synthesis and Strength of Evidence

One small trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Humor Therapy

Eligible Trial

Low et al. randomized 398 residents (diagnoses not reported) to humor therapy (n=189) or usual care (n=209).[87] Participants' mean age was 85 years and 77 percent were female. Participants in the intervention were provided personalized amusement from a special therapist and a home nurse (e.g., serenading, jokes, funny dress-up) in 9-12 weekly sessions. Usual care was not defined. Three scales assessed primary outcomes (agitation/aggression measured by CMAI, general behavior measured by NPI-NH, and MOSES) at baseline, postintervention (3 months), and 3-months postintervention. Differences between groups were not reported. One scale assessed secondary outcomes (patient distress, QoL measured by DEMQoL) at baseline, postintervention (3 months), and 3-months postintervention. Differences between groups were not reported. Intermediate outcomes and adverse effects were not reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Acupuncture

Eligible Trial

Rodriguez-Mansilla et al. randomized 120 nursing home residents from three nursing home and/or assisted living facilities in Spain to massage (n = 40), ear acupuncture (n = 40), or control (n = 40).[75] Details of this study are provided in the massage section. We discuss the massage versus no-treatment arms with the other massage trial, and the acupuncture versus no treatment arms here. The ear acupuncture group received application of Shenmen Muscle relaxant located in the peripheral inferior concha, close to the spleen and liver with adhesive herbal seeds of Wangbuliuxing (Semen Vaccariae Segetalis). The techniques were performed by a qualified acupuncturist. The seeds were placed with adhesive tape, and were replaced with new seeds every 15 days. The intervention lasted for 12 weeks. General behavior was measured with an investigator-designed instrument asking staff about the number of behavior alterations (not defined). General behavior improved more in the intervention groups than the control group at postintervention (3 months) ($p < 0.001$) and were maintained at 2 months after completing the treatment (5 months) ($p < 0.021$). No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence for the effectiveness of this intervention.[75]

Massage Versus Ear Acupuncture

Eligible Trial

Two arms of one trial previously discussed are used to assess the comparative effectiveness of massage versus ear acupuncture on agitation/aggression. Rodriguez-Mansilla et al.'s trial was previously described.[75] General behavior was measured with an investigator-designed instrument

asking staff to report the number of behavior alterations (not defined). General behavior improved by a similar amount with either intervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence for the comparative effectiveness of these interventions.

Acupressure

Eligible Trial

Lin et al randomized 133 individuals with dementia residing in six Taiwanese nursing home special care units to acupressure (n = 42), structured Montessori-based activities (n = 39), or presence (attention control) (n = 52).[88] The study used a double-blind crossover design. The mean age of study participants was 80.1 years and 26 percent were female. Acupressure was used to treat agitation/aggression using five acupoints (Fengchi, Baihui, Shenmen, Niguan, and Sanyinjiao). Acupuncture sessions were conducted for 15 minutes once a day, 6 days a week, for 4 weeks. Sessions consisted of warmup activities (5 minutes) and acupressure to each acupoint for 2 minutes. Montessori-based activities consisted of sensory stimulation (e.g., rhythmic music) and activities associated with daily living (e.g., scooping, pouring, and squeezing). This was done 6 days a week for 4 weeks. Attention control consisted of engaging subjects in conversation and attempting to maintain the subject's attention for 15 minutes. This was done 6 days a week for 4 weeks. Groups were defined by the sequence in which they received the intervention and analysis was at the patient-intervention level. Results were reported by group after all patients received all interventions. Agitation/aggression was measured with the CMAI. Mean differences before crossover were not reported for agitation/aggression or any intermediate or secondary outcomes, or adverse effects.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provides insufficient evidence for the effectiveness of this intervention.

Reminiscence

Eligible Trial

Ito et al. randomized 60 vascular dementia patients residing in three Japanese nursing home facilities to group reminiscence (n = 20), social contact (n = 20), and a control group (n = 20).[89] The mean age of study participants was similar across all three arms (mean age in group reminiscence in 82.9 years, social contact 81.9 years, and control 82.1 years). In all three groups there were more woman than men. A team of 10 professionals from psychology, speech therapy, occupational therapy, social work, and nursing were trained to deliver group reminiscence therapy or social contact. Group reminiscence was delivered to four residents at a time and sessions were delivered 1 hour a week for 3 months. Residents in the social contact group (four residents per session) received a 1 hour session of reality orientation. The social contact group also participated in a protocol-based conversation. The control group received supportive care. General behavior, measured using MOSES Multi-dimensional Observation Scale for Elderly

Patients, showed no difference between groups after the intervention. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Pleasant Experiences

Eligible Trial

Lichtenberg et al. randomized 20 residents from two dementia special care units to individually designed pleasant event one-on-one activity (n = 9) or usual care (n = 11).[90] The mean age of all residents was 85 years and 90 percent of participants were female. The behavioral treatment was an individually designed pleasant activity delivered by a trained nursing assistant three times a week for 20 to 30 minutes a session for 3 months. Pleasant activities were identified for the residents based on interviews with family caregivers. Repeated measures analysis of variance was used to evaluate treatment effects. No group differences were reported for general behavior as measured using the BEHAVE-AD instrument; both groups improved. A significant group time interaction occurred in favor of the intervention group ($p < 0.001$). No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provides insufficient evidence regarding the effectiveness of this intervention.

Multisensory Intervention Versus Recreational Activities

Eligible Trial

Baker et al. randomized 136 residents or day program participants with dementia in facilities in the United Kingdom, the Netherlands, and Sweden to multisensory stimulation (n = 65) or a group activity (n = 71).[44] The mean age of residents randomized to multisensory was 81 years, and the mean age of residents randomized to group activity was 83 years. The multisensory intervention involved one-to-one staff participant time in the sensory room where participants could experience touch, smell, sound, and sight. Group activities included activities such as playing card games or doing quizzes. Both multisensory and group activity sessions were conducted for 30 minutes twice a week for 4 weeks (a total of eight sessions). Pre-, mid- (after the fourth session), immediate post- (after the final session), and postintervention assessments (1 month after the final session) were taken. Changes in general behavior measured with several instruments (Behaviour Observation Scale for Intra-mural Psychogeriatrics; BRS; REHAB [general and deviant behavior]; and BMD [total, active/disturbed]) were similar with intervention and control. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provides insufficient evidence regarding the comparative effectiveness of these interventions.

Activities of Daily Living Intervention

Eligible Trial

Beck et al. randomized 127 nursing home residents with dementia and behavioral symptoms to five groups including an activities of daily living intervention (n = 28), a psychosocial activity intervention (n = 29), a combined activities of daily living/psychosocial activities group (n = 22), attention control (n = 29), or usual care (n = 19).[91] Those with severe activity limitations or some psychiatric or medical diagnoses that would restrict participation were excluded. The mean age of all study participants was 82.5 years and 81 percent were female. The interventions were conducted over 2 weeks by project-hired nursing assistants under the supervision of the principal investigator. The goal of the activities of daily living intervention was to reduce agitation/aggression during bathing, grooming, dressing, and eating the noon meal. It was administered 45 to 60 minutes per day during these activities and entails breaking down the tasks, guiding the person initially, and applying individualized problem solving. The psychosocial activity interventions required caregivers to apply 25 standardized modules to help with communication, self-esteem, and personal identity. The modules lasted up to 30 minutes a day depending on resident tolerance. The combined group had both interventions. The attention control group received a 30-minute interaction with a caregiver each day. General behavior measured using the Disruptive Behavior Scale showed similar effects across groups. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness or comparative effectiveness of these interventions.

Simulated Presence

Eligible Trial

Camberg et al. conducted a crossover RCT and randomized 54 nursing home residents with dementia and agitation/aggression to simulated family presence, attention control, or usual care.[92] The mean age of study participants was 82.7 years and 77 percent were female. Simulated family presence consisted of an audiotape made by a family member and delivered with a telephone call. Because the residents in the study were impaired in recent memory, the recording was perceived as new each time it was heard. Audiotapes were used at least twice a day Monday–Friday for 17 days over 4 weeks. Attention control consisted of an audio tape recording with readings from the newspaper. Attention control was similar to simulated family presence, but recordings were not personalized. Usual care consisted of routine management of behavioral symptoms (e.g., staff interactions, redirection, or physical restraints). Direct observation showed no difference between groups, but staff observation logs showed a greater reduction in behavioral symptoms after simulated presence. Residents showed 67 percent reduction in agitation/aggression after simulated family presence compared with 46 percent reduction after attention control and 59 percent reduction after usual care. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Enhancing Family Visits

Eligible Trial

McCallion et al. randomized 66 dementia residents of five nursing homes to a Family Visit Education Program (n = 32) or usual care (n = 34).[93] The mean age of residents was 86 years. In both the intervention (94%) and usual care groups (65%) there were more females than males. The intervention was a structured 8-week training for family members to make more constructive use of their visits. It consisted of four group sessions with role-playing and teaching, followed by a session where the trainer observed the family member with the resident for 20-30 minutes and gave 15 minutes of individualized feedback. Groups varied from four to eight participants. Agitation/aggression was measured with two versions of the CMAI (CMAI-O based on observations and CMAI-N based on nurse report) and general behavior with MOSES at baseline and 3 and 6 months postintervention. Significant group and time interactions were observed on the physically nonaggressive behavior subscale of the CMAI-N from baseline to 6 months. During this time, physically nonaggressive behavior decreased more for residents in the intervention than for residents in usual care ($p < 0.001$). During this time period, verbal behavior increased more for residents in the intervention group than in usual care. Finally, from baseline to 3 months, restraints were used less on residents in the intervention group than those in usual care ($p <0.024$). However, during this same period of time fewer psychotropic drugs were used in residents in usual care than those in the intervention group ($p<0.05$). No other intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provided insufficient evidence regarding the effectiveness of this intervention.

Electrostimulation

Eligible Trial

Hozumi et al. randomized 27 nursing home residents with dementia to electrostimulation (n = 14) or sham therapy (n = 13).[94] The age of residents varied between 58 and 86 years and 56 percent were female. Electrodes were attached to the forehead using a defined amount of current. Placebo participants had the same electrodes but were not connected to a device. Intervention was performed daily for 2 weeks. Behavioral symptoms were evaluated on the last day of the intervention. Different domains of agitation/aggression were assessed with an unknown scale. Intervention and control did not differ for behavioral disorders. No intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

One trial with study limitations and imprecise estimates provides insufficient evidence regarding the effectiveness of this intervention.

Multisensory Group Intervention

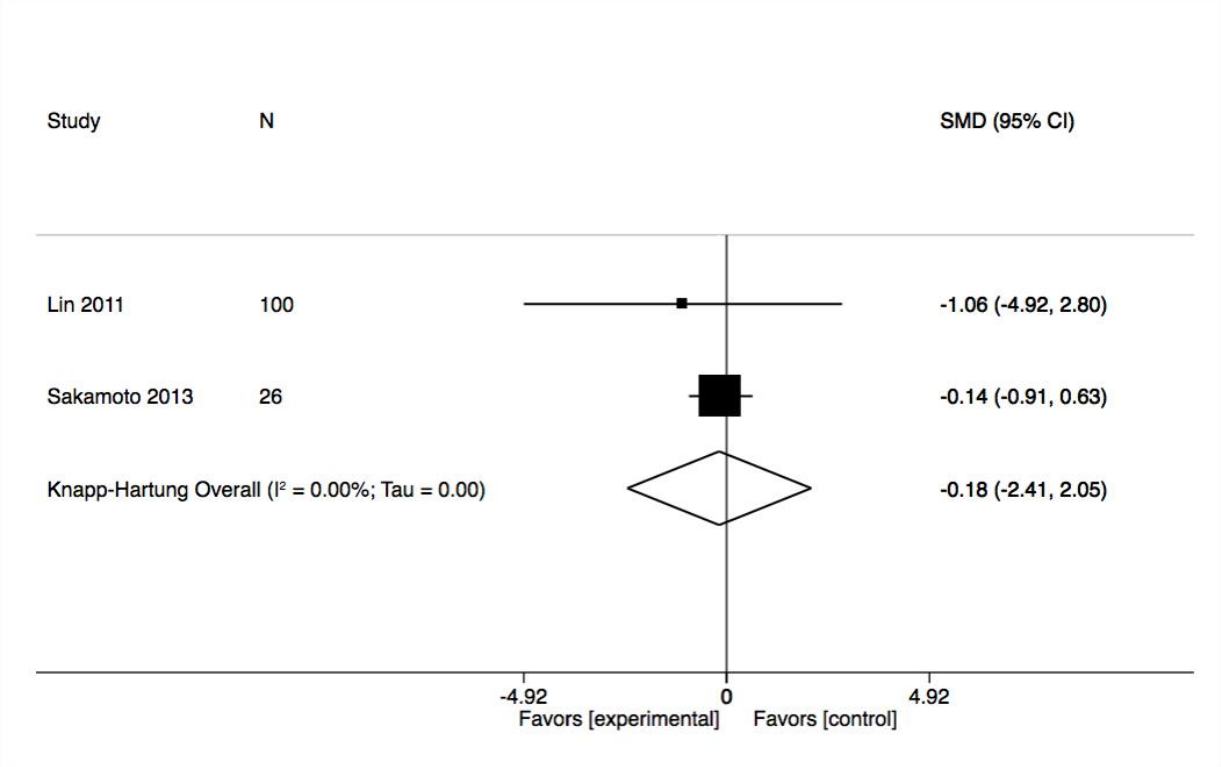
Eligible Trial

Robichaud et al. randomized 40 residents with dementia who resided in three institutions in Quebec City, Quebec, Canada, to a sensory integration program (n = 22) or usual leisure activities (n = 18).[95] Randomization was stratified according to dementia severity. The mean age of residents in the intervention group was 76.6 years and the mean age of residents in the control group was 80.1 years. Sensory integration incorporated reality orientation and movement approaches. Each session included five steps: (1) opening of the session, reality orientation; (2) activities emphasizing bodily responses: gross, proprioceptive, and vestibular movements; (3) sensory stimulations: taste, smell, touch, sight, hearing; (4) cognitive stimulations for organizing thought: memory, concentration, judgment; and (5) closing the session: socialization, pleasure, and relaxation. Subjects in the study group participated in three 45-minute group sessions per week for 10 weeks. Separate scores were obtained for two scales RMBPC (Revised Memory and Behavior Problem Checklist) (frequency, depression, memory, psychomotor slowness, disruptive behavior) and (reaction, depression, memory, psychomotor slowness, disruptive behavior). Each subject was evaluated at the beginning and end of the intervention program. General behavior measured with RMBPC was similar for intervention and control postintervention. No other intermediate outcomes, secondary outcomes, or adverse effects were reported.

Evidence Synthesis and Strength of Evidence

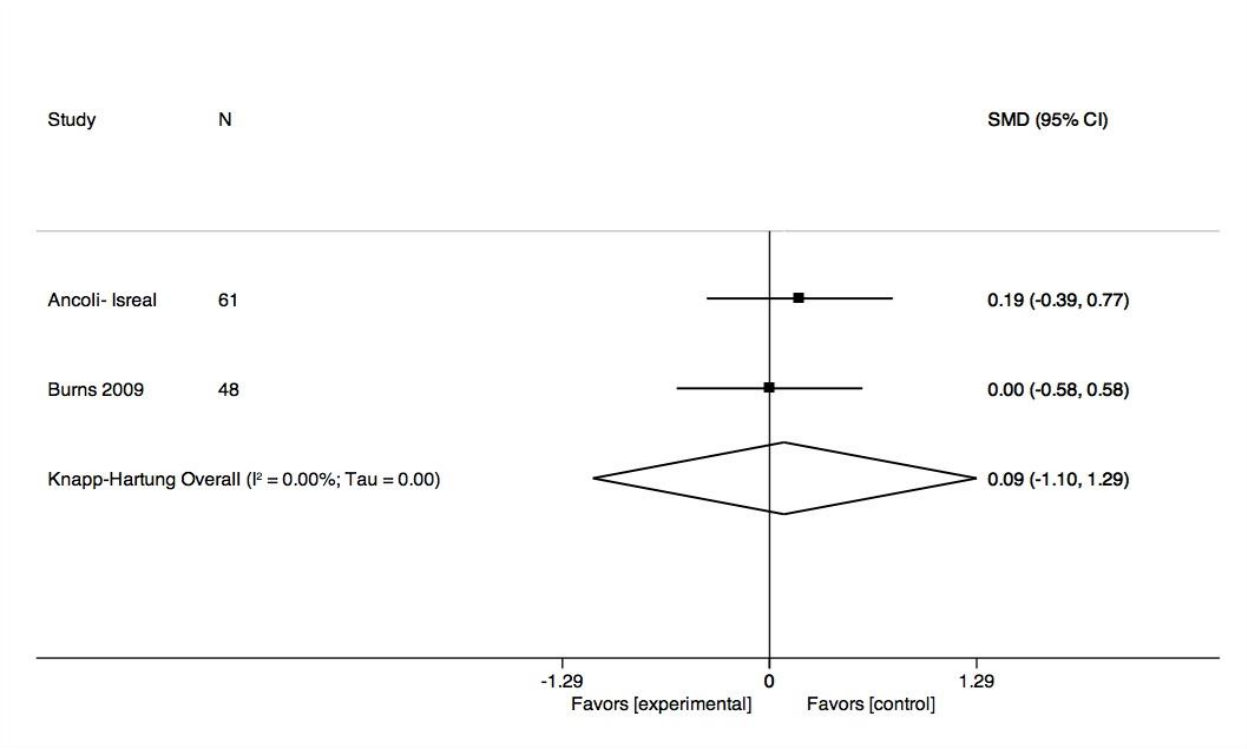
One trial with study limitations and imprecise estimates provides insufficient evidence regarding the effectiveness of this intervention.

Figure 3. Music therapy versus control (impact of treatment on agitation/aggression)



SMD=Standardized mean difference; CI=confidence interval.

Figure 4. Bright light versus standard light (impact of treatment on agitation/aggression)



SMD = Standardized mean difference; CI = confidence interval

Table 5. Patient-level interventions for agitation/aggression in nursing home and assisted living facility residents with dementia

Intervention-Comparison	Total Number of Studies (Number of Participants)	Strength of Evidence - Summary of Results
Agitation/Aggression		
Music vs. no treatment/attention control (for sustained reduction in agitation/aggression)	4 (233)	Low – agitation/aggression not improved
Music vs. no treatment/attention control (for immediate reduction in agitation/aggression)	1 (34)	Insufficient – no conclusions drawn
Music vs. comparison intervention (for sustained reduction in agitation/aggression)	4 (218)	Low – agitation/aggression not improved
Aroma therapy with Lavender vs. no treatment/attention control	3 (245)	Low – agitation/aggression not improved
Aroma therapy with Melissa vs. no treatment/attention control	1 (72)	Insufficient – no conclusions drawn
Aroma therapy with Melissa vs. comparison intervention	1 (77)	Insufficient – no conclusions drawn
Light therapy vs. no treatment/attention control	4 (225)	Low – agitation/aggression not improved
Therapeutic touch vs. no treatment/attention control	1 (51)	Insufficient – no conclusions drawn
Massage vs. no treatment/attention control	1 (34)	Insufficient – no conclusions drawn
Massage vs. comparison intervention	1 (55)	Insufficient – no conclusions drawn
Tailored activities vs. nontailored activities	4 (334)	Insufficient – no conclusions drawn
Tailored activities vs. tailored activities	2 (158)	Low – agitation/aggression not improved
Exercise vs. no treatment/attention control	No studies reporting	Insufficient – no conclusions drawn
Exercise vs. interactive control	No studies reporting	Insufficient – no conclusions drawn
Aroma-acupressure vs. no treatment/attention control	1 (113)	Insufficient – no conclusions drawn
Multisensory room vs. no treatment/attention control	1 (32)	Insufficient – no conclusions drawn
Multisensory room vs. interactive control	1 (32)	Insufficient – no conclusions drawn
Humor therapy vs. no treatment/attention control	1 (398)	Insufficient – no conclusions drawn
Acupuncture	No studies reporting	Insufficient – no conclusions drawn
Massage vs. ear acupuncture	No studies reporting	Insufficient – no conclusions drawn
Acupressure	1 (133)	Insufficient – no conclusions drawn
Structured activities	1 (133)	Insufficient – no conclusions drawn
Acupressure vs. structured activities	1 (133)	Insufficient – no conclusions drawn
Reminiscence	No studies reporting	Insufficient – no conclusions drawn
Pleasant experiences	No studies reporting	Insufficient – no conclusions drawn
Multisensory vs. recreation	No studies reporting	Insufficient – no conclusions drawn
Activities of daily living vs. psychosocial activity	No studies reporting	Insufficient – no conclusions drawn
Simulated presence	1 (54)	Insufficient – no conclusions drawn
Enhancing family visits	1 (66)	Insufficient – no conclusions drawn
Electro stimulation	1 (27)	Insufficient – no conclusions drawn
Group multistimulation vs. leisure activities	1 (40)	Insufficient – no conclusions drawn
General Behavior		
Music vs. no treatment/attention control (for sustained reduction in agitation/aggression)	2 (99)	Insufficient – no conclusions drawn
Music vs. no treatment/attention control (for immediate reduction in agitation/aggression)	No studies reported	Insufficient – no conclusions drawn
Music vs. comparison intervention (for sustained reduction in agitation/aggression)	2(125)	Insufficient – no conclusions drawn
Aroma therapy with Lavender vs. no treatment/attention control	2 (98)	Insufficient – no conclusions drawn
Aroma therapy with Melissa vs. no	No studies reported	Insufficient – no conclusions drawn

Intervention-Comparison	Total Number of Studies (Number of Participants)	Strength of Evidence - Summary of Results
treatment/attention control		
Aroma therapy with Melissa vs. comparison intervention	1 (77)	Insufficient – no conclusions drawn
Light therapy vs. no treatment/attention control	3 (133)	Low – general behavior not improved
Therapeutic touch vs. no treatment/attention control	2 (108)	Insufficient – no conclusions drawn
Massage vs. no treatment/attention control	1 (71)	Insufficient – no conclusions drawn
Tailored activities vs. nontailored activities	1 (87)	Insufficient – no conclusions drawn
Tailored activities vs. tailored activities	No studies reported	Insufficient – no conclusions drawn
Exercise vs. no treatment/attention control	1 (134)	Insufficient – no conclusions drawn
Exercise vs. interactive control	1 (170)	Insufficient – no conclusions drawn
Multisensory room + massage + exercise vs. no treatment/attention control	1 (39)	Insufficient – no conclusions drawn
Multisensory room vs. no treatment/attention control	1 (32)	Insufficient – no conclusions drawn
Multisensory room vs. interactive control	1 (32)	Insufficient – no conclusions drawn
Humor therapy vs. no treatment/attention control	1 (398)	Insufficient – no conclusions drawn
Acupuncture	1 (76)	Insufficient – no conclusions drawn
Massage vs. ear acupuncture	1 (75)	Insufficient – no conclusions drawn
Acupressure	No studies reported	Insufficient – no conclusions drawn
Acupressure vs. structured activities	No studies reported	Insufficient – no conclusions drawn
Reminiscence	1 (40)	Insufficient – no conclusions drawn
Pleasant experiences	1 (20)	Insufficient – no conclusions drawn
Multisensory vs. recreation	1 (136)	Insufficient – no conclusions drawn
Activities of daily living vs. psychosocial activity	1 (127)	Insufficient – no conclusions drawn
Simulated presence	No studies reported	Insufficient – no conclusions drawn
Enhancing family visits	1 (66)	Insufficient – no conclusions drawn
Electro stimulation	No studies reported	Insufficient – no conclusions drawn
Group Multistimulation vs. leisure activities	1 (40)	Insufficient – no conclusions drawn

Note: only one study reported an intermediate outcome; data were insufficient – no conclusions drawn

Table 6. Efficacy and comparative effectiveness of patient-level interventions for agitation/aggression in nursing home and assisted living facility residents with dementia

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Music - Efficacy		
Sakamoto, 2013[58] RCT Japan Music listening vs. interactive music vs. attention control n=39 Moderate risk of bias	**Treatment 1**: Music listening intervention with participants listening to music via CD **Treatment 2**: Interactive music intervention with participants listening to music on CD but also participating in an interactive activity (clapping, singing, dancing) **Comparison**: Attention control - 30 minutes once/week for 10 weeks - music facilitator	***Agitation/Aggression*** **Behave-AD Aggressiveness,** mean (SD) Baseline: 1.5 (1.8) vs. 2.5 (2.4) vs. 2.5 (3.1) Postintervention: 1.5 (0.9) vs. 0.7 (1.0) vs. 3.2 (3.0) 3-week postintervention: 1.3 (2.0) vs. 2.5 (2.2) vs. 2.9 (3.1) ***General behavior*** **Behave-AD,** Global mean (SD) Baseline: 0.9 (0.5) vs. 1.5 (0.7) vs. 1.3 (0.7) Postintervention: 0.8 (0.4) vs. 0.7 (1.0) vs. 1.5 (0.8) 3-week postintervention: 1.1 (0.5) vs. 1.2 (0.6) vs. 2.2 (0.9) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Lin, 2011[59] RCT Taiwan Group music therapy vs. usual care n=100 Moderate risk of bias	**Treatment**: Group music therapy intervention **Comparison**: usual daily activities (not otherwise specified) - 30-minute sessions twice weekly for 6 weeks (12 total sessions) - researcher trained in university music therapy programs	***Agitation/Aggression*** **C-CMAI,** mean (SD) Baseline: 43.12 (16.32) vs. 37.78 (11.04) Postintervention: 36.37 (10.64) vs. 38.55 (10.27) One month postintervention: 35.69 (9.99) vs. 37.75 (9.70) ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Raglio, 2010[60] RCT Italy Cyclical music therapy + standard care vs. standard care alone n=60 Moderate risk of bias	**Treatment**: In groups of 3 participants, participants and the music therapist interacted through musical improvisation on various instruments and with nonverbal behaviors; group also received standard care (educational activities and entertainment – reading, physical activities) **Comparison**: standard care - 3 cycles of 12 interactive sessions, 3 weekly 30-minute sessions; 1 month washout period between each cycle; total of 6 months - music therapist	***Agitation/Aggression*** **NPI Agitation Subscale,** mean (SD) Baseline: 3.13 (NR) vs. 3.87 (NR) Postintervention: 1.36(NR) vs. 3.00 (NR) 4-week postintervention: 1.57(NR) vs. 2.92 (NR) ***General behavior*** **NPI:** results presented graphically; authors report lower scores postintervention; between-group MANOVA of treatment effect - ($F_{1,51}$=4.84, p<0.05); difference likely not significant at postintervention. ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Remington, 2002[61] RCT United States Calming music vs. no treatment n = 26 (for these two groups) Moderate risk of bias	**Treatment**: taped calming music played from a CD player once **Comparison**: No treatment - 1 10-minute session - trained research assistant	***Agitation/Aggression*** **CMAI,** mean (SD) Baseline: 18.41 (11.19) vs. 21.76 (9.09) Immediately postintervention: 9.18 (11.11) vs. 21.88 (10.38) 10 minutes postintervention: 7.76 (9.55) vs. 20.88 (8.66) 20 minutes postintervention: 3.06 (5.44) vs. 20.47 (10.90) Repeated measures analysis of variance across all 4 groups: $F_{3,9}$=6.47; p<0.01 ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Music – Comparative Effectiveness		
Sakamoto, 2013[58] RCT Japan Music listening vs. interactive music n = 26 Moderate risk of bias	**Treatment 1**: Music listening intervention with participants listening to music via CD **Treatment 2**: Interactive music intervention with participants listening to music on CD but also participating in an interactive activity (clapping, singing, dancing) **Comparison**: Attention control - 30 minutes once/week for 10 weeks - music facilitator	***Agitation/Aggression*** **Behave-AD Aggressiveness,** mean (SD) Baseline: 1.5 (1.8) vs. 2.5 (2.4) Postintervention: 1.5 (0.9) vs. 0.7 (1.0) 3-week postintervention: 1.3 (2.0) vs. 2.5 (2.2) ***General behavior*** **Behave-AD Global,** mean (SD) Baseline: 0.9 (0.5) vs. 1.5 (0.7) Postintervention: 0.8 (0.4) vs. 0.7 (1.0) 3-week postintervention: 1.1 (0.5) vs. 1.2 (0.6) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Vink, 2013[63] RCT The Netherlands Group music therapy vs. recreational activity n=94 Moderate risk of bias	**Treatment**: Group music therapy **Comparison**: Recreational activity - 40 minute sessions twice/week for 4 months (up to 34 sessions) - music therapists, occupational therapists	***Agitation/Aggression*** **CMAI** Means– shown in figures; AMD NS (F=2.89; p=0.09) ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Cooke, 2010[62] RCT-Crossover Australia Music-reading vs. reading-music n = 47 Moderate risk of bias	**Treatment**: Live, somewhat tailored music program with facilitated engagement and song **Comparison**: interactive reading intervention with short stories, jokes, and quizzes - 40 minute sessions 3 times/week for 8 weeks (total of 24 sessions) - musician and reading group facilitator trained in working with persons with dementia	***Agitation/Aggression*** **CMAI-SF,** mean (95% CI) Baseline: 1.66 (1.42-1.91) vs. 1.54 (1.32-1.77) After first arm: 1.67 (1.49-1.85) vs. 1.66 (1.37-1.96) ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Remington, 2002[61] RCT United States Calming music vs. hand massage vs. calming music and hand massage vs. control n = 68 (4 arms) Moderate risk of bias	**Treatment 1**: taped calming music played from a CD player (new age arrangement of Pachelbel's Canon in D) **Treatment 2**: hand massage; light pressure and slow strokes to each hand for 5 minutes **Treatment 3**: music + massage simultaneously **Comparison**: No treatment - 1 10-minute session - trained research assistant	***Agitation/Aggression*** **CMAI,** mean (SD) Baseline: 18.41 (11.19) vs. 16.47 (9.94) vs. 22.00 (11.94) Immediately postintervention: 9.18 (11.11) vs. 10.35 (11.20) vs. 8.59 (7.87) 10 minutes postintervention: 7.76 (9.55) vs. 7.76 (9.55) vs. 7.06 (7.08) 20 minutes postintervention: 3.06 (5.44) vs. 3.06 (5.44) vs. 3.76 (4.40) ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Aromatherapy		
Yang, 2015[67] RCT Taiwan Aroma-acupressure vs. aromatherapy vs. treatment as usual n=186 Moderate risk of bias	**Treatment**: aroma-acupressure (5 acupuncture points pressed for two minutes each with 2.5% lavender oil) **Comparison 1**: aromatherapy (2.5% lavender oil applied to same 5 points without pressing) **Comparison 2**: treatment as usual (usual daily care routine, not otherwise specified) - 1 15-minute session (5 points pressed for 2 minutes, plus 5-minute warmup exercise) per day, 5 days per week over 4 weeks - research assistant, unclear who performed interventions	***Agitation/Aggression*** CMAI, Mean(SD) Postintervention: 43.24(10.00) vs. 41.08(8.24) vs. 41.72 (5.08) 3-week postintervention: 51.21(11.95) vs. 39.80 (7.27) vs. 42.13(5.53); significant decline of treatment effects in aroma-acupressure group (*p*-value NR) Unclear if significance tested between-group differences. ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** None **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Fu, 2013[64] RCT Australia Lavender vs. placebo water spray n = 45 (in these two arms) Moderate risk of bias	**Treatment**: Lavender treatments **Comparison**: water treatments - twice/day (morning and afternoon) 7 days/week for 6 weeks - researcher, trained research assistants	***Agitation/Aggression*** **CMAI – aggressive behaviors** No overall results reported; no statistically significant difference between groups on individual behaviors reported. ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Burns, 2011[68] RCT United Kingdom Active aromatherapy + placebo medication vs. placebo aromatherapy + active medication vs. placebo aromatherapy + placebo medication n=114 Moderate risk of bias	**Treatment**: Melissa essential oil (200mg dose) + placebo medication **Comparison 1**: Placebo aromatherapy (sunflower oil) + donepezil (5mg daily for 1 month, then increased to 10mg daily) **Comparison 2**: Placebos - aromatherapy/placebo administered twice daily for 1-2 minutes; medication/placebo administered daily; study length was 3 months - research nurse, caregivers	***Agitation/Aggression*** **PAS**, median(95% CI) change from baseline 12-week postintervention: -0.7 (-1.7, 0) vs. 0 (-1.7, 0.3) vs. -0.7 (-1.7, 0); p=0.56 ***General behavior*** **NPI**, mean(95% CI) change from baseline at 12-week postintervention: –7.2 (–12.6, –1.7) vs. –2.0 (–7.2, 3.2) vs. –10.0 (–17.2, –3.0); p=0.52 ***Patient Distress, QoL*** **Blau QoL**, mean(97% CI) change from baseline at 12-week postintervention: 17 (–13, 47) vs. –39 (–63, 15) vs. –2 (–34, 30); donepezil group significantly decreased in QoL compared with aromatherapy group (p=0.033) ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Fujii, 2008[65] RCT Japan Lavender aromatherapy vs. no treatment n = 28 Moderate risk of bias	**Treatment**: Lavender aromatherapy applied to clothing of the patients **Comparison**: No treatment - 3 times/day 1 hour after meals for 4 weeks - care staff, trained nurse	***Agitation/Aggression:*** NR ***General Behavior*** **NPI**, mean (SD) Baseline: 31 (10) vs. 32 (11) Postintervention: 18 (12) vs. 27 (12) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Lin, 2007[66] RCT-Crossover Hong Kong Lavender vs. sunflower aromatherapy n = 70 Moderate risk of bias	**Treatment**: Two drops of the treatment were placed on each side of the pillow of the participant during sleep at night; participants crossed over to the other treatment after a 2 week washout period **Comparison**: sunflower oil - 6 weeks (+2 week washout) - care home staff	***Agitation/Aggression*** **C-CMAI**, mean (SD) Baseline: 63.17 (17.81) vs. 63.94 (SD 17.67) Postintervention: 58.77 (16.74) vs. 63.90 (17.73) ***General Behavior*** **CNPI**, mean (SD) Baseline: 24.68 (10.54) vs. 24.33 (10.08)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
		Postintervention: 17.77 (7.52) vs. 24.41 (10.24) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Ballard, 2002[35] RCT United Kingdom Melissa essential oil vs. sunflower oil n = 72 Moderate risk of bias	**Treatment**: Melissa essential oil was combined with a base lotion and applied to patients' faces and arms **Comparison**: sunflower oil - twice/day for 4 weeks - care assistant	***Agitation/Aggression*** **CMAI,** Proportion making 30% decrease in score Postintervention: 60% vs. 14%, χ^2=16.3; p<.0001 **CMAI,** median change Postintervention: -22.0 vs. -6.5; Z=4.1; p<.0001 ***General Behavior:*** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** Prescribed additional psychotropic drugs during the study: 6% vs. 8%
Light		
Burns, 2009[70] RCT United Kingdom Bright light vs. standard light n = 48 Moderate risk of bias	**Treatment**: Bright light **Comparison**: Standard light - 2 hours of exposure daily over 2 weeks - nurse	***Agitation/Aggression*** **CMAI**, mean (SD) Baseline: 62.0 (18.4) vs. 57.5 (13.8) Week 4: 51.8 (22.8) vs. 50.9 (15.6) Week 8: 49.5 (SD 13.8) vs. 49.5 (SD 10.4) ***General Behavior*** **Crichton Royal Behavior Rating**, mean (SD) Baseline: 34.2 (6.5) vs. 35.6 (7.6) Week 4: 41.3 (2.9) vs. 42.8 (1.4) Week 8: 43.8 (3.4) vs. 44.2 (2.5) **MOUSEPAD**, mean (SD) Baseline: 13.5 (11.6) vs. 13.4 (8.8) Week 4: 7.8 (7.9) vs. 7.8 (SD 4.3) Week 8: 8.0 (7.8) vs. 7.7 (3.7) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Dowling, 2007[71] RCT United States Morning light vs. afternoon light vs. control n = 70 Moderate risk of bias	**Treatment 1**: Morning bright light with usual activities **Treatment 2**: Afternoon bright light with usual activities **Comparison**: usual activities with normal indoor light; activities not described - 1 hour per day on Mondays-Fridays for 10 weeks - research staff	***Agitation/Aggression*** **NPI Agitation/aggression**, mean (SD) Baseline: 5.3 (3.5) vs. 3.7 (2.4) vs. 5.8 (3.4) Postintervention: 5.5 (3.3) vs. 4.8 (2.6) vs. 4.3 (2.5) ***General Behavior*** **NPI**, mean (SD) Baseline: 29.4 (20.7) vs. 27.0 (15.7) vs. 24.1 (15.8) Postintervention: 26.3 (13.9) vs. 27.5 (16.5) vs. 19.6 (10.8) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Ancoli-Israel, 2003[69] RCT United States Morning bright light vs. evening bright light vs. dim light n = 92 Moderate risk of bias	**Treatment 1**: Morning bright light **Treatment 2**: Evening bright light **Comparison**: morning exposure to dim red light - 2 hours daily for 10 days - research staff	***Agitation/Aggression*** **CMAI** Data not provided; text reports no overall difference among treatment groups ($F_{16,453}$=0.99; p=0.46) **ABRS Verbal Agitation-morning,** mean (SD) Baseline: 0.19 (0.53) vs. 0.34 (0.71) vs. 0.18 (0.55) Days 6-10: 0.22 (0.59) vs. 0.20 (0.56) vs. 0.12 (0.47) Postintervention: 0.12 (0.45) vs. 0.20 (0.53) vs. 0.10 (0.40) **Agitation-ABRS Verbal Agitation-evening,** mean (SD) Baseline: 0.23 (0.59) vs. 0.27 (0.63) vs. 0.26 (0.59) Days 6-10: 0.27 (0.64) vs. 0.33 (0.68) vs. 0.16 (0.52) Postintervention: 0.25 (0.60) vs. 0.29 (0.67) vs. 0.18 (0.53) ***General Behavior:*** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Lyketsos, 1999[72] RCT-Crossover United States Bright light vs. dim blinking light n = 15 Moderate risk of bias	**Treatment**: Bright light; 1 week washout then cross-over **Comparison**: dim, blinking light - 1 hour every morning for 8 weeks (+ 1 week washout) - nursing staff	***Agitation/Aggression*** **Behave-AD Aggression subscale** No significant differences, did not present data (p>0.05) ***General Behavior*** **Behave-AD,** mean (SD) Baseline: 14.9 (3.83) vs. 13.7 (3.49) Week 4: 12.6 (SD 4.79) vs. 10.7 (4.85) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Massage		
Moyle, 2014[76] RCT Australia Foot massage vs. attention control n=55 Moderate risk of bias	**Treatment**: 10-minute foot massage; light pressure with unscented lotion. Crossover. **Comparison**: attention control – quiet presence (no talking or touching) - 4 hours (1-5pm) Monday-Friday for 3 weeks, 3 week washout, then 3 weeks of crossover treatment (9 weeks total) - research assistants (trained massage therapists)	***Agitation/Aggression*** **CMAI**, Mean(SD)– p-values reported for between group differences at baseline only Total postintervention: 27.76 (9.63) vs. 36.07 (9.72) Physical non-aggression postintervention: 10.08 (5.01) vs. 12.25 (4.52) Physical aggression postintervention: 5.36 (3.07) vs. 6.43 (3.50) Verbal nonaggression postintervention: 6.40 (3.44) vs. 9.57 (3.82) Verbal aggression postintervention: 5.92 (2.81) vs. 7.82 (3.76) ***General behavior*:** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Rodriguez-Mansilla, 2013[75] RCT Spain Massage therapy vs. no treatment control n = 71 Moderate risk of bias	**Treatment**: received back and lower limb massages **Comparison**: no treatment - 20 minute Monday-Friday for 3 months - physiotherapist, certified acupuncturist	***Agitation/Aggression:*** NR ***General Behavior*** **Behavior alterations** 3 months: 34/36 vs. 0/35 5 months: 28/35 vs. 32/36 ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Remington, 2002[61] RCT United States Hand massage vs. no treatment n = 34 (for these two groups) Moderate risk of bias	**Treatment**: taped calming music played from a CD player **Comparison**: No treatment - 1 10-minute session - trained research assistant	***Agitation/Aggression*** **CMAI,** mean (SD) Baseline: 16.47 (9.94) vs. 21.76 (9.09) Postintervention: 10.35 (11.20) vs. 21.88 (10.38) 10 minutes postintervention: 7.76 (9.55) vs. 20.88 (8.66) 20 minutes postintervention: 3.06 (5.44) vs. 20.47 (10.90) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Tailored vs. Nontailored Activity		
Van Haitsma, 2015[77] RCT United States Tailored-activity vs. attention control vs. treatment as usual n=180 Moderate risk of bias	**Treatment**: preference-based activity; one-to-one activity tailored to patients' preferences and abilities; preferences measured by Preferences for Everyday Living Inventory-Nursing Home questionnaire. Activities included exercise, music, reminiscence, snacks, etc. **Comparison 1**: attention control – one-to-one standard activity (reading magazine, conversing, etc.) **Comparison 2**: treatment as usual - approximately 6 10-minute sessions, 3 days per week, over 3 weeks - certified nursing assistants	***Agitation/Aggression*** **Nonverbal Behavior Observations-Aggression**, Mean (SE) Postintervention: 0.061 (0.04) vs. 0.117 (0.04) vs. 0.0 (0.02); aggression was significantly lower in usual care compared with attention control (p<0.01), all other comparisons between groups NS ***General behavior*** **Nonverbal Behavior Observations-General restlessness**, Mean (SE) Postintervention: 6.50 (5.66) vs. 5.28 (5.56) vs. 23.47 (3.60); significantly more restless behaviors observed in usual care compared with attention control of intervention (p<0.01), no difference between attention control and intervention groups ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Van der Ploeg, 2013[78] RCT – Crossover Australia Montessori activities vs. nonpersonalized activity n=44 Moderate risk of bias	**Treatment**: personalized one-on-one interactions using Montessori based activities **Comparison**: nonpersonalized activity - 4 weeks: 30 minute sessions twice weekly; crossover occurred after 2 weeks - performed by family members	***Agitation/Aggression*** **Target behavior present per minute**, mean (SD) Baseline: 16.7 (9.9) vs. 17.1 (9.8) During intervention: 8.4 (9.9) vs.10.0 (10.4) Postintervention: 17.6 (10.3) vs. 17.0 (9.4) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Cohen-Mansfield, 2012[79] RCT United States TREA vs. Staff Training n=125 Moderate risk of bias	**Treatment**: TREA (Treatment Routes for Exploring Agitation) designed to meet needs based on resident needs, interests, and preferences **Comparison**: staff training on behavior only - 2 weeks - care staff, research assistants, physician	***Agitation/Aggression*** **ABMI,** mean (SD) Baseline: 8.76 (5.61) vs. 7.16 (7.61) Postintervention: 2.08 (2.68) vs. 7.92 (9.09) 2-way repeated measures ANCOVA shows reduction larger with TREA ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Kovach, 2004[80] RCT United States BACE vs. comparison n=78 Moderate risk of bias	**Treatment**: BACE (Balancing Arousal Controls Excesses) controls the daily activity schedule so there is a balance between the time a person is in a high-arousal and a low-arousal state; consists of 3 phases: phase 1 is to make an assessment; phase 2 is to diagnose and plan a correction of the arousal imbalance; phase 3 is to implement a new activity schedule. **Comparison**: NR - total duration unclear; activities performed in 1-week blocks - research assistants, geriatric nurse practitioner, staff nurses	***Agitation/Aggression*** **Visual Analog Scale (0-100 based upon observation),** mean (SD) Baseline: 38.97 (20.54) vs. 32.59 (21.66) Postintervention: 30.54 (15.31) vs. 32.25 (20.16) (Pretest to Postintervention * group: $F_{1,69}$=4.26; p=0.43) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Tailored Activities vs. Tailored Activities		
Kolanowski, 2005[82] RCT – Crossover United States Skill based vs. Interest based vs. Skill and Interest based n=30 Moderate risk of bias	**Treatment 1**: activities tailored to skill level only **Treatment 2**: activities tailored to style of interest only **Treatment 3**: combination of both tailor activities. **Comparison**: participants served as own controls in crossover design; no specific comparison condition - up to 20 minutes per day for 12 consecutive days, with a 2-day washout period between treatments. - trained research assistants	***Agitation/Aggression*** **CMAI,** mean (CI) Baseline: 2.85 (2.0-3.7) Postintervention: 1.35 (0.5-2.2) vs. 1.09 (0.3-1.9) vs. 1.14 (0.3-4.0) ***General Behavior:*** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Kolanowski, 2011[81] RCT United States Functional level vs. personality style of interest vs. both vs. interactive control n=128 Moderate risk of bias	**Treatment 1**: Functional group - activities tailored to skill level but opposite their personality style of interest; activities tailored to skill level and functionally challenging. **Treatment 2**: Personality group - activities tailored to be functionally challenging for them; activities tailored to skill level and functionally challenging. **Comparison**: Interactive control - activities that were functionally challenging and opposite their personality. - up to 20 minutes twice per day (morning and afternoon) 5 days each week for 3 consecutive weeks - nursing staff, research assistants	***Agitation/Aggression*** ***CMAI,*** Least Square means (95% CI): Baseline: 1.62 (0.9-2.4) vs. 2.46 (1.7-3.2) vs. 1.86 (1.1-2.6) vs. 1.88 (1.1-2.6) Postintervention: 1.2 (0.3-2.0) vs.1.7 (0.9-2.5) vs.1.5 (0.6-2.3) vs.1.10 (0.3-1.9) ***General Behavior:*** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study Design Country Comparison n Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	Primary Outcome-Instrument Results Intermediate Outcome-Instrument Results
Therapeutic Touch		
Hawranik, 2008[74] RCT Canada Therapeutic touch vs. simulated touch vs. usual care n = 51 Moderate risk of bias	**Treatment**: Therapeutic touch **Comparison**: Simulated therapeutic touch **Comparison 2**: No additional treatment - 1 session of 30-40 minutes/day for 5 days - therapeutic touch practitioners	***Agitation/Aggression*** **CMAI-Physical aggression (# behaviors),** mean (SD) Baseline: 0.94 (0.83) vs. 0.75 (0.77) vs. 0.78 (0.81) Day 5: 0.18 (0.39) vs. 0.13 (0.34) vs. 0.11 (0.32) 2-week postintervention: 0.65 (0.70) vs. 0.38 (0.62) vs. 0.28 (0.57) **Agitation – Physical nonaggression (# behaviors),** mean (SD) Baseline: 1.4 (0.71) vs. 1.18 (0.83) vs. 1.39 (1.1) Day 5: 0.29 (0.69) vs. 0.25 (0.45) vs. 0.67 (0.91) 2-week postintervention: 1.24 (0.83) vs. 0.63 (0.81) vs. 0.83 (0.79) **Agitation – Verbal agitation (# behaviors),** mean (SD) Baseline: 1.88 (1.45) vs. 1.69 (1.25) vs. 2.33 (1.53) Day 5: 0.35 (0.70) vs. 0.38 (0.89) vs. 0.89 (0.96) 2-week postintervention: 0.88 (0.86) vs. 1.50 (1.59) vs. 01.33 (1.24) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Woods, 2005[73] RCT United States Therapeutic touch vs. placebo therapeutic touch vs. usual care n = 57 Moderate risk of bias	**Treatment**: Therapeutic touch **Comparison**: placebo therapeutic touch - twice daily for 5-7 minutes each session for 3 days - therapeutic touch practitioner	***Agitation/Aggression***: NR ***General Behavior*** **Modified ABRS,** mean (SD) Baseline: 1.55 (1.03) vs. 1.64 (1.87) vs. 1.53 (0.99) Postintervention: 1.03 (0.67) vs. 1.24 (1.26) vs. 1.48 (1.12) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Exercise		
Telenius, 2015[83] RCT Norway High-intensity exercise vs. attention control n=170 Moderate risk of bias	**Treatment**: intensive strength and balance exercises (warm-up, 2 lower body exercises, 2 balance exercises, 12-repetitions per exercise for strengthening exercises) performed in small groups of 3-6 participants **Comparison**: attention control - leisure activities (light physical activity, reading, games, listening to music, conversation) - twice weekly 50-60-minute sessions for 12 weeks - physiotherapists, occupational therapists, nursing staff, volunteers, activity leaders	***Agitation/Aggression:*** NR ***General behavior*** **NPI-Q**, Mean(SD) Total postintervention: 5.1 (6.0) vs. 5.4 (6.5); p=0.17 Agitation postintervention: 1.5 (2.2) vs. 1.7 (2.3); p=0.07 – change from baseline agitation significantly lower in intervention group ***Patient Distress, QoL*** **QUALID**, Mean(SD) Postintervention: 17.1 (7.0) vs. 17.4 (6.6); p=0.97 ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Rolland, 2007[84] RCT France Exercise vs. Usual care n = 134 Moderate risk of bias	**Treatment**: The group exercise intervention consisted of aerobic, strength, flexibility, and balance training **Comparison**: Routine medical care - twice weekly for 1 hour per session for 12 months (88 sessions total proposed to each subject) - research staff, occupational therapist	***Agitation/Aggression***: NR ***General Behavior*** **NPI,** mean (SD) Baseline: 10.7 (6.9) vs. 11.4 (7.7) 6 months: 8.2 (SD 8.0) vs. 9.2 (8.3) Postintervention: 8.3 (SD 8.9) vs. 8.9 (10.4) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** There were no significant group differences during the 12 months between the exercise program group and the routine medical care group in observed total number of falls (139 vs. 136), fractures (5 vs. 2), or deaths (7 vs. 8) **Neuroleptic Use:** NR
Unique Comparisons		
Hutson, 2014[85] RCT United Kingdom Sonas vs. treatment as usual n=39 Moderate risk of bias	**Treatment**: Sonas intervention to enhance communication through engagement in multisensory stimulation (listen to music, taste and smell food, looking at interesting items to reminisce, moving in stretches and light exercise, receive massages; singing and dancing invited) **Comparison**: engaged in usual activities (not further described) - 14 45-minute sessions over 7-8 weeks - care home staff trained in Sonas delivery	***Agitation/Aggression:*** NR ***General behavior*** **NPI-Q**, Mean(SD) Behavior - overall score, postintervention: 14.68 (16.38) vs. 9.31 (13.26) Behavior - severity, postintervention: 8.25 (6.09) vs.7.06 (4.91) Behavior - distress, postintervention: 7.72 (7.31) vs.4.38 (5.77) ***Patient Distress, QoL*** **QoL-AD**, Mean(SD) Postintervention: 32.26 (4.64) vs. 32.91 7.37) ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Maseda, 2014[86] RCT Spain Multisensory stimulation room vs. individualized activities vs. control n=32 Moderate risk of bias	**Treatment**: Multisensory stimulation room of nondirective stimulation and one-on-one time with therapist; included fiber-optic cables, water columns, vibrating water bed, mirror, video, music, aroma therapy, etc. **Comparison 1**: Directive, one-to-one individualized activity sessions to stimulate intellectually and physically (cards, quizzes, photograph viewing, etc.) **Comparison 2**: Treatment as usual (cognitive stimulation group sessions, activities for daily living training) - 2 30-minute weekly sessions over 16 weeks - psychologist, occupational therapist	***Agitation/Aggression*** **CMAI**: Results reported graphically ***General behavior*** **NPI-NH**: Results reported graphically ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Low, 2013[87] RCT Australia	**Treatment**: SMILE intervention used LaughterBosses and ElderClowns to engage residents through laughter and enjoyment; tailored activities to personality, mood,	***Agitation/Aggression*** **CMAI**, Mean (variance method NR) Postintervention: 43.4 (19.1) vs. 37.9 (10.0)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Humor therapy vs. usual care n=398 Moderate risk of bias	and physical and cognitive abilities (ex. through serenading, jokes, pretend tennis activity, etc.) **Comparison**: no intervention - 9-12 weekly sessions - ElderClown (trained performer experienced in healthcare settings), LaughterBoss (nominated care home staff member who encouraged intervention between ElderClown visits)	6-month postintervention: 42.0 (18.3) vs. 39.0 (11.7) ***General behavior*** **NPI-NH,** Mean (variance method NR) Postintervention: 20.0 (20.3) vs. 19.3 (15.7) 6-month postintervention: 23.2 (22.0) vs. 18.1 (16.8) **MOSES**, Mean(variance method NR) Postintervention: 17.6 (6.4) vs. 18.2 (6.0) 6-month postintervention: 18.1 (6.1) vs. 18.7 (6.3) ***Patient Distress, QoL*** **DEMQoL**, Mean(variance method NR) Postintervention: 93.7 (13.1) vs. 92.9 (12.7) 6-month postintervention: 92.0 (14.0) vs. 92.5 (15.4) ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Rodriguez-Mansilla, 2013[75] RCT Spain Massage therapy vs. ear acupuncture n = 75 Moderate risk of bias	**Treatment 1**: Massage therapy group received 20 minute back and lower limb massages Monday-Friday for 3 months **Treatment 2:** Ear acupuncture with adhesive herbal seeds, herbal seeds changed out every 15 days **Comparison**: no treatment - 3 months - physiotherapist, certified acupuncturist	***Agitation/Aggression:*** NR ***General Behavior*** **Behavior alterations** 3 months: 34/36 vs. 3/405 months: 28/35 vs. 33/40 ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Lin, 2009[88] RCT - Crossover Taiwan Acupressure vs. Montessori methods vs. presence n = 133 Moderate risk of bias	Three groups randomized to varying sequences of three conditions below: **Treatment 1**: Acupressure was applied to the hands in 15 minute sessions **Treatment 2:** Montessori methods included 45 minute sessions of sensory stimulation, demonstration, extension and conclusion for the following tasks: scooping, pouring, squeezing, fine motor skills, environmental care, and personal care **Comparison**: Presence consisted of companionship and conversation in 15 minute sessions - each treatment was received once/day 6 days/week for 4 weeks, and between each intervention period, there was 1 week of posttesting, 2 weeks of washout, and 1 week of pretesting before the next intervention - research team, Chinese medicine physician	***Agitation/Aggression*** **CMAI,** beta(SE) -2.113 (0.609) vs. -2.318 (0.610) vs. NR ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
Ito, 2007[89] Japan RCT Group reminiscence (GR) vs. Social contact (SC) vs. comparison n=60 Moderate risk of bias	**Treatment 1**: Group reminiscence approach and reality orientation was given once a week for 3 months to the subjects in the GR arm. **Treatment 2**: In the SC arm, a 1-hour session of reality orientation and conversation between participants took place in the same manner. **Comparison**: Only supportive care - 3 months - care provider, psychologist, speech therapists, occupational therapists, medical social workers, nurse	***Agitation/Aggression***: NR ***General behavior*** **MOSES,** mean (SD) Baseline: 78.8 (20.8) vs. 76.6 (22.2) vs. 75.9 (17.1) Postintervention: 78.1 (26.0) vs. 75.1 (16.6) vs. 75.9 (19.0) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Lichtenberg, 2005[90] RCT United States Pleasant events vs. usual care n = 20 Moderate risk of bias	**Treatment**: Pleasant events as instructed by The Pleasant Events Schedule for Alzheimer's disease; additional personalized activities for patients as suggested by nursing assistants **Comparison**: Usual care activity programming (not otherwise specified) - 3 times per week for 20 to 30 minutes over three months - trained nursing assistant	***Agitation/Aggression***: NR ***General Behavior*** **BEHAVE-AD,** mean (SD) Baseline: 1.9 (0.69) vs. 1.4 (0.78) Postintervention: 1.3 (0.30) vs. 2.2 (0.32) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Baker, 2003[44] RCT United Kingdom, Netherlands, and Sweden. Multisensory stimulation (MSS) vs. Comparison n=136 Moderate risk of bias NOTE: Because of low numbers in Sweden (only three participants in the MSS group), ANOVAs were carried out on UK and Netherlands data only.	**Treatment**: The key elements of MSS were to place emphasis on all the senses (except taste). - Light and sound effects were used, as well as materials for touching and smelling. - Light effects included bubble tubes, fiber-optic sprays, and moving shapes beamed across the walls. - Sound effects included 'new age' or pseudo-classical music, which did not distract individuals from exploring other stimuli as familiar music would. - Tactile stimulation used satin, cotton wool, shells, etc. - Tactile boards made up, used different textures such as rough/smooth, warm/cold, and hard/soft. - Sense of smell was stimulated using aromatherapy and lavender bags, etc. **Comparison**: engaged in activities like playing card, games, looking at photographs, doing quizzes, etc. - 8 30-minute sessions over 4 weeks. - nursing staff, occupational therapists, psychology assistants	***Agitation/Aggression***: NR ***General behavior*** **BRS,** mean(SD) *UK:* (n=492) Baseline: 15.8 (4.6) vs. 16.8 (5.1) Postintervention: 16.8 (4.8) vs. 17.6 (5.6) *NETHERLANDS:* Baseline: 16 (5.5) vs. 19.6 (6.4) Postintervention: 17 (5.6) vs. 20.4 (3.7) **REHAB,** mean (SD) *UK* (n=87) Baseline: 50.1 (30.0) vs. 55.3 (25.9) Mid-trial:49.7 (29.5) vs. 55.4 (25.5) Postintervention: 49.9 (29.3) vs. 58.6 (27.0) Postintervention: 54.2 (30.0) vs. 61.3 (28.2) **BMD (total score),** mean (SD) *UK* (n=83) Baseline: 56.4 (13.4) vs. 55.9 (16.6) Mid-trial:52.6 (14.4) vs. 55.1 (19.4) Postintervention: 53.4 (13.9) vs. 55.2 (19.7) Postintervention: 55.3 (16.4) vs. 55.5 (18.2) **GIP (total score),** mean (SD)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
		<u>*NETHERLANDS ONLY*</u> (n=26) Baseline: : 44.6 (10.1) vs. 53.6 (11.4) Postintervention: 46.2 (12.5) vs. 56.3 (12.6) Postintervention: 48.2 (13.6) vs. 59.6 (10.8) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Beck, 2002[91] RCT United States Activities of daily living intervention (ADL) vs. psychosocial activity (PSA) intervention vs. ADL and PSA combined intervention vs. placebo vs. no intervention n = 127 Moderate risk of bias	**Treatment 1**: ADL intervention: 45-60 minutes per day, PNAs used this intervention during bathing, grooming, dressing, and the noon meal, using strategies to complete an ADL by addressing specific cognitive deficits, using standard strategies of behaviors and communications techniques, and problem-oriented strategies to address particular disabilities **Treatment 2**: PSA intervention: 25 standardized yet tailored modules containing 5 psychosocial content areas and five sensory modalities, 15-30+ minutes per day **Treatment 3**: Combined intervention: 90+ minutes per day consisting of both the ADL and the PSA interventions **Comparison 1:** Placebo control - one on one interaction with PNA doing activities that the participant chose, 30 minutes/day **Comparison 2**: Usual care with no scheduled contact - 12 weeks of intervention (first 3 weeks considered baseline, 7 weeks of intervention, and 2 weeks of post-intervention) - professional nursing assistant	***Agitation/Aggression*** **DBS Physically Aggressive,** mean (SD) Baseline: 20.67 (30.52) vs. 85.87 (199.01) vs. 68.84 (126.18) vs. 49.26 (90.24) vs. 114.66 (202.89) Postintervention: 15.02 (26.10) vs. 82.82 (166.93) vs. 61.04 (127.78) vs. 59.67 (106.37) vs. 77.98 (173.15) 1-month postintervention: 44.18 (100.62) vs. 113.49 (235.71) vs. 92.68 (205.52) vs. 76.79 (165.45) vs. 130.92 (257.12) 2-month postintervention: 21.45 (SD 36.47) vs. 81.30 (SD 151.85) vs. 60.40 (SD 131.54) vs. 48.25 (SD 101.34) vs. 128.20 (SD 195.67) **DBS Vocally aggressive,** mean (SD) Baseline: 22.85 (32.10) vs. 49.64 (93.15) vs. 34.49 (55.91) vs. 47.20 (79.70) vs. 55.16 (74.70) Postintervention: 21.15 (26.54) vs. 37.90 (53.43) vs. 31.18 (33.85) vs. 32.69 (55.77) vs. 33.26 (47.06) 1-month postintervention: 30.72 (48.95) vs. 54.47 (90.33) vs. 36.95 (42.70) vs. 29.30 (47.60) vs. 64.72 (77.89) 2-month postintervention: 18.28 (24.55) vs. 40.26 (45.26) vs. 32.82 (51.32) vs. 30.18 (52.85) vs. 28.09 (37.02) **DBS Vocally agitated, mean (SD)** Baseline: 33.49 (84.39) vs. 46.92 (98.70) vs. 62.49 (98.97) vs. 50.10 (92.05) vs. 47.65 (97.22) Postintervention: 43.17 (72.10) vs. 52.50 (90.78) vs. 69.08 (107.29) vs. 48.59 (72.20) vs. 68.01 (116.62) 1-month postintervention: 43.48 (64.39) vs. 68.22 (98.89) vs. 82.14 (118.97) vs. 63.74 (95.30) vs. 84.50 (112.48) 2-month postintervention: 50.53 (117.95) vs. 48.89 (92.33) vs. 75.80 (129.67) vs. 54.11 (80.61) vs. 73.07 (117.12) ***General Behavior*** **DBS Total, mean (SD)** Baseline: 172.51 (191.47) vs. 348.02 (467.50) vs. 287.66 (373.73) vs. 325.96 (337.14) vs. 408.71 (427.24) Postintervention: 164.56 (154.95) vs. 303.24 (367.54) vs. 286.21

Study Design Country Comparison n Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	Primary Outcome-Instrument Results Intermediate Outcome-Instrument Results
		(365.78) vs. 336.80 (366.55) vs. 281.97 (410.85) 1-month postintervention: 207.22 (205.58) vs. 373.17 (533.05) vs. 374.10 (510.10) vs. 389.92 (434.43) vs. 418.31 (630.58) 2-month postintervention: 190.70 (291.06) vs. 300.20 (366.42) vs. 312.83 (433.18) vs. 319.15 (384.59) vs. 292.85 (405.15) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Family Involvement in Care or Activity		
Camberg, 1999[92] RCT - Crossover United States Simpres vs. placebo vs. usual care n=54 Moderate risk of bias	**Treatment**: Simpres audio tape was designed as a personalized interactive tape made by a family member; best loved memories of the dementia residents identified through assessment process and introduced to patient in a telephone conversation format using a continuous play audio tape system. **Comparison 1**: The placebo audio tape was a recording of a person reading emotionally neutral newspaper. **Comparison 2**: Usual care included the routine interventions nursing home staff used for behavior management e.g., staff interactions, redirection, or physical restraints. - 17 days of treatment and a 10-day washout period following each treatment. - nursing home staff, family members	***Agitation/Aggression*** **SCMAI** Total frequency of agitated behaviors under each treatment condition (variance NR): Simpres: 25.5 vs. 27.1 vs. 25.1 ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
McCallion, 1999[93] RCT United States Family Involvement vs. usual care n=66 Moderate risk of bias	**Treatment**: FVEP (Family Visit Education Program) was aimed at improving the quality of interaction between family members and nursing home residents; trainer observed the family member and resident interacting for 20-30 minutes and then provided an additional 15 minutes of feedback about the observations in a family meeting room (after the family member had completed his/her visit). **Comparison**: Participants in the usual care condition continued to engage in the usual social and recreational programming offered by each nursing facility. - delivered over 8 weeks and included 4 1.5-hour group sessions and 3 1-hour family conferences - trainer	***Agitation/Aggression*** **CMAI- Physically aggressive, observant,** mean (SD) Baseline: 0.0 (0.0) vs. 0.0 (0.0) 3-month: 0.3 (1.5) vs. 0.0 (0.0) 6-month: 0.0 (0.2) vs. 0.0 (0.0) **CMAI- Physically nonaggressive, observant,** mean (SD) Baseline: 0.5 (1.4) vs. 0.3 (1.2) 3-month: 1.4 (4.4) vs. 1.1 (6.0) 6-month: 0.2 (0.5) vs. 0.3 (1.9) **CMAI- verbally agitated, observant,** mean (SD) Baseline: 1.7 (3.2) vs. 0.5 (1.2) 3-month: 1.9 (3.8) vs. 0.9 (2.0) 6-month: 0.5 (1.2) vs. 0.8 (2.8) **CMAI- Physically aggressive, nurse,** mean (SD) Baseline: 12.5 (7.1) vs. 10.6 (4.6)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	**Primary Outcome-Instrument** **Results** **Intermediate Outcome-Instrument** **Results**
		3-month: 11.7 (6.1) vs. 9.7 (3.2) 6-month: 12.1 (6.9) vs. 10.1 (3.6) **CMAI- Physically nonaggressive, nurse,** mean (SD) Baseline: 14.3 (7.6) vs. 10.6 (5.6) 3-month: 12.5 (7.2) vs. 10.6 (5.2) 6-month: 11.4 (7.4) vs. 12.9 (6.2) **CMAI- verbally agitated, nurse,** mean (SD) Baseline: 10.6 (9.6) vs. 11.6 (7.7) 3-month: 13.9 (8.6) vs. 10.6 (7.5) 6-month: 12.7 (7.1) vs. 10.7 (7.0) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Hozumi, 1996[94] Japan RCT Electro-stimulation vs. placebo n=27 Moderate risk of bias	**Treatment**: Electro stimulation group had electrodes attached to forehead; the device (HESS-100) delivered repetitive rectangular electric pulses of 6-8V at increasing frequencies from 6-80Hz, each pulse lasting 0.2ms **Comparison**: Placebo had same electrodes but they were disconnected to actual device - 20 minutes each morning - doctor, nurse	***Agitation/Aggression*** **Behavior Disorder - Unknown scale,** mean (SD) Baseline: 1.20 (1.21) vs. 1.32 (1.23) 2-week postintervention: 0.95 (1.03) vs. 0.98 (1.13) ***General Behavior***: NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR
Robichaud, 1994[95] RCT Canada Sensory integration vs. usual care n = 40 Moderate risk of bias	**Treatment**: Sensory integration plus structured activities with various materials **Comparison**: Usual activities (not defined) - sensory integration 3 times/week over 10 weeks; structured activities session of 30-45 minutes - study author	***Agitation/Aggression***: NR ***General Behavior*** **RMBPC, Frequency,** mean (SD) Baseline: 1.43 (0.64) vs. 1.11 (0.46) Postintervention: 1.16 (SD 0.43) vs. 1.04 (0.37) **RMBPC – Disruptive Behavior,** mean (SD) Baseline: 0.91 (0.65) vs. 0.61 (SD 0.38) Postintervention: 0.54 (0.44) vs. 0.49 (0.37) ***Caregiver Distress*** **RMBPC – Reaction,** mean (SD) Baseline: 1.97 (0.87) vs. 1.45 (0.79) Postintervention: 1.21 (0.58) vs. 1.10 (0.60) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Neuroleptic Use:** NR

ABMI = Agitation Behavior Mapping Instrument; ABRS = Agitated Behavior Rating Scale; ANCOVA = analysis of covariance; ANOVA = analysis of variance; BACE = Balancing Arousal Controls Excesses; BEHAVE-AD = Behavioral Pathology in Alzheimer's disease; BMD = Behavior and Mood Disturbance; C-CMAI = Cohen-Mansfield Agitation Inventory-Community form; CI = confidence interval; CMAI = Cohen-Mansfield Agitation Inventory; CMAI-SF = Cohen-Mansfield Agitation Inventory-Short Form; CNPI = Checklist of Nonverbal Pain Indicators; DBS = Deep Brain Stimulation; DEMQoL = Dementia Quality of Life measure; FVEP = Family Visit Education Program; GIPB = Geriatric Indices of Positive Behavior; MANOVA = multivariate analysis of variance; MOUSEPAD = Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia; MOSES = Multidimensional observation scale for elderly patients; NPI = Neuropsychiatric Inventory; NPI-NH = Neuropsychiatric Inventory-Nursing Home; NPI-Q = Neuropsychiatric Inventory Questionnaire; NR = not reported; NS = not significant; QoL = quality of life; PAS = Pittsburg Agitation Scale; QUALID = Quality of Life in Late-stage Dementia; RCT = randomized controlled trial; REHAB = Rehabilitation Evaluation Hall and Baker tool; RMBPC = Revised Memory and Behavior Problem Checklist; SCMAI = Cohen-Mansfield Agitation Inventory, short form; SD = standard deviation; SE = standard error

Care Delivery-Level Nonpharmacologic Interventions for Agitation/Aggression in Individuals With Dementia in Long-Term Care Settings

Key Points

- Few trials studied comparisons and outcomes sufficiently similar to allow pooling data.
- Low strength evidence shows that dementia care mapping and person-centered care were similar to usual care in managing agitation/aggression in residents with dementia.

Overview

We identified 27 eligible trials that assessed care delivery level nonpharmacologic interventions for agitation/aggression in residents of nursing homes and assisted living facilities. Of these, eight were assessed as having a high risk of bias. These studies are described in Appendix D. Our analysis of the remaining 19 trials is provided below by intervention type. Trials with acceptable risk of bias examined a wide variety of care delivery interventions including dementia care mapping, patient-centered care, emotion-oriented care, and a variety of staff trainings, and environmental changes to assist way-finding. We grouped studies by intervention type and comparison. All studies were trials but they differed in the unit of randomization (i.e., at nursing home level, staff, or residents). In many of the studies the intervention was compared with "usual care" but the nature of this care was poorly specified. In some instances the intervention was added to this usual care; in others it was offered as an alternative. It was frequently not even clear if psychoactive medications were being given concurrently. Table 7 provides a summary of the results by intervention type and comparison. Table 8 provides results for trials analyzed. Small changes, even though statistically significant, may not be clinically significant. There have been efforts to create validated measures of minimal important differences (MID) for some topics but we could find no such data for agitation or aggression. We, therefore, simply comment when we judge that the size of the effect is not likely to be clinically significant.

Dementia Care Mapping

Eligible Trials

Three studies evaluated dementia care mapping (DCM) in nursing homes using cluster randomized designs.[96-98] DCM is a systematic approach to identifying and strategically responding to presumed causes of agitation/aggression and distress. The DCM process consists of observing care, the environment, and factors associated with resident wellbeing as identified by behavioral indicators, and then identifying positive and negative aspects of care delivery. Feedback is given to nursing home staff and used to inform action plans. In some cases, the intervention was conducted by both the trained staff and outside experts. The three studies that evaluated DCM ranged in size from 180 to 308.[96-98] Studies were similar in terms of resident characteristics with mean age of residents varying from 83 to 85 years and most were female. Two studies reported different characteristics of nursing facilities with the number of residents to staff ranging from 0.73 to 3.6.[96,97] Only one study reported care staff characteristics.[98]

Chenoweth et al. compared DCM (n = 109) with person-centered care (PCC) (n = 98) and usual care (n = 82) over a 4-month period.[96,99] Results for the PCC arm of the trial are presented in the PCC section. Nursing homes were randomized to treatment conditions, and dementia residents with need driven behavioral problems were invited by management and staff to participate in the study. Nursing homes in the DCM group had 52 beds, and 0.73 residents per staff member. Nursing homes randomized to usual care had 53 beds and 0.86 residents per staff member. The mean age of residents randomized to DCM was 83 years and most were female (83%). Mean age of patients in usual care was 85 years and 73 percent were female. In each intervention nursing home, two trained study investigators led DCM along with two care staff trained by a Bradford-trained expert in DCM. Study investigators and care staff conducted DCM for 6 hours over 2 days and then developed personalized care plans. Study investigators conferred with staff via regular teleconferences. Usual care consisted of normal practice of custodial and physical task oriented practices. Hierarchical linear models were estimated to test for treatment effects. With DCM, agitation/aggression declined compared with usual care as measured by the CMAI. At postintervention (4 months from end of intervention) CMAI score differed by 10.9 points (95% CI, 0.7 to 21.1) in favor of DCM compared with usual care. This represents a 5 percent improvement for patients in DCM relative to usual care and is unlikely to be clinically meaningful. There was no significant group or time by group interaction for general behavior as measured by the NPI, and DCM did not differ significantly from usual care for incidents (falls, injuries, drug errors, and behavioral events), and use of antipsychotic drugs.[96] Staff outcomes (burnout and general health) were reported in a second publication.[99] There was a significant reduction of burnout as measured by the Maslach Burnout Inventory emotional exhaustion subscale, but it is not clear if this is due to DCM or PCC. This study had a low risk of bias.

Rokstad et al. compared DCM (n = 158) and PCC (n = 138) with usual care (n = 150) over a 10-month period.[97] Results for the PCC arm of the trial are presented in the PCC section. DCM was used as a process tool to help staff deliver PCC. Nursing homes were randomized to treatment conditions. All residents with dementia were invited to participate in the study. On average, nursing homes had 24.1 residents per ward and 3.6 patients per staff member. The mean age of all residents was 85.7 years and 71.8 percent were female. Two staff members from nursing homes randomized to DCM participated in a detailed training course. All other staff randomized to DCM participated in a 3-hour lecture on DCM principles. The two trained staff members and study investigators then carried out DCM. Each DCM session consisted of 4-6 hours of observation per person with dementia. Following observations of staff and patient interactions, staff participated in feedback sessions with the care mappers. Observation and feedback sessions were held during the beginning of the study and again at 6 months. Nursing home staff randomized to DCM, PCC, and the control group received five DVDs with lectures about dementia. Other than the educational DVDs the control group did not receive any additional training. Linear mixed-models were estimated to test for treatment effects. Compared with the control group, patients cared for by staff in the DCM (-2.0 95% CI, -5.1 to 1.1) showed less agitation/aggression at postintervention on the Brief Agitation Rating Scale, but this was not significant. However, again compared with the control group, patients cared for by staff assigned to DCM experienced significant reductions on the overall NPI-Q (DCM -2.7; 95% CI: -4.6 to -0.7) and the NPI-Q agitation subscale (DCM -0.9; 95% CI: -1.7 to -0.04).[97] Although statistically significant, the difference may not be clinically meaningful.[38] This study had a moderate risk of bias due to possible selection bias (unbalanced on key baseline covariates) and high attrition.

A study by van de Ven et al. attempted to replicate the DCM component of the study by Chenoweth et al.[96,98] Nursing homes were randomized to DCM (resident n = 73) or usual care (resident n = 119). Managers in each home selected staff members to participate in the intervention. Residents were invited to participate in the study if they had dementia and at least one behavioral symptom. Residents lost to attrition were replaced. The mean age of residents in DCM (84.6 years) and usual care (83.5 years) was similar, and in both groups most residents were female. The mean age of care staff in DCM (43.6 years) and usual care (42.6 years) was similar, and in both homes 98 percent of care staff were female. Two staff members from each intervention nursing home participated in a basic and advanced DCM training program. All staff members in intervention nursing homes attended a seminar on the goals and methods of DCM. Staff trained in DCM conducted at least two cycles of mapping (observation, feedback, and action plans) over a 4-month period. Residents in usual care received the continuation of daily care practices. Linear-mixed effect models were used to evaluate treatment effects. DCM had no significant effect on patient agitation/aggression (CMAI mean difference in favor of usual care 2.4; 95% CI: -2.7 to 7.6). There was a significant interaction effect between group and time in favor of the control group on the NPI-NH scale (p = 0.022), but there was no difference in mean score at postintervention. In terms of staff outcomes, there was no significant group by time interaction in GHQ-12 scores (p = 0.432), or MJSS-HC (p = 0.069). This study had a moderate risk of bias due to possible selection bias (unclear methods of randomization) and high attrition.

Evidence Synthesis and Strength of Evidence Assessment

All eligible DCM studies assessed agitation/aggression. Chenoweth et al. was the only study to report an effect in favor of DCM on the primary measure of agitation/aggression. Rokstad et al. reported a significant improvement for DCM on a secondary outcome measure of agitation/aggression. However, both of these effects are small and unlikely to be clinically meaningful.[96,97] Both Chenoweth et al. and van de Ven et al. used the CMAI to evaluate agitation/aggression. Rokstad et al. evaluated agitation/aggression using the Brief Agitation Rating Scale, an instrument derived from the CMAI. The secondary outcome measure used by Rokstad et al. was the NPI-Q agitation subscale. To pool results, we standardized the mean between treatment group differences in the primary measure of agitation/aggression from each study. Figure 5 shows the pooled results of the three DCM studies. Low strength evidence shows that the effect of DCM on agitation/aggression in dementia is similar to control (standardized mean difference -0.12; 95% CI: -0.66 to 0.42). The meta-analysis model had an I^2 of 53 percent and Tau of 0.15. In a subsequent analysis we standardized the CMAI with the NPI-Q agitation subscale and again found similar effects with DCM and control.

Evidence for all other outcomes was insufficient. All three studies reported general behavior using a version of the NPI (e.g., NPI-Q and NPI-NH).[96-98] Only Rokstad et al. reported significant improvements in general behavior for the intervention group. Chenoweth reported no effect and van de Ven et al. reported a significant effect favoring the control. Studies varied on reporting of other outcomes of intermediate and secondary outcomes. Chenoweth et al. reported a null effect for DCM on neuroleptic use and injuries. This was the only study to report on neuroleptic use or injuries. None of the studies reported adverse events. Finally, van de Ven reported null effects of DCM on staff behavior and general health. This was the only study to evaluate staff outcomes.

Person-Centered Care

Eligible Trials

Three studies evaluated PCC interventions using cluster randomized designs.[96,97,100] PCC aims to foster personhood (e.g., positive relationships with others) as dementia progresses. It involves observations and feedback but involves less effort to identify underlying causes of behaviors than DCM. Three studies ranged in size from 141 to 346.[96,97,100] Studies were similar in terms of resident characteristics with the mean age of residents varying from 82 to 85 years. Two studies reported different characteristics of nursing facilities with the number of residents to staff ranging from 0.73 to 3.6.[96,97]

Chenoweth et al. compared PCC with usual care over a 4-month period. The study design is described in the DCM section above. The mean age of residents in PCC was 84 years and 74 percent were female. The number of beds in nursing homes randomized to PCC was 47 and there were 0.92 residents per staff member. Staff members in nursing homes randomized to PCC participated in a 2-day training session focused on interpreting behaviors as a form of communication. Sessions also highlighted techniques to develop care plans for residents. During the intervention period, staff discussed care plans with trainers. Hierarchical linear models were estimated to test for treatment effects. Compared with patients cared for by staff randomized to usual care, patients cared for by staff randomized to PCC had significantly less agitation/ aggression at 4 months after the intervention (mean difference in CMAI score 13.6 points; 95% CI: 3.30 to 23.9). This represents a 7 percent improvement for patients in PCC relative to usual care and is unlikely to be clinically meaningful. The NPI also showed a significant time trend favoring PCC ($p = 0.04$). However, the group and group by time interaction were not significant. There was no significant difference between PCC and usual care on incidents (falls, injuries, drug errors, and behavioral events) and antipsychotic drugs. Staff outcomes (burnout and general health) were evaluated in a separate study.[99] There was a significant treatment effect on the measure of burnout as measured by the Maslach Burnout Inventory emotional exhaustion subscale, but it is not clear if this is due to DCM or PCC. This study had a low risk of bias.

Rokstad et al. compared PCC with usual care over a 10-month period. The study design is described in the DCM section above. PCC was based on the VIPS framework (described as [V]aluing people with dementia, [I]ndividualized care, understanding the world from the [P]atient's perspective, and providing a social environment that supports the needs of patient[S]). The VIPS framework consists of 24 indicators used to ensure person-centered care. A staff nurse that participated in a 3-day training in the VIPS method led weekly 60-minute meetings during which the VIPS framework was used to evaluate a challenging patient-staff interaction. PCC and the control group received five DVDs with lectures about dementia. Other than the DVDs the control group consists of usual practice. Linear mixed-models were estimated to test for treatment effects. Compared with the control group, patients in the PCC group (-1.1; 95% CI: -3.8 to 1.6) showed a nonsignificant reduction in agitation/aggression measured using the Brief Agitation Rating Scale. However, patients in PCC had statistically significant reductions on the NPI-Q (mean difference -2.4; 95% CI: -4.1 to -0.6) and the NPI-Q agitation sub scale (mean difference -0.9; 95% CI: -1.6 to -0.1). However, these reductions may not be clinically meaningful. This study had a moderate risk of bias due to possible selection bias (unbalanced on key baseline covariates) and high attrition.

Fossey et al. compared a staff training and support program designed to reduce drug use for the management of agitation/aggression ($n = 181$) with usual care ($n = 168$) over a 12-month

period. Nursing homes were randomized to treatment and usual care. Residents with dementia were invited to participate in the study. The median age of residents in the treatment group was 82 years and 35 percent were female. The median age of residents in usual care was 82 years and 39 percent were female. Care staff characteristics were not provided. Staff members in the intervention group were trained in person-centered care methods and the use of nonpharmacologic behavioral management techniques. In addition, nursing homes randomized to the intervention agreed to work with a geriatric psychiatrist to review and adjust medications as needed. Treatment effects were evaluated using weighted *t* test and weighted linear regression. The authors adjusted for baseline neuroleptic use and region and found a nonsignificant decrease in the proportion of residents taking any neuroleptics in the intervention group compared with usual care at 12-month postintervention (-19.1; 95% CI: -41.7 to 3.0). Null effects were also observed for dose of neuroleptics and proportion of residents taking other psychotropics. Intervention and usual care did not differ significantly on agitation/aggression at 12 months (CMAI mean difference in favor of the intervention 0.3; 95% CI: -8.3 to 8.9) or on the number of aggression episodes (mean difference in favor of intervention group of percent of residents with >1 episode of aggression (-1.6; 95% CI: -12.7 to 15.8). This study had a moderate risk of bias due to detection bias (not adjusting for multiple comparisons) and high attrition.

Evidence Synthesis and Strength of Evidence Assessment

All eligible person-centered care studies assessed agitation/aggression. Chenoweth et al. was the only study to report a statistically significant effect of PCC on agitation/aggression. However, because the effect size was unlikely to be clinically meaningful, these results should not be interpreted as evidence of effectiveness due only to the statistical difference. Rokstad et al. reported a statistically significant reduction in agitation/aggression for PCC as assessed with one instrument, but not another. To pool results, we standardized the mean between treatment group differences at the final period of postintervention on the primary measure of agitation/ aggression from each study. Figure 6 shows the pooled analysis describing the effect of PCC on agitation/aggression in dementia. Low strength evidence shows that PCC and usual care have a similar effect on agitation/aggression in dementia (standardized mean difference -0.15; 95% CI: -0.67 to 0.38). The meta-analysis model had an I^2 of 56 percent and a Tau of 0.14.

Evidence for general behavior and intermediate outcomes was insufficient. Two of the three studies reported general patient behavioral outcomes; of these, Rokstad et al. reported a difference in general patient behavior in favor of PCC, and Chenoweth et al. reported a null effect. PCC had no effect on neuroleptic use or injuries. None of the studies reported staff outcomes.

Protocols To Reduce Use of Antipsychotics

Eligible Studies

Three studies used staff training and clinical protocols to reduce the use of antipsychotics. These studies have been grouped together.[100-102] The studies ranged in size from 258 to 659.[100-102] Resident characteristics were similar across studies, but neither study reported nursing facility or care provider characteristics.

Fossey et al. evaluated a clinical protocol to reduce antipsychotic use combined with person-centered care versus usual care. Results from this study were analyzed in both the person-centered care and in the reducing antipsychotics group. The authors adjusted for baseline

antipsychotic use and region and found no difference in the proportion of residents taking any antipsychotics at 12-month postintervention between intervention and control (mean difference favoring the intervention group -19.1; 95% CI: -41.7 to 3.0). Null effects were also observed at 12-month postintervention for dose of antipsychotics (mean difference in dose of antipsychotics favoring the intervention group -4.9; 95% CI: -20.0 to 29.9) and proportion of the population taking other psychotropics. Daily dose was translated into chlorpromazine daily equivalents using the British National Formulary. Additional details of this study are reported in the PCC section.

Rapp et al. evaluated a staff-training and behavior-based intervention also designed to reduce the use of antipsychotics. The intervention (n = 163) was compared with usual care (n = 141) at 10 months. Nursing homes were randomized to treatment conditions, and residents with dementia were invited to participate in the study. The mean age of study residents was 81.56 years and 73 percent were female. The intervention consisted of two 4-hour staff training sessions on the symptomatology and causes of behavioral symptoms of dementia. Staff members were also trained on the use of physical- and activity-based nonpharmacologic therapies for the management of behavioral symptoms. Finally, prescribers within nursing homes attended individual training sessions on the causes of behavioral symptoms and the use of a guideline-based prescribing for pharmacotherapy. The control group received treatment as usual. Repeated measures multivariate analysis of variance was used to evaluate treatment effects. At 10 months CMAI was significantly lower for residents in the treatment group than for residents in the control group (mean difference 6.24; 95% CI: 2.03 to 14.44). This represents a 3 percent improvement for residents in the treatment group compared with usual care, which may not be clinically meaningful. In addition, CMAI-aggression subscale scores significantly decreased in the intervention group (baseline mean sub score 14.03 SD = 5.82 and 10 month postintervention mean sub score 11.75 SD = 4.32) while increasing in the control group (baseline mean sub score 14.53 SD = 6.94 and 10 month postintervention mean sub score 17.12 SD = 11.07). The difference in mean change between intervention and control was significant (p = 0.012). No differences were observed between the intervention and control on the physically nonaggressive (p= 0.977) and verbally agitated (p = 0.357) subscales of the CMAI. At 10 months residents in the intervention group were prescribed fewer antipsychotics (mean difference of defined daily dosage 0.03; 95% CI: 0.01 to 0.05). The defined daily dosage was determined based on medication usage 2 weeks prior to assessment and was calculated using the German algorithm of the anatomic therapeutic chemicals. This study had a low-moderate risk of bias due to performance bias (unclear application of the intervention) and detection bias (not blinding assessors).

Zwijsen et al. compared a structured patient analysis form with a control group using a stepped-wedge randomized trial.[102] Nursing homes with dementia special care units were recruited to participate in the study. In total, 659 residents with dementia participated in the study. The mean age of residents was 84 years and 69 percent were female. Nursing staff characteristics were not provided. Staff randomized to the intervention (nursing assistants, physicians, and psychologist) participated in a 1-day seminar to learn about the analysis form. A postintervention seminar was conducted 2 weeks after the initial training. As part of the training, prescribers were provided information about the negative consequences associated with antipsychotics and the benefits of psychosocial interventions. The structured patient analysis form consisted of observing patient behavior to develop treatment goals and plans. Patients were evaluated after the implementation of the treatment plan. No information was provided regarding

the control condition. Mixed effects models were used to evaluate treatment effects at 20 months. Compared with the control group residents in the intervention experienced a significant but modest reduction in agitation/aggression as measured by the CMAI (-2.4; 95% CI: -4.30 - -0.60). This small reduction may not be clinically significant. There was no significant difference between groups in terms of general behavior as measured by the NPI-NH. Residents in the intervention group were prescribed fewer antipsychotics (OR: 0.54; 95% CI: 0.37 – 0.80). Finally, there was no difference in the use of restraints.

Evidence Synthesis and Strength of Evidence Assessment

Evidence was insufficient to draw conclusions regarding efficacy of interventions on reducing antipsychotic use, agitation/aggression, or any of the secondary outcomes. Rapp et al. reported a small but significant reduction in mean defined daily dose of antipsychotics in the intervention group. Zwijsen et al. also found a small reduction in the number of antipsychotics prescribed. In contrast, Fossey et al. reported no difference between intervention and control in terms of total antipsychotic use or dosing. To pool results, we standardized the mean between treatment group differences of antipsychotic dose. Results from Zwijsen et al. could not be pooled due to insufficient data regarding sample sizes in each treatment group. Figure 7 shows the forest plot of the effect of the interventions on antipsychotic dose. The pooled results indicated that the interventions had no effect on antipsychotic dose (standardized mean difference -0.28; 95% CI: -3.50 to 2.94). The meta-analysis model had an I^2 of 89 percent and a Tau of 0.34.

For agitation/aggression, Fossey et al. reported a null effect for the intervention. In contrast, Rapp et al. and Zwijsen et al. found significant reductions in agitation/aggression for the intervention group. To pool results, we evaluated the mean between treatment group differences at final period of postintervention on CMAI. Figure 8 shows the forest plot of the effect of interventions on agitation/aggression as measured by the CMAI. Again, results from Zwijsen et al. could not be pooled due to insufficient data. In pooled results, these studies had no effect on agitation/aggression (mean difference -4.5; 95% CI: -38.84 to 29.93). The meta-analysis model had an I^2 of 32 percent and a Tau of 2.39.

Emotion-Oriented Care

Eligible Studies

Two studies evaluated emotion-oriented care using cluster randomized designs.[103,104] Emotion-oriented care consists of understanding the resident's perception of the environment and the role of verbal and nonverbal communication in the caregiver-patient relationship. The two studies that evaluated emotion-oriented care ranged in size from 146 to 151. Resident characteristics were similar across both studies. However, only one study provided data on the characteristics of care staff.[103]

Finnema et al. compared emotion-oriented care combined with the guideline based Model-Care plan of the Dutch Association of Nursing Home Care (n = 46) versus the guideline based Model-Care plan alone (n = 53) (i.e., usual care) over 9 months. Nursing homes were randomized to treatment conditions, and residents with dementia were invited to participate in the study. The mean age of residents in the treatment group was 83.8 years and 81 percent were female. Similarly, the mean age of residents in usual care was 83.6 years and 81 percent were female. The mean age of care staff in both treatment groups was 30 years and 87 percent were

female. The emotion-oriented care component of the intervention consisted of a 2-day basic course for all staff in emotion-oriented care (e.g., staff members' experiences and application of nonverbal empathic skills). Five staff members from each intervention nursing home then participated in an advanced emotion-oriented care class. The 7-day advanced course (spread over 8 months) trained staff members on how to take life histories, acknowledge residents' experiences, and be alert to how past residents' experiences affect the present. Finally, one staff member per intervention nursing home was invited to participate in an adviser emotion-oriented training course. During this 10-day course (delivered over 9 months) the staff member was trained to organize and lead emotion-oriented care sessions for residents. These staff members were also responsible for the implementation of emotion-oriented care in their home institution. Two half-day training courses on the Model-Care plan were conducted in all intervention and usual care nursing homes. In both intervention and usual care homes, the staff training provided a methodological framework for developing individualized care plans. Multivariate analysis of variance was used to evaluate treatment effects. Residents cared for by staff randomized to the intervention group did not significantly improve agitation/aggression measures (CMAI, CMAI-PA, CMAI-VNA, BIP10-restless behavior). Compared with the usual care, staff that improved in the application of emotion-oriented care scored lower on stress reactions on the GHQ-28 ($p = 0.003$), but did not differ in stress perception scores as measured by the QOS ($p = 0.54$). This study had a low risk of bias.

Schrijnemaekers et al. compared an emotion-oriented intervention ($n = 77$) with usual care ($n = 74$). Homes for the elderly were randomized to treatment conditions and dementia residents with behavioral problems were invited to participate in the study. Homes for the elderly are similar to nursing homes, but all homes offered a structured day-care unit for residents during the day. At night, residents return to their room within the elderly home. The mean age of residents in the intervention group was 84.3 years and 90 percent were female. The mean age of residents in usual care was 85.9 years and 89 percent were female. All staff in the intervention nursing homes were trained on the goals and objectives of emotion-oriented care. In addition, eight staff caregivers in each intervention home participated in a 6-day training on emotion-oriented care. Hierarchical linear models were estimated to evaluate treatment effects. Overall there was no statistical difference between intervention and control on measures of agitation/aggression and psychotropic use. At the 6-month postintervention residents cared for by staff assigned to the control group had 2.3 fewer physically nonaggressive behaviors than in the treatment group (CMAI-PNA, $p < 0.001$). This represents a 1 percent improvement for usual care residents compared with residents in the intervention group, which may not be clinically meaningful. During the same time period, there were no statistical difference on the CMAI-aggression subscale, CMAI-verbal aggression subscale, or the GIP and GIP-subscales (nonsocial behavior, loss of decorum, rebellious behavior, and restless behavior). This study had a moderate risk of bias due to high detection bias (not blinding assessors).

Evidence Synthesis and Strength of Evidence Assessment

Evidence was insufficient to draw conclusions regarding efficacy of interventions on reducing antipsychotic use, agitation/aggression, or any of the secondary outcomes.

Both studies reported no effect for emotion-oriented care on the primary measure of agitation/aggression.[103,104] Schrijnemaekers et al. reported a significant reduction in the physically nonaggressive behavior subscale of the CMAI at 6 months for the control group, but staff who made the assessments were aware of treatment assignments. Moreover, this effect was

not sustained at 12 months. It was not possible to pool results because one study did not provide standard deviations for point estimates.[104] Finnema et al. reported significant improvement on staff stress reactions. Schrijnemaekers reported no significant differences on staff distress, burden, or quality of life. Neither study reported staff behavior outcomes, antipsychotic use, general behavioral outcomes, injuries, or adverse events.

Unique Comparisons

Eligible Studies

Twelve trials evaluated unique care-delivery level comparisons and could not be conceptually grouped. One study was conducted in an assisted living facility.[105] All other studies were conducted in nursing homes.[106-116] Studies varied in size from 31 to 306. Studies also varied in terms of unit of randomization and in reporting demographic characteristics of residents and care staff.

Deudon et al. compared an 8-week staff education and training program (n = 174) with a control group (i.e., usual care) (n = 132). Nursing homes were randomized. Staff members in each nursing home invited select dementia residents with behavioral symptoms to participate in the study. The mean age of residents in the treatment group was 86.5 years and 77 percent were female. In usual care, the mean age of residents was 86 years and 79 percent were female. Facility and care staff characteristics were not provided. A 90-minute training session was conducted in intervention nursing homes. The training session provided general information on dementia, behavioral symptoms, and the use of "how-to instruction cards." The instruction cards were for use in clinical practice and provided practical advice to care staff on how to deal with behavioral symptoms (e.g., recommendations on nonpharmacologic interventions). Trainers also visited intervention nursing homes to observe care staff. Following observations, the trainers provided feedback to staff and personalized training. Treatment effects were evaluated using Wilcoxon nonparametric test and linear mixed-effect models. At 8 and 20 weeks there was no difference between residents randomized to intervention versus control nursing homes on the CMAI and CMAI subscales.

Results from the linear mixed effects model indicated that the decline in agitation/aggression in the intervention group (CMAI coefficient -0.26 $p < 0.001$) was significantly different ($p = 0.001$) than the mean change observed in the control group (coefficient 0.02 $p = 0.797$). Similar results were observed on the physically nonaggressive and verbally nonaggressive subscales of the CMAI (difference in change between intervention and control $p < 0.001$). While these significant improvements for the intervention group, they represent small improvements and are unlikely to be clinically meaningful. Mean change did not differ significantly between residents in the intervention group and residents in the control group on the physically aggressive and verbally aggressive behavior subscales of the CMAI. Finally, no significant changes were observed on the NPI hyperactivity subscale or psychotropic use for the intervention and control groups. This study had a low-moderate risk of bias due to possible selection bias (unclear description of randomization), and possible attrition bias (unclear description of attrition).

Proctor et al. compared a staff-training program combined with psychosocial management of behavioral symptoms (n = 60) with a control group (i.e., usual care) (n = 60). Residential homes and nursing homes were randomized. In each home, staff members selected 10 residents with behavioral problems to participate in the study. Not all residents had dementia. The mean age of residents who completed assessments at baseline and 6 month postintervention was 83.1 years

and 83 percent were female. Facility and care staff characteristics were not provided. Staff training consisted of seven 1-hour seminars over 6 months on staff-identified topics (e.g., management of dementia and aggression). An experienced psychiatric nurse conducted the psychosocial management portion of the intervention. The psychiatric nurse visited intervention nursing homes and advised and supported staff in developing care plans for residents. The control group received treatment as usual. Generalized estimating equations were estimated to evaluate treatment effects. After adjusting for baseline differences, there was no statistical difference in behavioral symptoms for residents in the intervention group compared with residents in the control group at 6 month postintervention (difference on the Crichton scale -0.7; 95% CI: -3.0 to 1.6). This study had a low-moderate risk of bias due to potential selection bias (unbalanced on key baseline variables), potential performance bias (unclear description of the intervention), and potential detection bias (unclear if assessors were blinded).

Clare et al. compared a staff-training program using the AwareCare measure (n = 32) with a control group (i.e., usual care) (n = 33). Care homes were randomized, and care home managers identified and invited residents with severe dementia. Care home managers also identified select care staff to participate in the study. The mean age of residents in the intervention group was 82.3 years and 32 percent were female. The characteristics of residents in usual care were similar. The mean age of care staff in the intervention and control group was 38 years and most were female. The intervention was conducted over 8 weeks and consisted of training staff members to consider residents' awareness and use the AwareCare observational method. In addition, study investigators provided feedback to staff on communication with residents. Analysis of covariance was used to evaluate treatment effects. At 8 weeks from baseline, residents in the intervention group did not improve significantly compared with residents in the control group on behavioral (Positive Response Scale p = 0.62) or key staff outcomes (staff burnout and general health). This study had a low risk of bias.

Wenborn et al. compared an occupational therapy intervention that aimed to increase resident social activity (n = 104) with a control group (i.e., usual care) (n = 106). Care homes and nursing homes were randomized. Residents were invited to participate in the study if they had dementia. The mean age of residents in the intervention group was 84.2 years and 66 percent were female. In the usual care group the mean age of residents was also 84.2 years and 75 percent were female. The intervention consisted of an assessment of the care home's physical environment, a staff education program, and one-to-one staff coaching sessions. Five 2-hour sessions focused on teaching staff to how to identify resident interests and to engage residents in meaningful activities. A trained interventionist worked directly with staff and residents on providing meaningful activities. Usual care consisted of normal practice. Analysis of covariance and multilevel modeling was used to evaluate treatment effects. Resident behavior did not significantly differ between the intervention and control groups as measured by the CBS and CAPE-BRS at 4 or 12 months. The 12-month adjusted results were similar to unadjusted results. Finally, the groups did not differ significantly in use of total medications. This study had a low-moderate risk of bias due to potential performance bias (treatment fidelity is not clear) and potential attrition bias.

Kovach et al. compared a clinical protocol designed to enhance comfort in dementia patients and manage behavioral symptoms (n = 57) with an educational control (n = 57). Long-term care facilities were randomized. Residents with dementia were identified and invited to participate in the study. The mean age of residents in the treatment group was 87 years and 74 percent were female. In the control group, the mean age of residents was 87 years and 77 percent were female.

Staff members in the intervention group participated in a 7-hour training focused on the use of a protocol consisting of a physical and affective assessment followed by targeted therapy. Examples of targeted therapy include nonpharmacologic interventions, analgesics, or consultations with other practitioners. Staff members in the control group were given information on misconceptions about aging, dementia, and approaches to treating behaviors associated with dementia. Repeated measures analysis of variance was used to test for treatment effects. Staff nurses in both groups recorded patient behavior. Behavior was measured using BEHAVE-AD. At 2 weeks and 4 weeks post treatment there was no significant time by group interaction for the measure of behavior, and both intervention and control reported reductions in behavior (BEHAVE-AD). Following treatment, more subjects in the intervention returned to baseline behaviors than in the control group ($p = 0.002$). This study had a moderate risk of bias due to potential selection bias (method of randomization not clear) and detection bias (assessors not blinded).

Magai et al. compared a staff-training program in nonverbal sensitivity ($n = 41$) with a behavioral placebo group ($n = 23$) and a wait-list control group ($n = 27$). Three nursing homes were randomly assigned to treatment conditions. Within each nursing home dementia residents and care staff were invited to participate in the study. The mean age of residents across all groups was 85.9 years and 93 percent were female. The mean age of care staff in all groups was 41.6 years and all were female. Nonverbal sensitivity training consisted of 10 hour lectures over 2 weeks on issues of nonverbal communication and emotional expression. The lectures also covered cultural aspects related to patient affect, including basic emotions, personal emotional triggers, and body language. The behavioral placebo group also participated in 10 hour-long lectures over 2 weeks. Lectures focused on behavioral symptoms of dementia and not on patient affect. The wait-list control received usual care until after the study period, at which point they received training in nonverbal sensitivity. Repeated measures analysis of variance was used to evaluate treatment effects. There were no statistically significant time, treatment, or time by treatment interaction effects for patient symptomology (an aggregate measure incorporating CDS, CMAI, and BEHAVE-AD). This study had a moderate risk of bias due to potential selection bias (method of randomization not clearly explained and unbalanced on several baseline measures), and potential detection bias (potentially underpowered given no power calculation and small sample size [$N = 91$]).

McCallion et al. compared a nursing assistant communication skills program ($n = 49$) with a waitlist control group ($n = 56$). Two nursing homes participated in the study. Within each nursing home, one unit was randomized to the treatment group and the other to the control group. Data were also collected from dementia residents in the units that participated in the study. The mean age of residents in the treatment group was 84.5 years and 86 percent were female. In the control group, the mean age of residents was 83.3 years and 89 percent were female. The mean age of care staff in the treatment group was 40.9 years and 95 percent were female. Care staff in the control group had similar characteristics. For staff assigned to the intervention group, a master's level social worker led five 45-minute group sessions on knowledge of dementia, verbal and nonverbal communication, memory aids, and problem behaviors. Social workers also led four 30-minute individual sessions to help care providers identify barriers to communication, recognize verbal and nonverbal messages conveyed by residents, and provide feedback on the use of memory charts (e.g., the use of signs and labeling property to help residents). All social workers had experience with dementia patients and all participated in four half-day training sessions. Random effect regression models were estimated to evaluate treatment effects. Significant time

by group interactions were observed over 3 months (F = 7.76; p <0.01) and 6 months (F= 18.64, p<0.001) for the treatment group compared with the control group on the behavioral disturbance subscale of the CSDD. Over 3 months, there was also a significant time by group interaction (F = 17.59; p <0.001) on the physically nonaggressive behavior subscale of the CMAI in favor of the treatment group. Significant time by group interactions was also observed on the verbally aggressive behavior subscales of the CMAI at 3 (F = 32.97; p <0.001) and 6 months (F = 14.23; p <0.001) in favor of the treatment group. However, at 6 months, staff in the intervention group increased significantly in the use of restraints (F = 9.54; p <0.01). There was no difference in use of psychotropics. This study had a moderate risk of bias due to potential selection bias (unclear method of randomization and some baseline variables not balanced), potential detection bias (potentially underpowered given no power calculation and small sample size [N = 105]), and potential selection bias (staff attrition greater than 20 percent and information on resident attrition not provided).

Teri et al. evaluated an intervention aimed at improving interactions between care staff, the environment, and residents compared with usual care. Only an overall sample size was provided (n = 31). The two-phase study consisted of first a feasibility study and then a randomized trial conducted in the same site to evaluate the effect of the intervention compared with usual care. A sample of assisted living facilities that previously participated in a feasibility study was randomly assigned to treatment conditions. Dementia residents with behavioral problems were invited to participate in the study. The mean age of residents across both treatment conditions was 85.8 years and 87 percent were female. The mean age of staff across both groups was 37.4 years and 96 percent were female. Assisted living staff participated in two half-day workshops and four individualized sessions delivered over 2 months. Each training session was modular and focused on basic information on dementia, verbal and nonverbal skills for communicating with residents, maintaining pleasant events for residents, improving communication between staff and families, and using a framework of activators, behaviors, and consequences for identifying and decreasing resident distress. Staff in usual care received general information on needs of older adults and techniques for caring for residents with dementia. General linear models were estimated to evaluate treatment effects. Compared with usual care, residents in the intervention group had statistically significant improvements on behavioral outcomes. NPI scores declined 3.5 (SD 8.1) points in the intervention group and increased 2.7 (SD 10) points in the control group. The difference in change over time between intervention and control was significant (p = 0.031). This reflects an improvement in behavior for residents in the intervention. Total RMBP scores significantly declined (indicating improvement) in the intervention group (mean change from baseline -1.1 SD 1) and increased in the control group (mean change from baseline 0.2; SD 0.8). The difference in change was significant (p < 0.001) and favored residents in the treatment group. In addition, the difference in change on the ABID between the intervention and control was significant in favor of the intervention (mean change in intervention -3.8 SD 4.0, mean change in control -0.5 SD 6.7, significance of difference in change p <0.001). Staff also benefited from the intervention compared with the control, and significant differences were observed on NPI staff impact (mean change in intervention -1.2 SD 5.3, mean change in control 1.6 SD 4.2, significance of difference in change p = 0.022) and total RMBPC-reaction measures (mean change in intervention -0.7 SD 1.0, mean change in control 0.2 SD 0.8, significance of difference in change p <0.001). Although significant improvements in favor of intervention were observed, these improvements were small and may not be clinically meaningful. No significant difference was observed for staff job satisfaction. This study had a moderate risk of bias due to

potential selection bias (information on randomization not provided), using the same site for feasibility testing and implementation, potential detection bias (no power calculation and small sample size [residents N = 31, staff N = 25]), and potential attrition bias (information on attrition not provided).

Chapman, et al. compared the effectiveness of Advance Illness Care Teams (AICT) (n = 57) with usual care (n = 61). Participants were recruited from two large northeastern United States nursing homes. To be invited to participate in the study, residents had to have dementia, needed assistance with four or more ADLs, scored 23 or less on the MMSE, and scored 4 or more on the GDS. The mean age of residents in AICT was 85 years and 95 percent were female. The mean age of residents in usual care was 88 years and 98 percent were female. AICT consisted of staff teams applying a holistic approach (medical issues, meaningful activities, psychological problems, and behavioral concerns) to the care of dementia residents. Staff teams were multidisciplinary (medicine, nursing, social work, OT/PT, psychology, and nutrition). AICT teams met eight times (once a week) to develop and apply interventions across the holistic domains of the intervention.[114] Families were invited to the team meeting at week 3 and week 8. Residents randomized to usual care received normal care (e.g., medication management, nursing care, and social-recreational activities). Random effects regression models were used to evaluate treatment effects. Agitation/aggression was measured using the CMAI at baseline and 8 weeks. Physically nonaggressive behavior significantly declined in the treatment group compared with usual care ($p < 0.05$). No other significant group and time interactions were observed.

McGilton et al. compared a wayfinding intervention (n = 17) with a control group (n = 15).[115] Residents with dementia in the cognitive support units of a nursing home section of a large, university-affiliated geriatric center were invited to participate in the study. Residents were being relocated to a new facility, which meant that all residents needed to learn their new environments, enabling the investigators to look at the effects of the wayfinding. The study started 6 weeks post-relocation to a new building. The mean age of residents in the treatment group was 86.2 years and 94 percent were female. The mean age of residents in the control group was 89.2 years and 67 percent were female. Wayfinding includes backwards chaining intervention, which focuses on residents' ability to find their way to a specific location. Intervention lasted for 30 minutes, three times a week, for 4 weeks. Outcomes included the Pittsburgh Agitation Scale. Repeated measures analysis of variance was used to evaluate treatment effects. At 3 months after the intervention there was no significant group and time interaction on the measures of agitation/aggression.

Galik et al. compared function-focused care (n = 53) with an attention control group (n = 50).[116] Residents with dementia from four nursing homes were invited to participate in the study. The mean age of residents was 83.7 years and 67 percent were white. Nursing assistants were predominantly female (96 percent), nonwhite (96 percent), and had worked within their respective facility for an average of 5.8 years. Function-focused care consisted of four components: (1) an environmental and policy assessment; (2) 30 minute in-service educational seminar for nursing staff on function-focused care (e.g., having residents walk to the dining room) and 15 minute seminar on engaging residents to participate in functional activity; (3) individualized goals were developed; and (4) ongoing education and support was provided to staff implementing function-focused care. To implement the intervention, a research nurse provided up to 10 hours of support for 6 weeks to nursing homes in the intervention group. In addition, within each intervention, nursing home staff champions were identified. Staff in nursing homes randomized to the attention control group received a 30-minute in-service

educational seminar on function-focused care. This was the same seminar provided to staff in the intervention group (i.e., step two of the intervention). Generalized estimating equations were used to evaluate treatment effects. Agitation and aggression were measured using the CMAI. At 6-months there was no statistical difference in CMAI score between intervention and attention control. Residents in the intervention group had significantly fewer falls (28% vs. 50%). There were no other differences between groups in terms of adverse events as measured by emergency room visits for falls, inquires post fall, and death. At baseline and 3-months staff in the intervention group reported higher job satisfaction as measured by the Job Attitude Scale, but by 6-months there was no statistically significant difference between staff. Finally, at 6-months staff in the intervention group engaged in functional focused care more often than staff in the control group as measured by the Restorative Care Behavior Checklist.

Evidence Synthesis and Strength of Evidence Assessment

Twelve trials studied interventions that could not be conceptually grouped with other studies.[105-116] These trials typically had small sample sizes and methodological problems, so evidence was insufficient for all comparisons and outcomes. To evaluate any trends across the studies, we plotted standardized effects of each intervention on agitation/aggression in a forest plot (Figure 9). All of the interventions reported null effects on agitation/aggression, and the forest plots provide evidence of consistency across studies. Studies have wide confidence intervals indicating an overall lack of precision.

Reports of other outcomes of interests in these studies was sparse. Five studies reported general behavioral outcomes. Four of these studies reported a null effect,[106,111-113] and one study reported an effect in favor of treatment.[105] Two studies reported no effect on antipsychotic use.[106,109] None of the other studies reported medication use. Two studies reported multiple outcomes related to staff behavior and distress.[105,112] Results were mixed, with both no effect and effects in favor and against the intervention. No other outcomes were reported.

Table 7. Care delivery-level interventions for agitation/aggression in nursing home and assisted living facility residents with dementia

Intervention-Comparison	Total Number of Studies (Number of Participants)	Strength of Evidence - Summary of Results
Agitation/Aggression		
Dementia care mapping	3 (643)	Low – agitation/aggression not improved
Person-centered care	3 (813)	Low – agitation/aggression not improved
Protocols to reduce antipsychotic use	3 (1,263)	Insufficient – no conclusions drawn
Emotion-oriented care	2 (297)	Insufficient – no conclusions drawn
General Behavior		
Dementia care mapping	3 (643)	Insufficient – no conclusions drawn
Person-centered care	2 (467)	Insufficient – no conclusions drawn
Protocols to reduce antipsychotic use	1 (659)	Insufficient – no conclusions drawn
Emotion-oriented care	No studies reported	Insufficient – no conclusions drawn
Intermediate Outcomes		
Dementia care mapping	1 (180)	Insufficient – no conclusions drawn (staff behavior)
	2 (339)	Insufficient – no conclusions drawn (staff distress)
	1 (158)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
Person-centered care	2 (505)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
	1 (159)	Insufficient – no conclusions drawn (staff distress)
Protocols to reduce antipsychotic use	3 (1,263)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
	1 (659)	Insufficient – no conclusions drawn (staff behavior)
Emotion-oriented care	1 (151)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
Secondary Outcomes		
Dementia care mapping	1 (159)	Insufficient – no conclusions drawn (injuries)
	1 (180)	Insufficient – no conclusions drawn (staff distress/burden/quality of life)
Person-centered care	1 (159)	Insufficient – no conclusions drawn (injuries)
Protocols to reduce antipsychotic use	No studies reported	Insufficient – no conclusions drawn
Emotion-oriented care	1 (146)	Insufficient – no conclusions drawn (staff distress/burden/quality of life)

Table 8. Efficacy and comparative effectiveness of care delivery interventions for agitation/aggression in nursing home and assisted living facility residents with dementia

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Dementia Care Mapping			
Chenoweth, 2009[96] Jeon, 2012[96,99] RCT Australia Dementia Care Mapping vs. Usual Care k=3; n=159 Low risk of bias	**Treatment**: Staff training and implementation of dementia-care mapping; sessions focused on observing positive and negative care delivery. Following observations feedback was provided to nurses and care plans were developed **Comparison**: Addressed custodial and physical task oriented practices (e.g., unwarranted use of physical restraints, tendency to ignore psychosocial needs, and limited options for resident choice) - 6 hours a day for 2 days - Study investigators and two care staff from nursing home trained by Bradford-trained experts	***Agitation/Aggression*** **CMAI** AMD (CI)=-10.9 (-21.1 to -0.7) ***General Behavior*** **NPI, baseline** Adjusted Mean (SE)=12.7 (5.1) vs. 16.9 (5.3) **NPI, postintervention (4 months)** Adjusted Mean (SE)=16.8 (5.1) vs. 20.2 (5.4) **NPI, postintervention (8 months)** Adjusted Mean (SE)=12.7 (5.1) vs. 16.9 (5.3) Hierarchical linear model: p-value for group: 0.68 Hierarchical linear model: p-value for group and group x time: 0.30 ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR ***Incidents*** **Falls, injuries, drug errors, behavioral events, baseline** Adjusted Proportion=0.40% vs. 0.25% **Falls, injuries, drug errors, behavioral events, postintervention (4 months)** Adjusted Proportion=0.49% vs. 0.37% **Falls, injuries, drug errors, behavioral events, postintervention (8 months)** Adjusted Proportion=0.46% vs. 0.37% Hierarchical linear model: p-value for group and group: 0.15 Hierarchical linear model: p-value for group x time: 0.89	***Staff Behavior:*** **NR** ***Antipsychotic Use*** **Baseline** Adjusted Proportion=0.15% vs. 0.19% **postintervention (4 months)** Adjusted Proportion=0.19% vs. 0.14% **postintervention (8 months)** Adjusted Proportion=0.15% vs. 0.14% Hierarchical linear model: p-value for group: 0.01 Hierarchical linear model: p-value for group x time: 0.66 ***Staff Distress:*** **MBI-Emotional Exhaustion** **Baseline** Mean (SE) = 17.3 (1.7) vs. 12.4 (2.3) **postintervention (4 months)** Mean (SE) = 14.8 (1.8) vs. 14.5 (2.5) **postintervention (8 months)** Mean (SE) = 12.9 (1.8) vs. 16.6 (2.5) Repeated Measures ANCOVA: p-value for group x time: 0.028 (combined intervention groups vs. usual care) **MBI-Depersonalization** **Baseline** Mean (SE) = 3.5 (0.6) vs. 4.3 (0.8) **postintervention (4 months)** Mean (SE) = 3.6 (0.6) vs. 3.8 (0.9) **postintervention (8 months)** Mean (SE) = 3.0 (0.6) vs. 4.9 (0.8) Repeated Measures ANCOVA: p-value for group x time: 0.66

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
			MBI-Personal Accomplishment **Baseline** Mean (SE) = 35.7 (1.4) vs. 31.2 (2.1) **postintervention (4 months)** Mean (SE) = 36.2 (1.3) vs. 33.8 (1.9) **postintervention (8 months)** Mean (SE) = 36.1 (1.3) vs. 36.9 (1.8) Repeated Measures ANCOVA: p-value for group x time: 0.17 **GHQ-28** **Baseline** Mean (SE) = 0.9 (0.3) vs. 0.5 (0.4) **postintervention (4 months)** Mean (SE) = 1.5 (0.4) vs. 1.2 (0.5) **postintervention (8 months)** Mean (SE) = 0.7 (0.4) vs. 1.2 (0.5) Repeated Measures ANCOVA: p-value for group x time: 0.92 ***Staff Burden:*** NR ***Staff QoL:*** NR
Rokstad, 2013[97] RCT Norway Dementia Care Mapping vs. Usual Care K=3; n=308 Moderate risk of bias	**Treatment**: Staff received 3-hour lecture on dementia-care mapping; used as a process tool to develop care staff skills in person centered care **Comparison**: All three treatment groups received five DVDs with lectures about dementia. No other information regarding the control group was provided. - dementia-care mapping at beginning of study and 6-months - two care staff members from nursing home were trained	***Agitation/Aggression*** ***Brief Agitation Rating Scale*** MC (p-value between group)=-1.5 vs. 0.2 (0.06) Multivariate regression: Coefficient (CI) = -2.0 (-5.1 to 1.1) ***Agitation-NPI-Q Agitation*** MC (p-value between group)=-0.3 vs. 0.5 (<0.01) Multivariate regression: Coefficient (CI) = -0.9 (-1.7 to -0.04) ***General Behavior – NPI-Q*** MC (p-value between group) =-0.2 vs. 1.4 (<0.01) Multivariate regression: Coefficient (CI) = -2.7 (-4.6 to -0.7) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Van de Ven, 2013[98] RCT Netherlands Dementia Care Mapping vs. Usual Care K=3; n=180 Moderate risk of bias	**Treatment**: Nursing homes given a briefing on dementia-care mapping (observation, feedback, action plan); two staff trained and certified **Comparison**: Continuation of daily care practices; practices could vary by facility. Additional details were not provided. - 2 dementia-care mapping cycles - two staff from each nursing home were trained	***Agitation/Aggression*** ***CMAI*** MD (CI)= 2.4 (-2.7 to 7.6) ***General Behavior*** **NPI-NH, baseline** Mean (SE)=5.35 (0.94) vs. 6.28 (0.88) **NPI-NH postintervention (4 months)** Mean (SE)=7.19 (0.95) vs. 4.45 (0.88) **NPI-NH postintervention (8 months)** Mean (SE)=6.28 (0.92) vs. 4.13 (0.86) *Linear mixed-effect model* *p-value for group: 0.23* *Linear mixed-effect model* *p-value for group * time: 0.02* ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior*** ***QEAW emotion reactions, baseline*** Mean (SE)=13.69 (1.51) vs. 9.48 (1.40) ***QEAW emotion reactions,*** **postintervention (4 months)** Mean (SE)=23.38 (1.67) vs. 25.97 (1.59) ***QEAW emotion reactions,*** **postintervention (8 months)** Mean (SE)=53.28 (1.20) vs. 53.09 (1.12) *Linear mixed-effect model* *p*-value for group: 0.719 *Linear mixed-effect model* *p*-value for group * time: 0.015 ***Antipsychotic Use:*** NR ***Staff Distress*** **GHQ 12, baseline** Mean (SE)=17.48 (0.33) vs. 16.67 (0.29) **GHQ 12 postintervention (4 months)** Mean (SE)=15.72 (0.38) vs. 14.89 (0.34) **GHQ 12 postintervention (8 months)** Mean (SE)=14.57 (0.37) vs. 14.42 (0.32) Linear mixed-effect model p-value for group: 0.122 Linear mixed-effect model p-value for group * time: 0.43 ***Staff Burden:*** NR ***Staff QoL*** **MJSS-HC, baseline** Mean (SE)=76.98 (1.36) vs. 77.29 (1.44) **MJSS-HC, postintervention (4 months)** Mean (SE) =76.40 (1.34) vs. 75.10 (1.43) **MJSS-HC, postintervention (8 months)** Mean (SE)=78.08 (1.40) vs. 75.58 (1.46) Linear mixed-effect model p-value for group: 0.56 Linear mixed-effect model p-value for group * time: 0.069

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
Person-Centered Care			
Chenoweth, 2009[96] Jeon, 2012[99] RCT Australia Dementia Care Mapping vs. Usual Care k=3; n=141 Low risk of bias	**Treatment**: Training in person centered care using the Bradford University training manual; focused on teaching caregivers to interpret behavior as a form of communication **Comparison**: Addressed custodial and physical task oriented practices (e.g., unwarranted use of physical restraints, tendency to ignore psychosocial needs, and limited options for resident choice) - 2-day training session + 2 nursing home visits by study investigators to implement person-centered care + conference calls between investigators and staff - study investigators	***Agitation/Aggression*** **CMAI** AMD (CI) =-13.6 (-23.9 to -3.3) ***General Behavior*** **NPI, baseline** Adjusted Mean (SE)=21.3 (6.8) vs. 16.9 (5.3) **NPI, postintervention (4 months)** Adjusted Mean (SE)=16.8 (5.1) vs. 20.2 (5.4) ***General Behavior*** **NPI, postintervention (8 months)** Adjusted Mean (SE)=13.5 (5.1) vs. 15.3 (5.3) Hierarchical linear model: p-value for group: 0.68 Hierarchical linear model: p-value for group x time: p = 0.30 ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR ***Incidents*** **Falls, injuries, drug errors, behavioral events, baseline** Adjusted Proportion=0.43% vs. 0.25% **Falls, injuries, drug errors, behavioral events, postintervention (4 months)** Adjusted Proportion=0.53% vs. 0.37% **Falls, injuries, drug errors, behavioral events, postintervention (8 months)** Adjusted Proportion=0.44% vs. 0.37% Hierarchical linear model: p-value for group and group: 0.15 Hierarchical linear model: p-value for group x time: 0.89	***Staff Behavior:*** NR ***Antipsychotic Use*** **Baseline** Adjusted Proportion=0.42% vs. 0.19% **postintervention (4 months)** Adjusted Proportion=0.30% vs. 0.14% **postintervention (8 months)** Adjusted Proportion=0.34% vs. 0.14% Hierarchical linear model: p-value for group: 0.01 Hierarchical linear model: p-value for group x time: 0.66 ***MBI-Emotional Exhaustion*** **Baseline** Mean (SE) = 14.3 (1.5) vs. 12.4 (2.3) **postintervention (4 months)** Mean (SE) = 16.0 (1.7) vs. 14.5 (2.5) **postintervention (8 months)** Mean (SE) = 15.1 (1.6) vs. 16.6 (2.5) Repeated Measures ANCOVA: p-value for group x time: 0.028 (group means either treatment group compared with usual care) ***MBI-Depersonalization*** **Baseline** Mean (SE) = 3.4 (0.6) vs. 4.3 (0.8) **postintervention (4 months)** Mean (SE) = 3.2 (0.6) vs. 3.8 (0.9) **postintervention (8 months)** Mean (SE) = 2.9 (0.6) vs. 4.9 (0.8) Repeated Measures ANCOVA: p-value for group x time: 0.66 ***MBI-Personal Accomplishment*** **Baseline** Mean (SE) = 34.1 (1.3) vs. 31.2 (2.1) **postintervention (4 months)** Mean (SE) = 35.5 (1.2) vs. 33.8 (1.9)

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
			postintervention (8 months) Mean (SE) = 35.2 (1.1) vs. 36.9 (1.8) Repeated Measures ANCOVA: p-value for group x time: 0.17 ***GHQ-28*** **Baseline** Mean (SE) = 0.9 (0.2) vs. 0.5 (0.4) **postintervention (4 months)** Mean (SE) = 1.3 (0.3) vs. 1.2 (0.5) **postintervention (8 months)** Mean (SE) = 1.1 (0.3) vs. 1.2 (0.5) Repeated Measures ANCOVA: p-value for group x time: 0.92 ***Staff Burden:*** NR ***Staff QoL:*** NR
Rokstad, 2013[97] RCT Norway Dementia Care Mapping vs. Usual Care k=3; n=288 Moderate risk of bias	**Treatment**: A 24-indicator framework to evaluate person-centered care; three nurses from each ward attended a 3-day training seminar on person-centered care, then led intervention **Comparison**: All three treatment groups received five DVDs with lectures about dementia. No other information regarding the control group was provided. - 3-day training seminar; 3-hour class to all staff regarding the VPM methodology; 45-60 minutes weekly staff meetings to analyze patient-nurse interactions, meetings chaired by nurse trained in VPM method - 3 nursing home staff	***Agitation/Aggression*** ***Brief Agitation Rating Scale*** MC (p-value between group) = -1.2 vs. 0.2 (0.17) Multivariate regression: Coefficient (CI) = -1.1 (-3.8 to 1.6) ***NPI-Q Agitation*** MC (p-value between group) = -0.5 vs. 0.5 (<0.01) Multivariate regression: Coefficient (CI) = -0.9 (-1.6 to -0.01) ***General Behavior*** ***NPI-Q*** MC (p-value between group) = -0.7 vs. 1.4 (<0.01) Multivariate regression: Coefficient (CI) = -2.4 (-4.1 to -0.6) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Fossey, 2006*[100] RCT England Clinical Protocol Combined with Person Centered Care vs. Usual Care k=3; n=346 Moderate risk of bias *This study fits in person-centered care and reducing antipsychotics	**Treatment**: Staff training in delivery of person centered care and understanding the role of the environment in the patient caregiver relationship; training in Cohen-Mansfield behavioral management technique **Comparison**: - weekly supervision over 10 months - psychologist, occupational therapist, or nurse to staff caregivers, study investigators provided weekly supervision; prescribers worked with study psychiatrists 2-days a week	***Agitation/Aggression*** **CMAI** AMD (CI) = -0.3 (-8.3 to 8.9) ***Agitation*-% of population with >1 episode of aggression** MD (CI) = -1.6% (-12.7% to 15.8%) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior:*** NR ***Antipsychotic Use*** ***% taking antipsychotics*** MD (CI) = -19.5% (-47.1% to 3.0%) ***Dose of antipsychotics*** AMD (CI) = -4.0% (-29.9% to 22.0%) ***% taking other psychotropic*** MD (CI) = 5.9% (-27.2% to 15.5%) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Reducing Antipsychotics			
Fossey, 2006*[100] RCT England Clinical Protocol Combined with Person Centered Care vs. Usual Care K=2; n=346 Moderate risk of bias *This study fits in person-centered care and reducing antipsychotics	**Treatment**: Staff training in delivery of person centered care and understanding the role of the environment in the patient caregiver relationship; training in Cohen-Mansfield behavioral management technique **Comparison**: - weekly supervision over 10 months - psychologist, occupational therapist, or nurse to staff caregivers, study investigators provided weekly supervision; prescribers worked with study psychiatrists 2-days a week	***Agitation/Aggression*** **CMAI** AMD (CI) = -0.3 (-8.3 to 8.9) **% of population with >1 episode of aggression** MD (CI) = -1.6% (-12.7% to 15.8%) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR	***Staff Behavior:*** NR ***Antipsychotic Use -% taking antipsychotics*** MD (CI) = -19.5% (-3.0% to 41.7%) ***Antipsychotic Use -Dose of antipsychotics*** AMD (CI) = -4.0% (-29.9% to 22.0%) ***% taking other psychotropic*** MD (CI) = 5.9% (-27.2% to 15.5%) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Rapp, 2013[101] RCT Germany Clinical Protocol vs. Usual Care K=2; n=258 Low-Moderate risk of bias	**Treatment**: home staff received training on general information about dementia; use of activity-based interventions **Comparison**: 13 nursing homes provided group activity twice a week for 45 min; 5 nursing homes provided activity sessions once a week for 45 minutes. Not all residents in a usual	***Agitation/Aggression*** **CMAI** AMD (CI) = -6.24 (-14.14 to -2.03) **CMAI aggressive behavior subscale** F-value (p-value) group x time: 6.442 (0.012) **CMAI physically nonaggressive behavior** F-value (p-value) group x time: 0.001 (0.977) **CMAI verbally agitated behavior**	***Staff Behavior:*** NR ***Antipsychotic Use*** **Dose of antipsychotic** AMD (CI) = -0.03 (-0.05 to -0.03) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
	care home participated in group activity (approximately 29.7% did at baseline). Activity therapy optional for residents in usual care. - staff trained in two 4-hour sessions; activity interventions 1-2 days a week for 45 minutes; prescribers trained individually for 4 hours - prescribers, nursing home staff	F-value (p-value) group x time: 0.853 (0.357) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** **NR**	
Zwijsen, 2014[102] RCT Netherlands Clinical Protocol vs. Usual Care n=659 Moderate risk of bias	**Treatment**: Training in using structured form to evaluate behaviors and develop individualized treatment goals **Comparison**: NR - 1 day of training at study commencement, postintervention meeting 2 weeks later; study lasted 20 months - Nursing staff, physicians, and psychologists	***Agitation/Aggression*** **CMAI** Linear mixed effect model coefficient for difference in MC (CI): -2.5 (-4.3 - -0.6) in favor of intervention. **NPI-Agitation** Number of agitated behaviors OR (CI): 0.81 (0.50 – 1.32). ***General Behavior:*** Total number of NPI symptoms post intervention OR: estimated from figure 0.60 (NS). ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior:*** **Restraint use**: NS - detailed data not provided ***Antipsychotic Use:*** Number of prescriptions post intervention OR (CI): 0.54 (0.37 – 0.80) in favor of treatment ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Emotion Oriented Care			
Finnema, 2005[103] RCT Netherlands Emotion oriented care vs. Control k=2; n=146 Low risk of bias	**Treatment**: Basic course for all nursing home care staff on emotion-oriented care (staff experience and understanding resident experiences); advanced course for select staff focused on making life histories and acknowledging patient experiences; advisor course for select staff focused on implementation on emotion oriented care (these staff also led emotion-oriented group sessions for residents). **Comparison**: working in accordance with the guidelines of the Model-Care	***Agitation/Aggression*** **CMAI** Multivariate Analysis of Variance Adjusted Means (F-test, p-value): 3.34 vs. 3.63 (0.43, 0.51) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress*** **Stress reactions GHQ 12** Multivariate Analysis of Variance Adjusted Means improved and not improved (F-test, p-value): treatment 15.42 and 20.47 and control 19.14 and 14.19 (9.11, 0.003). **Staff distress-Stress perception QOS** Multivariate Analysis of Variance Adjusted Means improved and not improved (F-test, p-value): treatment 23.02 and 24.73

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
	plan of the Dutch Association of Nursing Home Care. No other details provided. - basic course: 2 days; advanced course: 7 days over 8 months; advisor course: 10 days over 9 months - nursing assistants		and control 22.59 and 23.70 (1.51, 0.54) ***Staff Burden:*** NR ***Staff QoL:*** NR
Schrijnemaekers, 2002[104] RCT Netherlands Emotion Oriented Care vs. Usual Care n =151 Moderate risk of bias	**Treatment**: All nursing home staff received clinical lesson on goal of emotion-oriented care; eight staff caregivers received training in emotion-oriented care **Comparison**: nursing homes' procedures prior to entering the study - lesson: 1 hour; three half-day supervision meetings - professional training organization teacher	***Agitation/Aggression*** **CMAI-verbal aggression** Day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.04 (NS) 3-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 1.54 (NS) 6-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.78 (NS) 12-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.41 (NS) Ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.14 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.07 (NS) 6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -1.10 (NS) 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -1.41 (NS) **CMAI aggression** Day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.04 (NS) 3-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.59 (NS) 6-month day-care unit caregivers linear multilevel model adjusted MD per month (p-	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Psychotropic Use*** Ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.00 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.00 (NS) 6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.07 (NS) 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.02 (NS) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
		value): 0.12 (NS) 12-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.67 (NS) Ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.13 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.87 (NS) 6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.83 (NS) 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -1.18 (NS) **CMAI physical nonaggression** Day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.03 (NS) 3-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.70 (NS) 6-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): -0.85 (NS) 12-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.97 (NS) Ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.14 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.28 (NS) 6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -2.26 (<0.01) in favor of control 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -1.27 (NS) **GIP nonsocial**	

Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
		Day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.04 (NS) 3-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.35 (NS) 6-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.84 (NS) 12-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.08 (NS) Ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.05 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 1.96 (NS) 6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 1.78 (NS) in favor of control 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 1.01 (NS) **GIP loss of decorum** Day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.01 (NS) 3-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.47 (NS) 6-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.38 (NS) 12-month day-care unit caregivers linear multilevel model adjusted MD per month (p-value): 0.18 (NS) Ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.00 (NS) 3-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.05 (NS)	

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
		6-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): 0.05 (NS) in favor of control 12-month ward unit caregivers linear multilevel model adjusted MD per month (p-value): -0.10 (NS) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	
Unique Comparisons			
Deudon, 2009[106] RCT France Staff education vs. Control n=306 Low-Moderate risk of bias	**Treatment**: Teaching session on dementia to nursing home care staff; use of how-to instruction cards providing practical advice on how to deal with behaviors **Comparison**: Usual care defined as care according to own practices and procedures - 90-minute session; trainings available 2-hours twice a week - trainers	***Agitation/Aggression*** **CMAI** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.26 (0.05) vs. 0.02 (0.06) [0.001] **CMAI physically nonaggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.02 (0.002) vs. -0.003(0.03) [<0.0001] **CMAI verbally nonaggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.02 (0.003) vs. 0.001 (0.004) [<0.001] **CMAI physically aggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.001 (0.002) vs. 0.004 (0.002) [0.142] **CMAI verbally aggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.01 (0.004) vs. -0.001 (0.004) [0.571]	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR **Baseline** Mean (SD) =2.52 (1.3) vs. 2.68 (1.65) **Postintervention (8 weeks)** Mean (SD) =2.62 (1.3) vs. 2.76 (1.6) **Postintervention (20 weeks)** Mean (SD) =2.51 (1.3) vs. 2.81 (1.6) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
		General Behavior **NPI-Hyperactivity factor** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.25 (0.2) vs. 0.35 (0.2) [0.032] ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	
Proctor, 1999[110] RCT England Staff Education and Care Planning vs. Usual Care n=120 Low-Moderate	**Treatment**: Nursing home staff received educational seminars on dementia; weekly psychiatric nurse visits to support developing care plans. **Comparison**: Usual care not defined - seven 1-hour seminars - psychiatric nurse	***Agitation:*** NR ***General Behavior*** ***CRB*** AMD (CI) = -0.7 (-3.0 to 1.6) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Clare, 2013[112] RCT England Staff Training in Aware Care vs. Usual Care k=1; n=65 Low risk of bias	**Treatment**: Nursing home staff received training on resident awareness and use of AwareCare measures; staff observation and weekly support **Comparison**: Homes in the control group received no input - 8 week course (two 90-minute sessions + 6 weeks observation and weekly support) - accredited trainer	***General Behavior*** ***PRS*** Analysis of Covariance Adjusted Means (SE): 37.39 (2.32) vs. 34.71 (2.17) Analysis of Covariance F-test (p-value) of group * time: 0.25 (0.62) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	***Staff Behavior*** ***MBI Depersonalization*** Analysis of Covariance Adjusted Means (SE): 1.32 (0.04) vs. 0.53 (0.07) Analysis of Covariance F-test (p-value) of group * time: 2.55 (0.12) ***Antipsychotic Use:*** NR ***Staff Distress*** **GHQ** Analysis of Covariance Adjusted Means (SE): 6.63 (0.82) vs. 7.12 (1.05) Analysis of Covariance F-test (p-value) of group * time: 0.22 (0.64) ***Staff Burden*** **Emotional Exhaustion** Analysis of Covariance Adjusted Means (SE):12.36 (0.07) vs. 12.38 (0.07) Analysis of Covariance F-test (p-value) of group * time: 0.00 (0.99) ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Wenborn, 2013[111] RCT United Kingdom Activity Intervention vs. Usual Care n=159 Low-Moderate risk of bias	**Treatment**: Education sessions to nursing home staff to improve knowledge and skill; one-to-one coaching; occupational therapy assessment of physical environment **Comparison**: Usual care consisted of care consistent with procedures of the home. Homes were allowed to implement their own training or any new activity provision they sought fit. - five 2-hour sessions over 16 weeks - occupational therapists, study investigators	***Agitation/Aggression*** **CBS** 4-week MD (CI) = 1.15 (-9.23 to 11.52) 12-week AMD (CI) = 4.13 (-21.10 to 29.36) ***General Behavior*** **CAPE BRS** 4-week MD (CI) = 1.08 (-0.18 to 2.34) 12-week AMD (CI) = 0.52 (-1.63 to 2.67) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR **Total Medications** 4-week MD (CI) = 0.10 (-0.53 to 0.34, 0.66) 12-week AMD (CI) = -0.15 (-0.55 to 0.24) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Chapman, 2007[114] RCT United States Advanced illness care team vs. usual care n = 118 Moderate risk of bias	**Treatment**: Advanced illness care team (AICT) intervention addressed 4 domains of care (medical issues, meaningful activities, psychological problems, and behavioral concerns); care teams of staff working in each of the units at the nursing homes (medicine, nursing, social work, psychology, PT, OT, nutrition. Residents and families were invited to participate in a planning meeting of each AICT **Comparison**: Usual care (waitlist control) participants received typical services and received treatment after the 8 week usual care period - care team met five times during the intervention period; planning meetings during weeks 3 and 8 - licensed clinical social workers (study authors)	***Agitation/Aggression*** **CMAI – Aggressive behavior,** mean (SD) Baseline: 1.18 (0.47) vs. 1.23 (0.48) 8 weeks: 1.10 (0.25) vs. 1.16 (0.39) **CMAI – Physically nonaggressive behavior,** mean (SD) Baseline: 1.64 (1.10) vs. 1.36 (0.52) 8 weeks: 1.30 (0.60) vs. 1.29 (0.49) **CMAI – Verbally agitated behavior,** mean (SD) Baseline: 1.44 (0.48) vs. 1.44 (0.61) 8 weeks: 1.28 (0.42) vs. 1.36 (0.53)	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Kovach, 2006[113] RCT United States Training in Serial Trial Intervention vs.	**Treatment**: long-term care nurses led in an educational seminar on how to use STI method (a five step process used to identify needs and apply therapy to meet the need)	***General Behavior*** **BEHAVE AD, baseline** Mean (SD) =7.43 (6.75) vs. 6.80 (5.47) **BEHAVE AD, Postintervention (2 weeks)** Mean (SD) =5.56 (5.64) vs. 6.15 (5.55)	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Usual Care n=114 Moderate risk of bias	**Comparison**: Nurses in the control group were taught common misconceptions about dementia, the physical effects of aging, causes of dementia, stages of Alzheimer's disease, and approaches to treating behaviors associated with dementia. - 7-hour seminar - 2 advanced practice nurses	**BEHAVE AD, Postintervention (4 weeks)** Mean (SD) =4.68 (4.06) vs. 4.96 (4.39) Repeated Measures Analysis of Variance F-test (p-value) group x time: 0.70 (0.5) ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	
McGilton, 2003[115] RCT Canada Way-finding vs control n = 32 Moderate risk of bias	**Treatment**: Way-finding intervention included backward chaining **Comparison**: NR - 30 minutes 3x/week for 4 weeks - research assistant	***Agitation/Aggression*** **Pittsburgh Agitation Scale,** mean (SD) Baseline: 2.4 (1.6) vs. 1.8 (1.3) 1 week post-intervention: .87 (0.88) vs. 0.92 (1.0) 3 months post-intervention: 1.8 (1.1) vs. 0.92 (0.99)	***Staff Behavior: NR*** ***Antipsychotic Use: NR*** ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR
Magai, 2002[108] RCT United States Staff Training vs. Behavioral Placebo and Wait-list Control n=95 Moderate risk of bias	**Treatment**: Nursing home staff received training in nonverbal sensitivity **Comparison**: No information provided; placebo control group participated in training sessions but the sessions focused on cognitive and behavioral aspects of dementia and did not focus on patient affect - ten 1-hour sessions over 2 weeks - clinical psychologist	***Agitation/Aggression*** **Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD** **Baseline** Mean (SD) =83.7 (51.2) vs. 25.2 (5.2) vs. 40.6 (7.8) **Postintervention (3 weeks)** Mean (SD) =69.1 (36.1) vs. 49.6 (27.2) vs. 75.4 (41.4) **Postintervention (6 weeks)** Mean (SD) =69.1 (36.1) vs. 49.6 (27.2) vs. 75.4 (41.4) **Postintervention (9 weeks)** Mean (SD) =71.8 (37.6) vs. 44.6 (23.7) vs. 63.1 (42.0) **Postintervention (12 weeks)** Mean (SD) =65.5 (37.7) vs. 39.2 (15.2) vs. 61.6 (31.1) Repeated Measures Analysis of Variance F-test (p-value) for group: 2.28 (NS) Repeated Measures Analysis of Variance F-test (p-value) for group x interaction: 1.15 (NS)	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
		General Behavior: NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	
McCallion, 1999[109] RCT United States Staff Education vs. Usual Care n=105 Moderate risk of bias	**Treatment**: Nursing home staff received education in knowledge of dementia, verbal and nonverbal communication, memory aids, and problem behaviors **Comparison**: No intervention-related activity - five 45-minute group sessions and four 30-minute individual conferences - master's level social worker	***Agitation/Aggression*** **CSDD behavioral disturbance, baseline** Mean (SD) =2.00 (1.58) vs. 1.13 (1.06) **CSDD behavioral disturbance, Postintervention (3 months)** Mean (SD)=1.32 (1.40) vs. 0.98 (1.13) **CSDD behavioral disturbance, Postintervention (6 months)** Mean (SD)=1.26 (1.17) vs. 1.29 (1.29) Random effects regression F-test (p-value) 3-month group: 49.20 (NS) Random effects regression F-test (p-value) 3-month group x interaction: 7.76 (<0.01) F-test (p-value) 6-month group: 23.46 (NS) F-test (p-value) 6-month group x interaction: 18.64 (<0.001) **CMAI aggressive behavior, Baseline** Mean (SD)=15.16 (9.81) vs. 13.25 (7.52) **CMAI aggressive behavior, Postintervention (3 months)** Mean (SD)=11.00 (5.35) vs. 12.46 (6.82) **CMAI aggressive behavior, Postintervention (6 months)** Mean (SD)=12.21 (8.31) vs. 12.02 (6.22) Random effects regression F-test (p-value) 3-month group: 0.23 (NS) Random effects regression F-test (p-value) 3-month group x interaction: 8.67 (NS) F-test (p-value) 6-month group: 6.02 (NS) F-test (p-value) 6-month group x interaction: 0.92 (NS) **CMAI physically nonaggressive behavior, baseline**	***Staff Behavior*** **Restraints Use, baseline** Mean (SD) =1.20 (1.34) vs. 1.82 (1.62) **Restraints Use, Postintervention (3 months)** Mean (SD) = 1.53 (1.56) vs. 2.04 (1.78) **Restraints Use, Postintervention (6 months)** Mean (SD) = 1.88 (1.82) vs. 1.75 (1.42) *Random effects regression* *F-test (p-value) 3-month group:* 43.99 (NS) F-test (p-value) 3-month group x interaction: 0.00 (NS) F-test (p-value) 6-month group: 7.20 (NS) F-test (p-value) 6-month group x interaction: 9.54 (<0.01) ***Antipsychotic Use:*** NR **Psychotropic Use, mean (SD)** Baseline, 0.98 (1.41) vs. 1.62 (1.70) **Postintervention (3 months)** 0.93 (1.39) vs. 1.7 (1.82) **Postintervention (6 months)** 1.30 (2.15) vs. 1.57 (1.71) Random effects regression F-test (p-value) 3-month group: 37.48 (NS) F-test (p-value) 3-month group x interaction: 1.78 (NS) F-test (p-value) 6-month group: 4.99 (NS) F-test (p-value) 6-month group x interaction: 1.61 (NS) ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL:*** NR

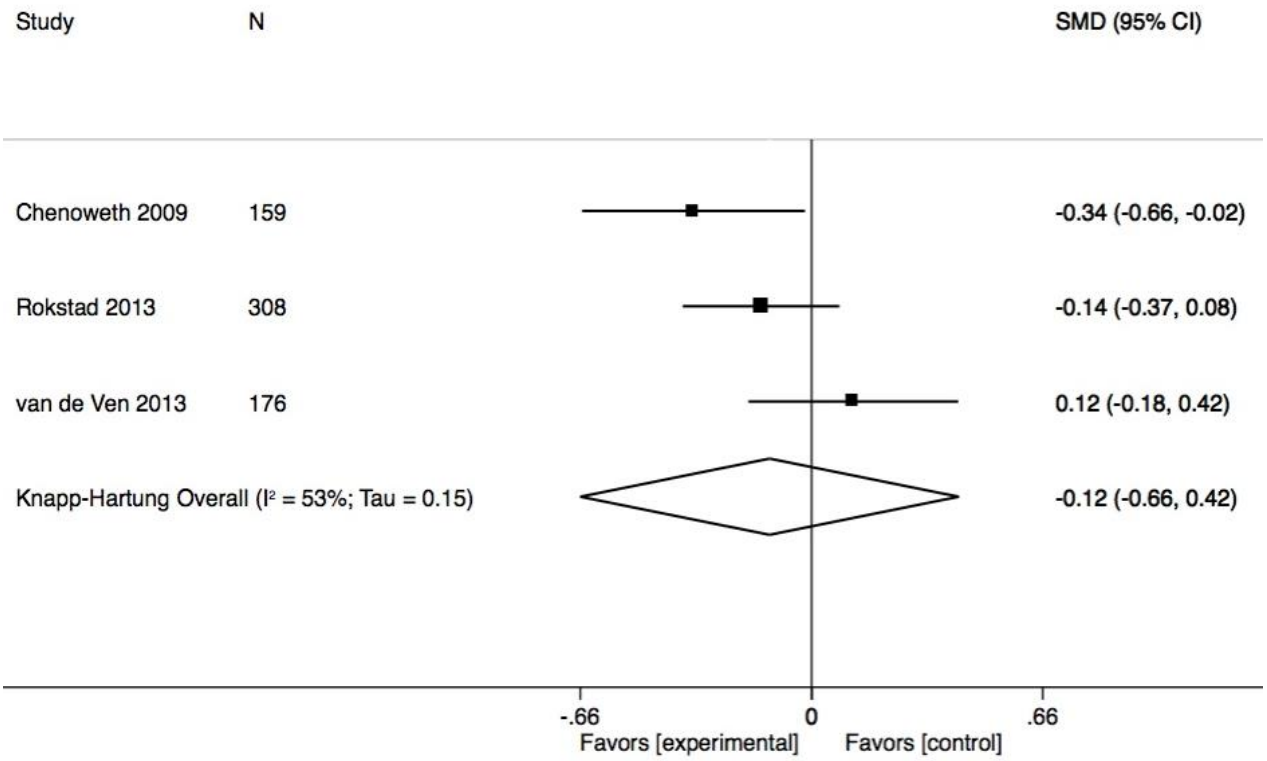
Study Design Country Comparison k= ; n= Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
		Mean (SD)=12.49 (6.34) vs. 11.09 (5.47) **CMAI physically nonaggressive behavior, Postintervention (3 months)** Mean (SD)=10.36 (4.72) vs. 11.86 (6.54) **CMAI physically nonaggressive behavior, Postintervention (6 months)** Mean (SD)=11.38 (5.99) vs. 10.38 (6.32) Random effects regression F-test (p-value) 3-month group: 0.56 (NS) F-test (p-value) 3-month group x interaction: 17.59 (<0.001) F-test (p-value) 6-month group: 7.78 (NS) F-test (p-value) 6-month group x interaction: 0.26 (NS) **CMAI verbally aggressive behavior, baseline** Mean (SD)=16.22 (10.31) vs. 10.44 (6.21) **CMAI verbally aggressive behavior, Postintervention (3 months)** Mean (SD)=11.3 8 (7.13) vs. 11.52 (6.71) **CMAI verbally aggressive behavior, Postintervention (6 months)** Mean (SD)=12.88 (8.39) vs. 12.05 (6.86) Random effects regression F-test (p-value) 3-month group: 38.65 (NS) F-test (p-value) 3-month group x interaction: 32.97 (<0.001) F-test (p-value) 6-month group: 38.82 (NS) F-test (p-value) 6-month group x interaction: 14.23 (<0.001) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries*:** NR	
Teri, 2005[105] RCT United States Staff Training vs. Usual Care n=31	**Treatment**: Assisted living staff received workshops focused on dignity and respect of patient and caregiver skill development + individualized sessions **Comparison**: Usual on-site training (general information on needs of older,	***Agitation/Aggression*** **ABID** AMC (SD)=-3.8 (4.0) vs. -0.5 (6.7) ***General Behavior*** **NPI** AMC (SD)= -3.5 (8.1) vs. 2.7 (10.0)	***Staff Behavior:*** NR ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden*** **NPI (staff impact)** AMC (SD)= -1.2 (5.3) vs. 1.6 (4.2)

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Moderate risk of bias	memory-impaired adults) - 2-half day workshops; 4 individual sessions - clinical psychologist (study author), graduate nursing student	**RMBPC Total Score Frequency** AMC (SD)= -1.1 (1.0) vs. 0.2 (0.8) **RMBPC Disruption Frequency** AMC (SD)= -0.2 (0.2) vs. 0.0 (0.3) ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR	**RMBPC (reaction)** AMC (SD)= -0.7 (1.0) vs. 0.2 (0.8) **RMBPC-disruption (reaction)** AMC (SD)= -0.1 (0.3) vs. 0.0 (0.0) ***Staff QoL*-Job Satisfaction** AMC (SD)= 0.2 (0.4) vs. 0.00 (0.05)
Galik, 2014[116] RCT United States Function-focused Care vs. Attention Control n =103 Moderate risk of bias	**Treatment**: Nursing home staff were trained in engaging residents to optimize physical activities; key intervention components included nursing home environment assessment, staff education, development of function focused goals and physical activities **Comparison**: Attention control reduced educational seminars on function focused care. - sites received intervention for 10 hours per week for 6 months total - research nurse	***Agitation*** **CMAI baseline** Control M (SE): 19.06 (1.05) Treatment M (SE): 16.57 (0.69) p-value difference between control and treatment: 0.08 **CMAI 3-months** Control M (SE): 18.95 (1.21) Treatment M (SE): 17.04 (0.69) p-value difference between control and treatment: 0.01 **CMAI 6-months** Control M (SE): 19.48 (1.46) Treatment M (SE): 17.83 (0.89) p-value difference between control and treatment: 0.36 ***General Behavior:*** NR ***Patient Distress:*** NR ***Nursing Home Admission:*** NR ***Injuries:*** NR ***Harms/Adverse Events*** **Falls 6-months** Control N (%): 25 (50) Treatment N (%): 15 (28) p-value difference between control and treatment: 0.02 **Emergency room visits for falls 6-months:** Control N (%): 5 (10) Treatment N (%): 1 (2) p-value difference between control and treatment: 0.08	***Staff Behavior:* Self-efficacy for Restorative Care** **Activities Function Focused Activities - The Restorative Care Behavior Checklist baseline** Control M (SE): 0.55 (0.04) Treatment M (SE): 0.63 (0.04) p-value difference between control and treatment: 0.18 **Function Focused Activities - The Restorative Care Behavior Checklist 3-months** Control M (SE): 0.61 (0.04) Treatment M (SE): 0.71 (0.04) p-value difference between control and treatment: 0.12 **Function Focused Activities - The Restorative Care Behavior Checklist 6-months** Control M (SE): 0.40 (0.06) Treatment M (SE): 0.66 (0.05) p-value difference between control and treatment: 0.001 ***Antipsychotic Use:*** NR ***Staff Distress:*** NR ***Staff Burden:*** NR ***Staff QoL*** **Job Satisfaction (Job Attitude Scale) baseline** Control M (SE): 35.00 (1.02) Treatment M (SE): 39.37 (0.93)

Study **Design** **Country** **Comparison** **k= ; n=** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
		Injuries post falls 6-months Control N (%): 5 (10) Treatment N (%): 5 (9) p-value difference between control and treatment: 0.92 **Deaths 6-months** Control N (%): 3 (6) Treatment N (%): 5 (9) p-value difference between control and treatment: 0.45	p-value difference between control and treatment: 0.002 **Job Satisfaction (Job Attitude Scale) 3-months** Control M (SE): 33.35 (1.19) Treatment M (SE): 37.85 (0.93) p-value difference between control and treatment: 0.003 **Job Satisfaction (Job Attitude Scale) 6-months** Control M (SE): 35.13 (1.24) Treatment M (SE): 36.89 (1.00) p-value difference between control and treatment: 0.280

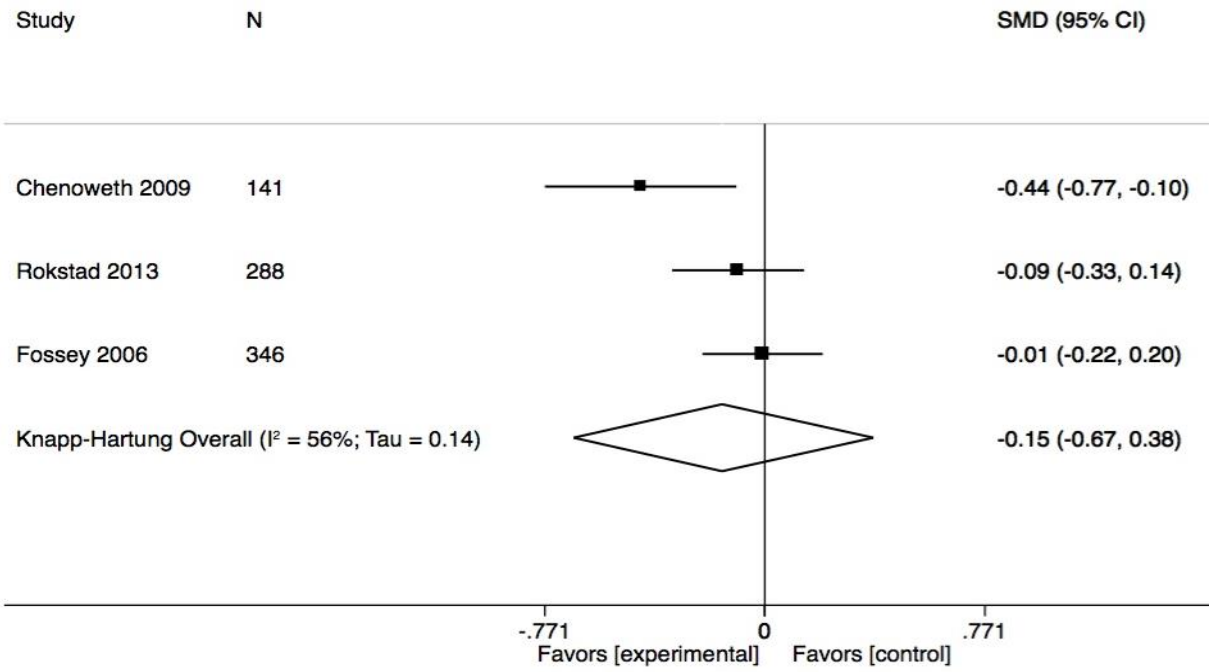
ABID=Agitated Behavior in Dementia; BEHAVE-AD=Behavioral Pathology in Alzheimer's disease; BMD=Behavior and Mood Disturbance; = General Health Questionnaire; MBI = Maslach Burnout Inventory; MOSES=Multi-dimensional Observation Scale for Elderly Patients; NPI=Neuropsychiatric Inventory; REHAB=Rehabilitation Evaluation Hall and Baker; RMBPC=Revised Memory and Behavior Problem Checklist

Figure 5. Random effects meta-analysis for the effect of dementia care mapping on agitation/sggression



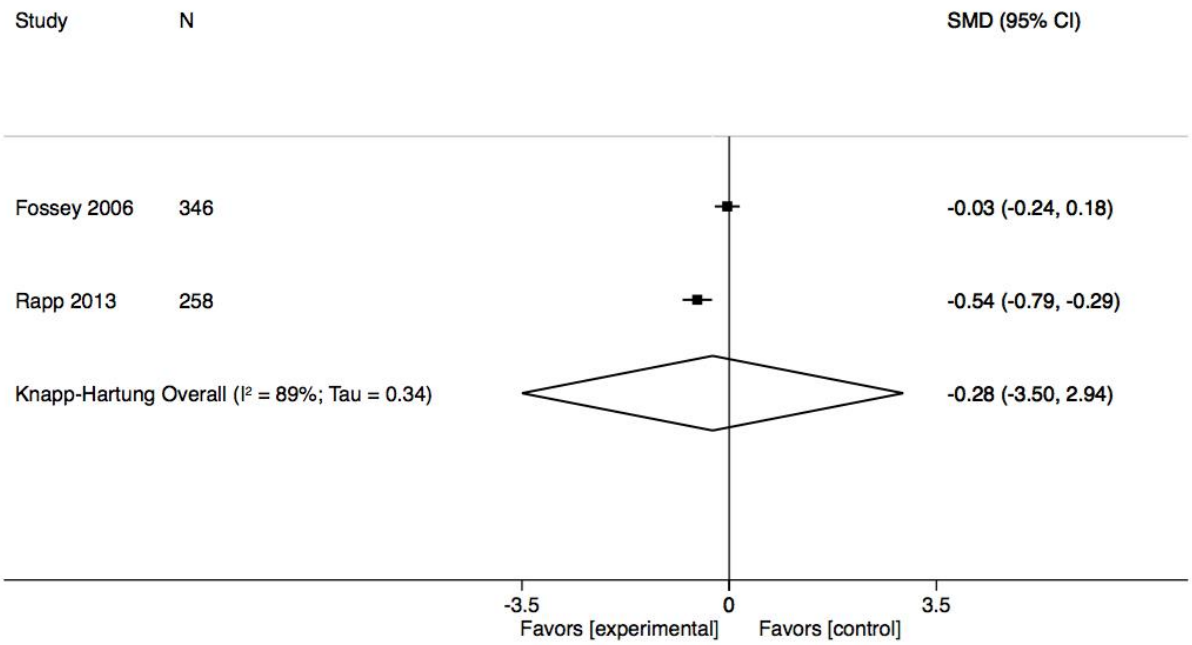
SMD = standardized mean difference; CI = confidence interval

Figure 6. Random effects meta-analysis for the effect of person-centered care on agitation/aggression



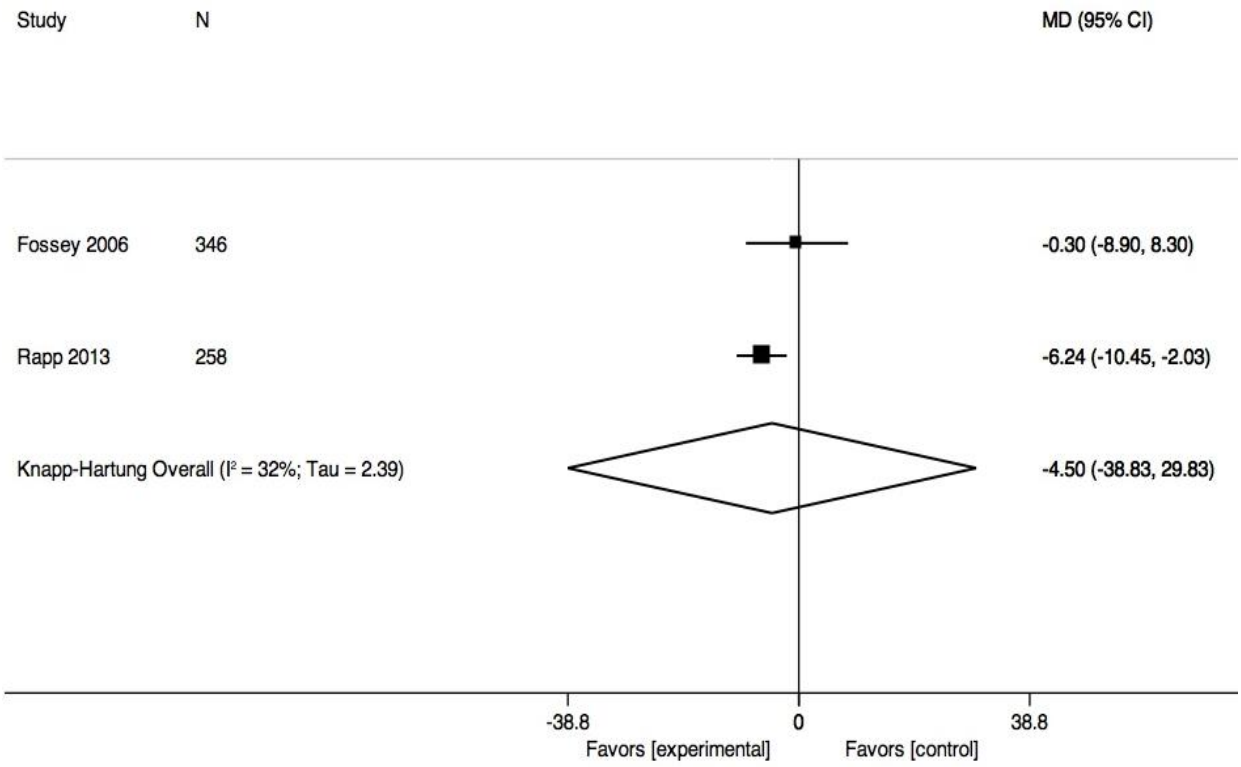
SMD=Standardized mean difference; CI=confidence interval;

Figure 7. Random effects meta-analysis for the effect of clinical protocols on dose of antipsychotics



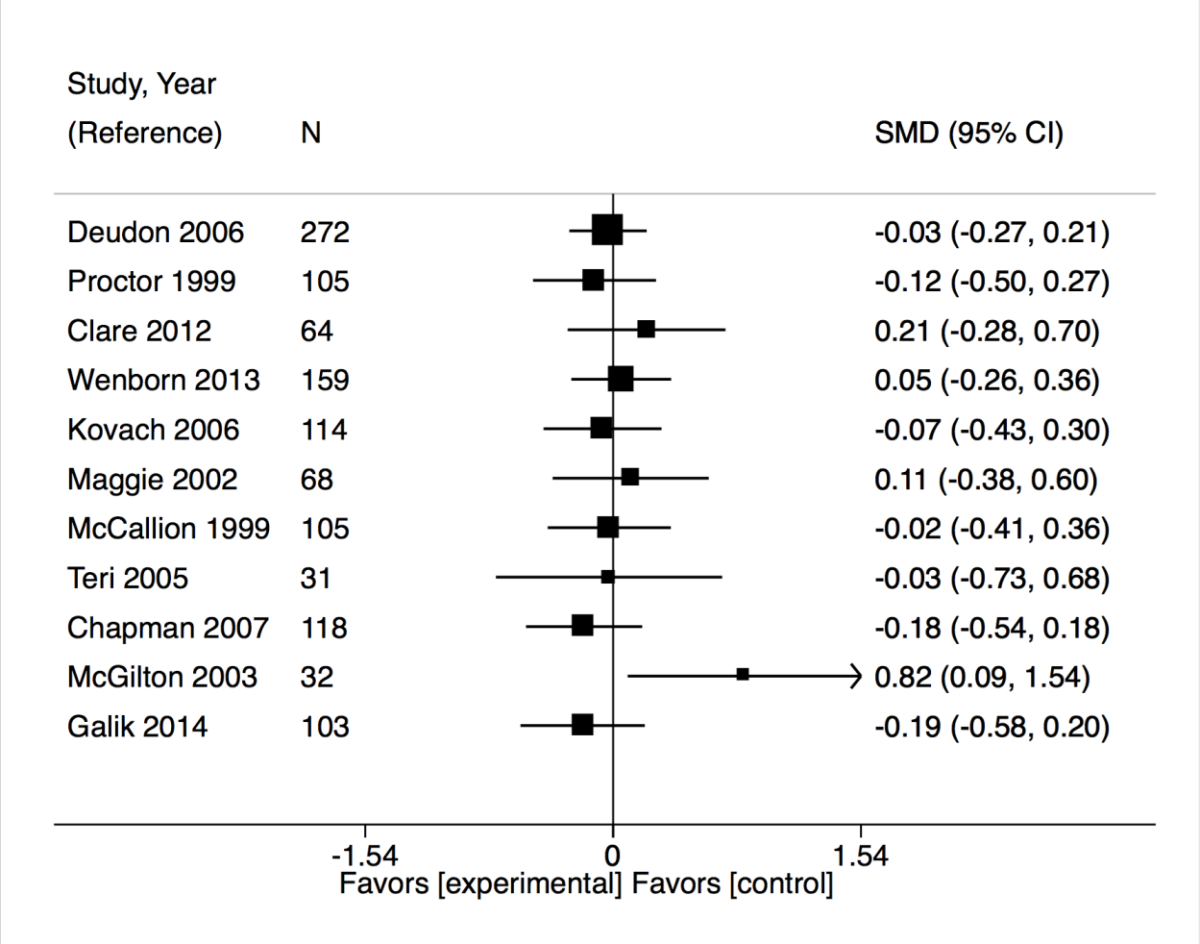
SMD=Standardized mean difference; CI=confidence interval

Figure 8. Random effects meta-analysis for the effect of clinical protocols on agitation/aggression



SMD = Standardized mean difference; CI = confidence interval

Figure 9. Unique comparisons and effect on agitation/aggression



SMD = standardized mean difference; CI = confidence interval

Patient-Level Interventions for Community-Dwelling Individuals With Dementia

Key Points

- We identified few trials studying patient-level interventions in community-dwelling dementia patients.

Overview

We identified five trials that examined patient-focused interventions for managing agitation/aggression in community-dwelling individuals with dementia.[36,117-120] Three of these were assessed as having high risk of bias and were not included in the analysis[117,118,120] (Appendix D). Table 9 summarizes the results of these trials and Table 10 lists results for relevant outcomes.

Multisensory Stimulation

Eligible Trial

Baker et al., randomized 50 community-dwelling individuals with dementia to a multisensory stimulation intervention (n = 25) or an interactive control group (n = 25).[36] The mean age of patients was 78 years and 50 percent were female. Participants had moderate to severe cognitive impairment with a majority diagnosed with Alzheimer's disease (66%) followed by vascular dementia (14%) or a mixed diagnosis (20%). The intervention group received eight standardized 30-minute multisensory stimulation sessions twice weekly for 4 weeks. The multisensory stimulation sessions included unpatterned stimuli, efforts to stimulate all nontaste senses, nondirective enabling approaches by staff, and no intellectual demand of the patient. The interactive control received eight standardized 30-minute sessions composed of activities typically used with individuals with dementia and geared to the individual's interests twice weekly for 4 weeks. Five different scales assessed primary outcomes (patient agitation/aggression measured with the REHAB deviant behavior subscale and the BRS Social Disturbance subscale, general behavior measured using the REHAB general behavior subscale, the Behavior and Mood Disturbance Scale, and the Behavioral Rating Scale) at baseline, 2 weeks, 4 weeks, and 1 month after sessions were completed. Change from baseline was similar with multisensory stimulation or activities in agitation/aggression and general behavior outcomes once differences in baseline characteristics were taken into consideration. No intermediate or secondary outcomes were reported.

Evidence Synthesis and Strength of Evidence

One small study provides insufficient evidence on the effectiveness of patient-level multisensory stimulation intervention for treatment of agitation/aggression in community-dwelling individuals with moderate to severe dementia for all outcomes.

Art Therapy

Eligible Trial

Hattori et al. randomized 43 community-dwelling individuals with dementia to an art therapy intervention (n=22) or interactive control group (n=21).[119] The mean age of participants was 74 years and 54 percent were female. Participants had mild cognitive impairment and met Alzheimer's disease diagnostic criteria, although actual diagnosis was not reported. The intervention group received 12 weekly 45-minute coloring sessions in hospital, in addition to daily 15-minute sessions at home over 12 weeks. Participants were given abstract patterns which revealed birds and animals to color at their own pace. The interactive control received arithmetic exercises of simple addition and multiplaction to do at their own pace in daily 15-minute sessions. Two scales assessed primary outcomes (general behavior measured with Dementia Behavior Disturbance Scale, patient distress - QoL measured with SF-8) at baseline and post-treatment. Percent of responders showing a 10 percent or greater improvement for the mental subscale of the SF-8 was significantly higher in the intervention group compared with control post-intervention. No other between-group results were significant. One scale assessed secondary outcomes (caregiver burden measured with Zarit Burden Index [ZBI]) at baseline and post-treatment. ZBI results were not significant. No intermediate outcomes were reported.

Evidence Synthesis and Strength of Evidence

One small study provides insufficient evidence on the effectiveness of patient-level art therapy intervention for treatment of agitation/aggression in community-dwelling individuals with moderate to severe dementia for all outcomes.

Table 9. Patient-level interventions for agitation/aggression in community-dwelling individuals with dementia

Intervention-Comparison	Total Number of Studies (Number of Participants)	Strength of Evidence - Summary of Results
Primary Outcomes		
Agitation/Aggression		
Multisensory vs. activity	1 (50)	Insufficient – no conclusions drawn
General Behavior		
Multisensory vs. activity	1 (50)	Insufficient – no conclusions drawn
Art therapy vs. activity	1 (43)	Insufficient – no conclusions drawn
Intermediate Outcomes		
Caregiver Burden	1 (43)	Insufficient – no conclusions drawn

Table 10. Efficacy and comparative effectiveness of interventions delivered directly to caregivers of community-dwelling individuals with dementia

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Hattori, 2011[119] RCT Japan Art therapy vs. math exercise n=43 Moderate risk of bias	**Treatment:** coloring abstract patterns **Comparison:** addition and multiplication problems - 45 minute weekly sessions in hospital for 12 weeks, plus 15 minute daily session at-home - industrial designer/artist, speech therapists	***Agitation/Aggression:*** NR ***General Behavior*** **Dementia Behavior Disturbance Scale**, Mean (SD) Postintervention: 16.8 (12.9) vs. 14.5 (12.7) ***Patient Distress, QoL*** **SF-8 (physical and mental subscales)**, Mean (SD) Postintervention physical: 50.5 (4.0) vs. 47.3 (6.7) Postintervention mental: 53.4 (3.3) vs. 52.9 (6.7) ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden:*** **ZBI**, Mea (SD) Postintervention: 16.9 (9.1) vs. 16.5 (10.5) ***Caregiver Distress:*** NR ***Caregiver QoL:*** NR
Baker, 2001[36] RCT United Kingdom Multicomponent sensory stimulation vs. specialized activity n=50 Moderate risk of bias	**Treatment:** Nondirective **s**timulation of all nontaste senses (music, aromas, tactile objects, special lighting) **Comparison:** interactive control received standardized sessions for the same amount of time geared towards their interests - 8 30-minute sessions (twice weekly) for 1 month - nurse, occupational therapist, psychologist	***Agitation/Aggression*** **REHAB deviant behavior,** AMD (CI) Postintervention: -.32 (-.55 to -.09) **BRSD social disturbance,** AMD (CI) Postintervention: -.32 (-.55 to -.09) ***General Behavior*** **REHAB general behavior,** MD (CI) Postintervention: ND **BMD,** MD Postintervention: ND ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden:*** NR ***Caregiver Distress:*** NR ***Caregiver QoL:*** NR

AMD=adjusted mean difference; **BMD**=Behavior and Mood Disturbance; **BRSD**=Behavior Rating Scale for Dementia; **CI**=confidence interval; **MD**=mean difference; **ND**=no difference; **NR**=not reported; **QoL**=quality of life; **RCT**=randomized controlled trial; **REHAB**=Rehabilitation Evaluation Hall and Baker; **SD**=standard deviation; **SF-8**=short form 8; **ZBI**=Zarit Burden Index

Caregiver-Level Interventions for Community-Dwelling Individuals With Dementia

Key Points

- Evidence for most comparisons was insufficient to conclude whether caregiver-level interventions were effective in managing agitation/aggression in community-dwelling individuals with dementia. This was largely due to heterogeneous comparisons and small sample sizes. Trials often showed no difference between intervention and comparison, but differences were typically too imprecise to conclude a lack of efficacy.
- Evidence was sufficient to draw conclusions for only five comparison-outcome pairs:
  - Low strength evidence shows that interventions targeting caregiver skills and knowledge were similar to no treatment in managing care recipient general behavior.
  - Low strength evidence shows that interventions targeting caregiver skills and behavior were similar to no treatment in managing caregiver burden.
  - Low strength evidence shows that interventions targeting caregiver skills and behavior were similar to attention control in managing care recipient agitation/ aggression.
  - Moderate strength evidence shows that interventions targeting caregiver skills and behavior are better than attention control in managing caregiver distress.
  - Moderate strength evidence shows that interventions targeting caregiver skills and behavior are better than attention control in improving caregiver confidence in caregiving.

Overview

Twenty-eight references reporting on 27 unique RCTs studied caregiver interventions for managing agitation/aggression in community-dwelling individuals with dementia.[121-148] Eight records reported comparisons and outcomes that were assessed as having a high risk of bias (Appendix E).[123,124,133,137,142,148-150] These studies were not used in our qualitative analysis; they are described in Appendix E. This results in 20 references of 20 unique trials with an acceptable risk of bias to use in analysis. We grouped trials using previously proposed taxonomy.[151] We first identified the primary functional domain addressed by the intervention (i.e., either knowledge or skills for eligible interventions). We then assessed a secondary functional domain addressed by the intervention (i.e., knowledge, skills, behavior, or affect). We discuss the interventions by the primary and secondary functional domains addressed and conducted a qualitative analysis because interventions and outcomes were heterogeneous and pooling was not appropriate. Table 11 summarizes the results of these interventions and Table 12 lists results for relevant outcomes.

Interventions Addressing Caregiver Knowledge and Skills

We identified two eligible trials that primarily addressed knowledge and secondarily addressed skills.[136] Guerra et al. randomized 58 caregiver-care recipient dyads to intervention (n = 29) or waitlist (n = 29).[136] The mean age of caregivers was 51 years and 85 percent were female. The mean age of care recipients was 82 years and 74 percent were female. The intervention used the Helping Carers to Care model, designed for use in diverse low- and middle-income countries. The intervention was delivered by ‘junior’ psychologists and social

workers. It is unclear what 'junior' means in this perspective. Three modules were delivered through five 30-minute weekly sessions that included assessment, basic education about dementia, and tailored training for identified problem behaviors. The waitlist group received the intervention after 6 months. Postintervention assessments occurred after 6 months. Patient agitation/aggression was not specifically measured; general behavior measured with the NPI-Q severity scores. General behavior was similar between groups at 6-month postintervention. Care recipient quality of life measured with the DEMQOL. Adjusted standardized mean changes was similar between intervention and comparison groups at 6-month postintervention. Intervention and comparison groups also showed similar postintervention changes in secondary outcomes of caregiver burden, distress, and quality of life as measured by the ZBI, the NPI-Q caregiver distress score, and the WHOQOL-BREF, respectively.

In their Minnesota Family Workshop trial, Ostwald et al. randomized 117 caregiver-care recipient dyads to an intervention group (n = 72) or waitlist (n = 45).[144] A high percentage of the caregivers were female (65%) while a little more than half of the care recipients were male (51%). The mean age of caregivers was 66 years and the mean age of care recipients was 77 years. The intervention group received seven weekly 2-hour training sessions in a classroom format, including homework and readings. The first four sessions included general education and videos about dementia and its impacts on others. The fifth session included videos of the participants being assessed with the Cognitive Performance Test, the results of which were given to participants. The final two sessions included skill development and mastery. Care recipients were invited to a daycare-like setting with activities tailored to their functional level. The waitlist group received the intervention after 5-6 months. Postintervention assessments occurred at 3 months and 5 months after baseline. Patient general behavior was measured using RMBPC, disruptive behaviors subscale.[144] Mean scores were similar with intervention and comparison at both postintervention time points. No intermediate outcomes were measured. Two secondary outcomes were reported. Caregiver burden as measured by the ZBI was similar with intervention and comparison, but there was a significant intervention by time interaction ($F [2, 156] = 5.53$, $p=0.005$). Caregiver distress measured by the RMBPC response to disruptive behaviors was similar in both groups at both time points with a significant intervention by time interaction ($F [2, 164] = 4.60$, $p=0.01$).

Evidence Synthesis and Strength of Evidence

These small trials provided insufficient evidence to draw conclusions about the effectiveness of caregiver interventions addressing knowledge and skills managing agitation/aggression in community-dwelling individuals with dementia.

Interventions Addressing Caregiver Knowledge and Affect

One trial studied an intervention with objectives of improving caregiver knowledge primarily and affect secondarily. Chien et al. randomized 88 caregiver-care recipient dyads to personalized dementia care management (n=44) or standard care (n=44).[125] The mean age of caregivers was 44 years and 64 percent were female The mean age of care recipients was 68 years and 43 percent were female. Caregivers attended 12 2-hour sessions every other week over 6 months. A trained case manager identified problem areas and designed a personalized program to educate the caregiver about dementia care, family role and strength rebuilding, and community support resources. Caregivers in the comparison group attended monthly education sessions, received educational materials, and care recipients received "usual" pharmacotherapy (not specified) and

social and recreational activities. General behavior was measured with the NPI at baseline, 6 months (immediate postintervention), and 6-month postintervention. Mean neuropsychiatric symptoms at immediate postintervention were significantly lower in the intervention group compared with the comparison group. It was unclear if this significance was sustained at 6-month postintervention. Two scales assessed secondary outcomes (caregiver burden measured by Family Caregiver Burden Inventory, caregiver QoL measured by WHO-QoL) at baseline, posttreatment, and 6-month postintervention. Mean burden was significantly lower and mean QoL was significantly higher in the intervention group at immediate postintervention compared with comparison. It was unclear if this significance was sustained at 6-month postintervention. No intermediate outcomes were reported.

Evidence Synthesis and Strength of Evidence

These trials provided insufficient evidence to draw conclusions for any outcome.

Interventions Addressing Caregiver Skills and Knowledge

We identified six trials studying interventions addressing caregiver skills and knowledge. Five of these trials compared interventions targeting skills and knowledge with no treatment. One compared the intervention with an antipsychotic medication.

De Routrou et al. randomized 167 caregiver-patient dyads to a psychoeducational program (n=79) or usual care (n=78).[126] The mean age of caregivers was 65 years and 68 percent were female. The mean age of patients was 79 years and 60 percent were female. Patients had been diagnosed with Alzheimer's disease. Caregivers attended weekly 2-hour sessions over 12 weeks. Small groups of 6-10 caregivers were led by psychologists and experienced geriatric health professionals to deliver education on dementia, problem-solving techniques, emotion-centered coping, behavior management, communication skills, and available resources. Caregivers in the comparison group were on a waitlist; usual care was not defined. General behavior was measured with NPI at baseline, postintervention (3-month intervention) and 3-month postintervention. Mean neuropsychiatric symptoms at postintervention and 3-month postintervention were not significantly different between groups. Caregiver burden was measured with the ZBI at baseline, postintervention (3-month intervention), and 3-month postintervention. Mean caregiver burden at postintervention and 3-month postintervention was not significantly different between groups. No intermediate outcomes were reported.

Klodnicka et al. randomized 50 caregivers to a psychoeducational communication intervention (n=25) or usual care (n=25).[139] The mean age of caregivers was 62 years and 82 percent were female. Patients had been diagnosed with cognitive problems likely associated with early stages of Alzheimer's disease. Caregivers attended weekly 90- to 120-minute sessions over 5 weeks. Sessions provided education on communication difficulties relating to cognitive limitations and incorporated skill modelling and performance. Caregivers in the comparison group received an information pamphlet on memory and communication. General behavior was measured with the RMBPC at baseline, 1 week postintervention, and 6-weeks postintervention. Adjusted mean problem behaviors at postintervention and 6-weeks postintervention were lower in the intervention group compared with usual care. No secondary or intermediate outcomes were reported.

Gallagher-Thompson et al. randomized 70 caregivers to receive a psychoeducation skill training DVD (n=36) or educational DVD (n=34).[127] The mean age of caregivers was 59 years and 87 percent were female. The mean age of care recipients was 83 years and gender was not

reported. Care recipients had significant memory loss or deteriorating cognition for at least 6 months. Caregivers in the intervention group watched 2.5 hours of footage over 4 months of role-played situations with narrations, accompanying workbook, and exercises to practice at home. Psychoeducation focused on dementia, managing difficult behaviors (recognizing and changing stressful behaviors), managing stressful family situations (communication with family and healthcare providers), and accessing other resources (legal issues, community resources, preparing for end-of-life). Caregivers in the comparison group received two DVDs of information on dementia. General behavior was measured with the RMBPC at baseline and postintervention (4 month intervention). Mean problem behaviors at postintervention were no different between groups. No secondary or intermediate outcomes were reported.

Ulstein et al. randomized 180 caregiver and care recipient dyads to a tailored education and training program with caregiver psychosocial components (n = 90) or usual care (n = 90).[152] The mean age of caregivers was 65 years and 64 percent were female. The mean age of care recipients was 76 years and 56 percent were female. The intervention took place over 4.5 months and included a 3-hour physician-led education session that included information about the course of dementia and different treatment options. The intervention also included six 2-hour group meetings focused on communication techniques, problem-solving, and cognitive techniques. Usual care was not defined. Outcomes were assessed postintervention and at postintervention (12 months). General behavior measured with the NPI-S was similar with intervention and comparison postintervention and at postintervention. No intermediate outcomes were reported. Caregiver burden measured with the Relatives' Stress Scale (RSS) was similar with intervention and comparison postintervention and at postintervention.

Gitlin et al. in their REACH trial, randomized 255 caregiver-care recipient dyads to an Environmental Skill-Building Program (ESP) or usual care.[153] The mean age of caregivers was 61 years, 76 percent were female, 45 percent were white, and 53 percent were African American. The mean age of care recipients was 81 years and 68 percent were female. The ESP intervention included five 90-minute home visits and one 30-minute telephone contact over 6 months with an occupational therapist, developing a tailored plan after a needs assessment at the first home visit with the caregiver. The tailored plans could address or recommend environmental factors, education, and community resources. Caregivers were given a form outlining the tailored strategies. In future visits, the dementia education was reinforced, caregivers were observed using previously discussed strategies, strategies were further refined, and new recommendations were given regarding cognitive restructuring and validation. The 6-month analysis included 190 caregivers (89 in ESP group and 101 in usual care). General behavior measured with the RMBPC frequency scale was similar with intervention and comparison. Intermediate outcomes of mastery managing behaviors measured with the Caregiving Mastery Index and ability to manage caregiving measured by the Perceived Change Index were similar between groups. Caregiver distress measured with the RMBPC reaction to disruptive behaviors scale was also similar with intervention and comparison.

One trial evaluated interventions primarily aimed at educating caregivers about dementia and how to address common situations.[154] For caregivers, mean age was 65.5 years and 68.2 percent were female. For care recipients, mean age was 75 years, 55 percent were female, and 86 percent were white. Teri et al. randomized 148 caregiver and care recipient dyads to a behavior management group (n = 41), an antipsychotic treatment group with haloperidol (n = 34), trazodone (n = 37), and placebo (n = 36).[154] The only treatment arms relevant to our KQ were behavior management and haloperidol. The behavior management intervention consisted of 11

therapist-led sessions (eight weekly and three biweekly) over 4 months. The sessions provided information about Alzheimer's disease, strategies for decreasing agitation/aggression, structured assignments, and videotape training. Treatment began with 0.5 mg per day and was increased at the next visit by 0.5 mg per day unless the subject had at least moderately improved behavior, significant adverse events were noted, or the maximum dose was reached (3 mg/day). Assessments occurred at baseline, 9 weeks (midpoint of intervention period), 4 months (conclusion of intervention), and 3 months, 6 months, and 12 months postintervention. Agitation/aggression was measured with three different instruments: a dichotomous variable measuring improvement based on change in Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC); continuous variables based upon scores on the ABID frequency scale, and the CMAI. General behavior was measured with the BRSD. Changes from baseline were similar between the behavior management and haloperidol treatment groups for each of these instruments. No intermediate outcomes were reported. Changes in caregiver burden, measured with the Screen for Caregiver Burden (SCB), and changes in caregiver distress, as measured with the ABID reaction scale, also were similar in these two treatment groups.[145,154] Harms comparison was important for this study because one arm was an antipsychotic. Behavior management had statistically significantly fewer symptoms of parkinsonian gait and bradykinesia (0% and 0%, respectively) compared with haloperidol (22% and 33%, respectively). There were no differences between groups for the following adverse effects: drooling, dry mouth, dizziness, akathisia, rigidity, dyskinesia, drowsiness, tremor, and fatigue.

Evidence Synthesis and Strength of Evidence

Low strength evidence shows that interventions targeting caregiver skills and knowledge were similar to no treatment in managing patient general behavior. Evidence was insufficient to draw conclusions for any other outcome. Few trials measured similar outcomes, and when they did, methodological limitations and imprecision were apparent. Often trials did not show statistical differences in outcomes, but precision was not sufficient to conclude a lack of effectiveness.

Interventions Addressing Caregiver Skills and Behavior

We identified nine trials that primarily addressed caregiver skills and secondarily behavior. Gonzalez et al. randomized 102 caregivers to group resourcefulness training (n=50) or no treatment (n=52).[134,155] The mean age of caregivers was 60 years and 97 percent were female. The mean age of patients was 80 years and 58 percent were female. Patients had been diagnosed with Alzheimer's disease. Caregivers attended weekly 2-hour sessions over 6 weeks. Groups of five to seven caregivers were led by a registered nurse to identify problem behaviors and management strategies, such as coping skills, problem solving, priority setting, and decisionmaking. Participants in the comparison group received a binder of information on Alzheimer's disease, availability of community resources, and information on recent research. One scale assessed primary outcomes (general behavior measured with RMBPC) at baseline, postintervention (6-week intervention), and 3-month postintervention. Adjusted mean problem behavior frequency at postintervention and 3-month postintervention was not significantly different between groups. One scale assessed secondary outcomes (caregiver burden measured with Caregiver Role Strain—global strain subscale) at baseline, postintervention (6-week intervention), and 3-month postintervention. Adjusted mean caregiver burden at postintervention

and 3-month postintervention was not significantly different between groups. No intermediate outcomes were reported.

Huang et al. randomized 129 caregiver-care recipient dyads to a behavior management program with telephone support (n=63) or written instructions with social telephone postintervention (n=66).[138] The mean age of caregivers was 55 years and 75 percent were female. The mean age of patients was 80 years and 54 percent were female. Patients had been diagnosed with dementia. Caregivers received in-home visits from a study nurse 1 week, 2 weeks, 3 months, and 6 months after study initiation, as well as monthly phone calls during the 6 months. Training focused on enhancing behavior management, self-efficacy, and preparedness to identify stressors and problem behaviors, and ultimately to modify the environment to decrease these stressors. The attention comparison received in-home visits of general information on dementia with written informational materials. One scale assessed primary outcomes (agitation/aggression measured by CMAI) at baseline, 2 weeks, 3 months, and 6 months postintervention. The number of aggressive behaviors reported at postintervention was not significantly different between groups. No secondary or intermediate outcomes were reported.

Gitlin et al. randomized 237 caregiver-care recipient dyads in their Care of Persons with Dementia in their Environments (COPE) trial.[131] The mean age of caregivers was 62 years, 89 percent were female, 70 percent were white, and 28 were African American. The mean age of the care recipients was 82 years; 68 percent were female, 70 percent were white, and 27 percent were African American. The staff used scripts to ask caregivers about challenges, mailed informational brochures, and reviewed materials in subsequent calls to the caregivers. The intervention consisted of up to 10 sessions with an occupational therapist, one face-to-face session with an advance practice nurse, and one telephone session with an advanced practice nurse over 4 months. Each caregiver was exposed to all of the components of the intervention, including: assessments, caregiver education, and caregiver training to address caregiver-identified concerns and help them reduce stress. Tailored training was given to all caregivers in problem-solving, communication, engaging patients in activities, and simplifying tasks, based on their concerns and patient capabilities. The comparison group (n = 107 for analysis) received up to three 20-minute telephone calls from trained research staff over 4 months. Postintervention agitation/aggression (ABID scores) and patient quality of life (QoL-AD) were similar with intervention and comparison. Caregivers in the intervention group reported greater confidence using activities to manage behaviors measured with an investigator-developed Likert scale with five questions (adjusted mean difference 0.81; 95% CI: 0.30-1.32; Cohen *d*=0.54). Effect size was moderate according to Cohen's *d*; scores declined from baseline by 1 percent in the control group and improved by 14 percent in the intervention group.[131] Caregiver burden measured using the perceived change in wellbeing improved more in the intervention group (15% vs. 4%; adjusted mean difference 0.22; 95% CI: 0.08-0.36; Cohen *d*=0.30). This between-group difference represented a small effect size according to Cohen *d*.

In their Advancing Caregiver Training (ACT) trial, Gitlin et al. randomized 272 care recipient dyads to ACT (n = 137) or no treatment (n = 135).[132] The mean age of caregivers was 66 years, 82 percent were female, and 69 percent were white. The mean age of care recipients was 82 years, 53 percent were female, and 69 percent were white. ACT participants received up to 11 home and telephone contacts by health professionals over 4 months, including up to nine occupational therapy sessions and two nursing sessions. Caregivers identified behaviors most upsetting to them. Health professionals then identified communication and environmental triggers of care recipient behaviors along with undiagnosed patient health conditions (through

blood and urine samples). Health professionals then trained caregivers in strategies to modify triggers and reduce care recipient upset. Three telephone contacts to reinforce strategy use occurred between 4 and 6 months. Comparison participants were offered a 2-hour in-home education and problem behavior management workshop after the 6-month postintervention. Caregivers selected a wide variety of behaviors to target during the intervention. Frequently mentioned targeted behaviors included refusing care (15%), repetitive questioning (11%), argumentation (8%), waking up at night (8%), toileting problems (8%), verbal aggression (8%), wandering (7%), inappropriate behavior (i.e., loud, destructive) (6%), upset or agitation (5%), safety concerns (5%), and delusions (5%).[132]

Postintervention outcomes were assessed at 4 months for 117 dyads in the intervention group and 122 dyads in the comparison group, and postintervention outcomes at 6 months for 106 dyads in the intervention group and 114 dyads in the comparison group. ACT caregivers were more likely than comparisons to report reductions in the problem behavior (67.5% vs. 45.8%; χ^2=8.7; p=.002). The percentage of caregivers who reported that symptoms worsened (18.4% vs. 31.7%; p>.05) or stayed the same (14.0% vs. 22.5%; p>.05) was similar in the intervention and comparison groups. Confidence managing target problem behavior as measured by an investigator-developed Likert scale, improved more with intervention than control (20% vs. 10%; adjusted mean difference 0.33; 95% CI: 0.08-0.58; Cohen's *d*=.30). The effect size was small according to Cohen's *d*.[132] ACT participants reported significantly higher confidence managing behaviors at postintervention on an investigator-developed postintervention questionnaire to ascertain perceived benefits ([unadjusted] 71.9% vs. 29.1%; χ^2=41.1; p=.001). Secondary outcomes were reported at postintervention (4 months) and at postintervention (6 months).[132] Caregiver burden as measured by ZBI was similar with intervention and comparison postintervention, but had significantly improved with a moderate effect size with intervention at postintervention (adjusted mean difference -1.61; 95% CI: -3.13 to -0.09; *d*=.67). The effect size was moderate according to Cohen's *d*; mean scores in the intervention group were over 10 percent higher than in the comparison group at 6 months. Caregiver behavior upset overall improved more with intervention than comparison at both time points (adjusted mean difference -1.07; 95% CI: -1.57 to -0.56; Cohen's d=.47 at 4 months; and -0.82; 95% CI: -1.34 to -0.29; Cohen's d=.43 at 6 months). Effect size was moderate according to Cohen's *d*; mean scores in the intervention group were over 15 percent higher than in the comparison group at both time points. Perceived change in caregiver wellbeing improved with intervention compared with comparison at both time points (adjusted mean difference 0.45; 95% CI: 0.29 to 0.62; Cohen's d=.62 at 4 months; and 0.29; 95% CI: 0.14 to 0.44; Cohen's d=.43 at 6 months). Effect sizes were moderate according to Cohen's *d*; mean scores in the intervention group were over 10 percent higher than in the comparison group at both time points.

In another trial, Gitlin et al. randomly assigned 60 caregiver and care recipient dyads to the Tailored Activity Program (TAP) (n = 30) or a waitlist (n = 30).[129] The mean age of caregivers was 65 years and 88 percent were female. Caregivers were primarily white (77%). The mean age of care recipients was 79 years and 43 percent were female. TAP dyads received six 90-minute home visits and two 15-minute telephone contacts by occupational therapists over 4 months. Care recipient interests were ascertained and individual programs were presented to the caregiver at the next visits, including activities, goals, and implementation plans. Caregivers were instructed to use deep breathing techniques to manage stress. Waitlist participants received the intervention after the 4-month assessment. Fifty-six dyads were included in the analysis. Agitation/aggression was measured using an investigator-created checklist documenting the

occurrence of 24 behaviors (16 from the ABID scale; two from the RMBPC [repetitive questioning/hoarding]; four from previous research [wandering, incontinent incidents, shadowing, boredom], and two others defined by each caregiver). The caregiver completed checklists were used to create two indices, number of behaviors occurring and the mean frequency of occurrence. All behaviors appear to be weighted equally. We classified this outcome as patient agitation/aggression because over half of the questions were from an agitation/aggression scale. Behavioral occurrences decreased more with intervention than comparison (adjusted mean difference = -0.32 points; 95% CI: -0.55-0.09, Cohen's *d*=0.72). Changes in the number of behaviors reported was similar with intervention and comparison. A binary analysis of specifically agitated behaviors showed a larger reduction with intervention than comparison (adjusted mean difference = 0.6; 95%; CI: 0.01-0.56, Cohen's *d*=0.75). The effect size was moderate according to Cohen *d*. Three intermediate outcomes measured using 5-item Likert scales improved more with intervention than comparison. Caregiver mastery improved more with intervention (adjusted mean difference 0.34; 95% CI: 0.08 to 0.60; Cohen's d=.55). Effect size was moderate according to Cohen *d*; mean score improved by nearly 10 percent with intervention but stayed the same with comparison. Confidence using activities improved more with intervention (adjusted mean difference 1.67; 95% CI: 0.41 to 2.94; Cohen's d=.74). Effect size was moderate according to Cohen *d;* mean score improved by nearly 40 percent with intervention, but only 3 percent with comparison. Strategy use improved more with intervention than control (adjusted mean difference 0.25; 95% CI: 0.04 to 0.46; Cohen's d=.71). Effect size was moderate according to Cohen *d*; mean score improved by less than 6 percent with intervention and 4 percent with comparison. Reductions in secondary outcomes of caregiver burden measured with the Zarit Burden and caregiver behavior upset measured on a Likert scale were similar with intervention and control

Bourgeois et al. randomized 63 caregivers to patient-focused skills training (n=22), caregiver-focused skills training (n=21) or attention control (n=20).[122] The mean age of caregivers was 73 years and 54 percent were female. The mean age of patients was 75 years and 46 percent were female. Patients met diagnostic criteria for probable Alzheimer's disease. Caregivers received 12 weekly 1-hour in-home training sessions and attended one 3-hour group workshop to enhance skills training. The patient-focused group received training to identify problem behaviors, antecedents and consequences of problem behaviors, and develop a management plan. The caregiver-focused group received training to increase coping skills through increasing pleasant events, improving problem-solving, and learning relaxation techniques. The comparison group was an attention control which received general information and suggestions for problem behaviors. Two scales assessed primary outcomes (aggression/agitation measured by BEHAVE-AD aggressivity/activity disturbance subscale, general behavior measured by BEHAVE-AD total score) at baseline, postintervention (3-month intervention), 3 months postintervention, and 6 months postintervention. Both patient-change ($p<0.05$) and caregiver change ($p<0.01$) groups reported significantly lower aggressivity scores than comparison at 6-month postintervention. The caregiver change group reported significantly lower total scores than comparison at 6-month postintervention ($p<0.01$). Secondary and intermediate outcomes were not reported.

Gerdner et al. randomly assigned 241 caregiver and care recipient dyads, of which 237 were included in the analysis.[128] The mean age of caregivers in the final analysis was 65 years and 74 percent were women. Caregivers were primarily white (94%). The mean age of care recipients was 77. The intervention group (n = 132) received individualized care plans that may

have included structured routines and rest periods, environmental modifications, and care recipients' past interests in activities. Care plan information was communicated in person, environmental techniques were taught to the caregivers, and care plan information was provided in a written format. The intervention group participants received 4 hours of contact over two in-home visits 1 week apart. The comparison group (n = 105) received general information about Alzheimer's disease, community resources, a caregiver book, and other brochures. The comparison group participants received two 1-hour in-home visits scheduled 2 weeks apart, and were offered the intervention after study completion. Assessments occurred at baseline, 3 months, 6 months, and 12 months. One primary outcome, general behavior, was measured using the Memory and Behavior problems checklist frequency and analyzed based upon relationship with care recipient using a hierarchical linear model; no overall results were provided. Behavior problems increased significantly as reported by nonspouse caregivers in the comparison group (hierarchical linear model estimate 0.77; SE=0.36; $p<.001$) relative to the intervention group. Behavior problems were similar between spouse caregivers in intervention and comparison groups. No intermediate outcomes were reported. One secondary outcome, caregiver distress, was measured with the Memory and Behavior problems checklist reaction and analyzed using a hierarchical linear model without separating estimates by relationship. Caregivers in the intervention group decreased reactions to problem behaviors compared with those in the comparison group (hierarchical linear model estimate -0.39; SE 0.18; $p<.01$). Effect sizes for both of these outcomes is likely small given the 0 to 96 range on the instruments.

Gormley et al. randomized 62 caregiver-care recipient dyads to a behavioral management program (n = 34) or comparison group (n = 28).[135] The intervention group received four sessions of behavior management training over 2 months. The mean age of caregivers was 68 and 60 percent were female. The mean age of care recipients was 76 and 53 percent were female. Caregivers were trained to identify precipitating factors for aggressive behaviors and subsequent sessions focused on tailored behavioral interventions and modifications. The comparison group received an equivalent number of sessions, consisting of discussions with caregivers and care recipients on care-related issues and recommendations for community resources. Postintervention agitation/aggression measured with the RAGE instrument and general behavior measured with BEHAV-AD were similar with intervention or comparison. Postintervention proportion of care recipients taking antipsychotic drugs and caregiver burden measured with the ZBI was also similar with intervention and comparison.

Marriott et al. randomized 42 caregiver-care recipient dyads to three groups: a family intervention group (n = 14), an interview comparison group (n = 14), and a no-interview comparison group (n = 14).[140] The mean age of caregivers was 64 years and 69 percent were female. The mean age of care recipients was 77 years and 71 percent were female. The family intervention consisted of caregiver education (three sessions), stress management (six sessions), and coping skills training (five sessions) over a total of 14 sessions delivered biweekly. Total treatment duration was 7 months. Caregivers in the family intervention also received the Camberwell Family Interview (CFI), booklets about Alzheimer's disease, and booklets listing available services. The interview comparison group received the CFI, taking approximately 90 minutes, and the assessments. The no-interview comparison group received only the assessments. Assessments were conducted at baseline, postintervention, and at 3 months postintervention. General behavior, measured with the MOUSE-PAD instrument was similar across groups at each time point. The study reported a significant difference between the

intervention group and the no-interview comparison but not the interview comparison group postintervention. No group differences were seen at postintervention. No intermediate or secondary outcomes were reported.

Evidence Synthesis and Strength of Evidence

Trials studying skills-behavior interventions used several types of comparisons. Two trials compared interventions with no treatment. Evidence on behavior was insufficient, but low strength evidence shows that skills-behavior interventions were similar to no treatment in managing caregiver burden. Evidence was insufficient for all other outcomes.

Five trials compared interventions targeting caregiver skills-behaviors with attention controls. Low strength evidence shows that these interventions are similar to attention control in managing care recipient agitation/aggression. However, moderate strength evidence shows that these interventions are better than attention control in improving caregiver caregiving abilities and managing caregiver distress. Evidence on other outcomes was insufficient.

Two trials compared interventions targeting caregiver skills-behaviors with sham treatments. These data provide insufficient evidence to draw conclusions for any outcome.

Trials rarely reported adverse effects. The interventions studied have a low risk for adverse effects.

Interventions Addressing Caregiver Skills and Affect

There were two eligible trials that studied interventions primarily addressing caregiver skills and secondarily affect. Belle et al., in their Resources for Enhancing Alzheimer's Caregiver Health (REACH) II trial, randomly assigned 642 caregiver-care recipient dyads to a multicomponent intervention (n=323) or an occasional contact comparison (n=319).[121] The mean age of the caregivers included in the final analysis was 61 years and 85 percent were female. Of those caregivers included in the final analysis, 32 percent were Hispanic or Latino, 37 percent were white/Caucasian, and 32 percent were black/African American. The multicomponent intervention consisted of education and training to address problem behaviors as well as caregiver psychosocial support to address depression, burden, and self-care/healthy behaviors through 12 in-home or telephone sessions delivered over a 6-month period. Assessments occurred at baseline and 6 months. Results were reported by racial/ethnic group; overall results were not reported. Two primary outcomes were reported. Patient general behavior was measured using three questions from the RMBPC (covering domains of memory, depression, and disruption). We classified this outcome as general behavior as it consisted of components other than agitation/aggression. No intermediate outcomes were reported. The secondary outcome of caregiver burden was measured using 11 of the 12 items on the brief ZBI. The frequencies reported on the checklist and scores from the ZBI were used to calculate the number of dyads making clinically significant changes (defined as an unadjusted standardized change of +/- 0.5 standard deviation or more from baseline to postintervention). In the Hispanic/Latino subgroup, intervention caregivers were more likely than comparison caregivers to report that problem behaviors decreased (45% vs. 23%) and less likely to report that they worsened (13% vs. 28%). With a net of 36 percent (95% CI: 13.2 to 56.7) more intervention caregivers reporting a clinically significant improvement compared with the comparison caregivers. Hispanic/Latino caregivers in the intervention and comparison groups reported admission of care recipient to nursing home at similar rates. Hispanic/Latino intervention and comparison caregivers reported similar change in burden postintervention. White/Caucasian intervention and comparison

caregivers reported similar changes in problem behaviors, admission of care recipient to nursing home, and caregiver burden. Black/African American intervention and comparison caregivers reported similar changes in problem behaviors and admission of care recipient to nursing home, but the intervention was associated with greater improvement in burden. Net burden was reduced in 23 percent more with intervention than comparison.

Mittelman et al. randomized 406 caregiver-care recipient dyads to counseling (n = 203) or usual care (n = 203).[141] The mean age of caregivers was 71 years; 60 percent were female and 91 percent were white. The caregiver intervention included two individual and four family counseling sessions over the course of 4 months. The counseling sessions were tailored but focused on communication, problem solving, and management of patient behavior, caregiver support, and education and resources related to Alzheimer's disease. Each session was 1 to 3 hours long. After 4 months, caregivers in the treatment group were required to join weekly support groups. Counselors were continuously available for caregivers and families to deal with various problems. The comparison subjects received usual care (not described). Postintervention occurred every 4 months for the first year and every 6 months thereafter for 4 years after the start of the study. This publication reports agitation/aggression measured with the Memory and Behavior Problems Checklist. Data on problem behavior frequency and reaction were analyzed with a mixed model growth curve. Memory and Behavior Problem Checklist frequency was similar with intervention and comparison as indicated by the nonsignificance of the group variable and the group-time interaction in the model. Our secondary outcome of caregiver distress measured with the Memory and Behavior Problem Checklist reaction improved more with intervention than comparison as indicated by negative estimates and significance of the intervention variable (estimate -2.90; SE=1.27; p=.0226) and the intervention-time interaction (-1.86; SE=0.89; p=.04). The effect sizes are small and may not be clinically meaningful given the score range of 0–96 for this instrument.

Evidence Synthesis and Strength of Evidence

Two trials compared interventions addressing caregiver skills and affect with no treatment. This evidence was insufficient to draw conclusions given methodological limitations, imprecision, and inconsistent or unknown consistency with regard to specific outcomes, for all outcomes.

Table 11. Caregiver-level interventions: evidence summary

Comparison	Outcome K=total trials; n= total dyads	Evidence Summary
Knowledge-skills vs. no treatment/waitlist/ information control Guerra, 2012[136] Ostwald 1999[144]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior K=2; n=140	Insufficient – no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL k=1; n=56	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=2; n=140	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL k=1; n=56	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver behavior k=1; n=84	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)

Comparison	Outcome K=total trials; n= total dyads	Evidence Summary
Knowledge-affect vs. attention control Chien, 2008[125]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior K=1; n=88	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=1; n=88	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress/QoL k=1; n=88	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver behavior	Insufficient – no data
Skills-knowledge vs. waitlist, usual care, or info control De Rotrou, 2011[126] Klondnica, 2011[139] Gallagher-Thompson, 2010[127] Ulstein, 2007[152] Gitlin, 2003[130]	Care recipient agitation/aggression	Insufficient – no data
	Care recipient general behavior K=5; n=657	Skills-knowledge interventions similar to no treatment on care recipient general behavior (Low strength evidence – moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=2; n=337	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL	Insufficient – no data
	Caregiver behavior k=1; n=190	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
Skills-knowledge vs. haloperidol Teri, 2000[154]	Patient agitation/aggression K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Patient general behavior K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver behavior	Insufficient – no data
Skills-knowledge vs. placebo Teri, 2000[154]	Patient agitation/aggression K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, imprecise)
	Patient general behavior K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver distress/QoL K=1; n=75	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise)
	Caregiver behavior	Insufficient – no data
Skills-behavior vs. waitlist/information control 3 Gitlin, 2008[129] Gonzalez, 2014[134] Marriot, 2000[140]	Patient agitation/aggression K=1; n=56	Insufficient– no conclusions drawn (moderate risk of bias, imprecise)
	Patient general behavior K=2; n=144	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=2; n=158	Skills-behavior interventions similar to no treatment on caregiver burden (Low strength evidence – moderate risk of bias, indirect)

Comparison	Outcome K=total trials; n= total dyads	Evidence Summary
	Caregiver distress/QoL K=1; n=56	Insufficient– no conclusions drawn (moderate risk of bias, unknown consistency)
	Caregiver behavior k=1; n=56	Insufficient– no conclusions drawn (moderate risk of bias, unknown consistency)
Skills-behavior vs. attention control 5 Gitlin, 2010a[131] Huang, 2013[138] Gitlin, 2010b[132] Gerdner, 2002[128] Marriot, 2000[140]	Patient agitation/aggression K=3; n=575	Skills-behavior interventions similar to attention control on care recipient agitation/aggression (Low strength evidence – moderate risk of bias, imprecise)
	Patient general behavior K=1; n=102	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL K=1; n=209	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient psychoactive medication	Insufficient – no data
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=2; n=448	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress K=3; n=685	Skills-behavior interventions improve caregiver distress more than attention control (Moderate strength evidence – moderate risk of bias)
	Caregiver behavior K=1; n=239	Skills-behavior interventions improve caregiver confidence more than attention control (Moderate strength evidence – moderate risk of bias)
Skills-behavior vs. sham treatment 2 Gormley, 2001[135] Bourgeois, 2002[122]	Patient agitation/aggression K=2; n=125	Insufficient– no conclusions drawn (moderate risk of bias, imprecise)
	Patient general behavior K=2; n=125	Insufficient– no conclusions drawn (moderate risk of bias, imprecise)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient taking psychotropic medication K=1; n=62	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Care recipient nursing home admission	Insufficient – no data
	Caregiver burden K=1; n=62	Insufficient– no conclusions drawn (moderate risk of bias, indirect, imprecise, unknown consistency)
	Caregiver distress/QoL	Insufficient – no data
	Caregiver behavior	Insufficient – no data
Skills-affect Belle, 2006[121] Mittelman, 2004[141]	Care recipient agitation/aggression	Insufficient – no data
	Patient general behavior K=2; n=924	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Care recipient distress/QoL	Insufficient – no data
	Care recipient psychoactive drug use	Insufficient – no data
	Care recipient nursing home admission K=1; n=518	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Caregiver burden K=1; n=518	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, inconsistent)
	Caregiver distress/QoL K=1; n=406	Insufficient– no conclusions drawn (moderate risk of bias, imprecise, unknown consistency)
	Caregiver behavior	Insufficient – no data

QoL=Quality of Life

Table 12. Efficacy and comparative effectiveness of caregiver-level interventions for community-dwelling individuals with dementia

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Interventions addressing knowledge-skills (k=2)			
Guerra, 2011[136] RCT United States Caregiver intervention vs. waitlist n=56 Low risk of bias	**Treatment**: Basic education about dementia; training regarding specific problem behaviors - five weekly 30-minute sessions - junior psychologists and social workers **Comparison**: Waitlist	***Agitation/Aggression***: NR ***General Behavior*** **NPI-Q severity score** ASMD (CI): -0.10 (-0.66 to 0.48) ***Patient Distress, QoL*** ***DEMQOL*** ASMD (CI): 0.32 (-0.84 to 1.48) ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** **ZBS** ASMD (CI): -1.02 (-0.53 to 0.51) ***Caregiver Distress*** **NPI-Q carer distress score** ASMD (CI): -0.09 (-0.64 to 0.48) ***Caregiver QoL*** ***WHO-QoL-Brief, Psych*** ASMD (CI): 0.10 (-0.47 to 0.68)
Ostwald, 1999[144] RCT United States General stress mediation model Psychoeducational intervention vs. waitlist n=84 Low to moderate risk of bias	**Treatment**: Education about dementia and how it affects patient, caregivers, family system; develop and strengthen caregivers' practical skills for dealing with caregiving tasks on a day-to-day basis; strengthen caregivers' feelings of confidence and belief that they are able (competent) to deal with issues, day in and day out; facilitating the family's ability to work collaboratively to find solutions to current management problems - 7 weekly 120-minute sessions - study investigators, interdisciplinary faculty (nurses, occupational therapists, family therapists, educators) **Comparison**: Waitlist	***General Behavior*** **RMBPC, disruptive behavior subscale** Baseline, mean (SD): 6.75 (5.55) vs. 5.32 (4.10) 3-months, mean (SD): 6.16 (5.26) vs. 4.87 (3.54) 5-months, mean (SD): 6.35 (5.20) vs. 6.68 (4.50) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** **ZBS** Baseline, mean (SD): 56.18 (13.29) vs. 56.54 (15.97) 3-months, mean (SD): 56.82 (11.83) vs. 55.43 (15.91) 5-months, mean (SD): 54.13 (11.29) vs. 59.81 (15.23) ***Caregiver distress*** **RMBPC, caregiver response to disruptive behavior subscale** *Baseline, mean (SD): 6.76*

Study Design Country Comparison n Study Risk of Bias	Intervention Description [Intensity, Duration, Qualifications Interventionist]	*Primary Outcomes-Instrument* Results	*Intermediate/Secondary Outcomes-Instrument* Results
			(6.27) vs. 5.20 (5.10) *3-months, mean (SD): 5.00 (5.38) vs. 4.42 (4.23)* *5-months, mean (SD): 4.08 (4.44) vs. 5.73 (4.42)* ***Caregiver QoL:*** NR
Interventions addressing knowledge-affect (k=1)			
Chien, 2008[125] Hong Kong Dementia care management vs. standard care n=88 Moderate risk of bias	**Treatment:** Personalized care management program including education on dementia care, family role and strength rebuilding, and community support resources; training to target problem areas identified by case manager - 12 2-hour sessions every other week over 6 months - trained case manager **Comparison:** Monthly education sessions, pharmacotherapy, social and recreational activities for patients, and educational materials for caregivers	***Agitation/Aggression***: NR ***General behavior*** NPI, mean (SD) Postintervention: 68.1 (10.2) vs. 84.5 (9.8) 6 month postintervention: 64.2 (11.8) vs. 85.1 (12.1); significant lower symptom severity in treatment group (p<0.01) ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR ***Adverse effects***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden*** Family Caregiver Burden Inventory, mean (SD) Postintervention: 56.7 (15.7) vs. 63.0 (15.1) 6 month postintervention: 48.3 (13.9) vs. 65.9 (16.3); significantly lower burden in treatment group (p<0.001) ***Caregiver QoL*** WHO-QoL, mean (SD) Postintervention: 75.1 (16.8) vs. 69.8 (16.7) 6 month postintervention: 81.4 (16.0) vs. 65.2 (17.5); higher QoL in treatment group (p<0.001)
Interventions addressing skills-knowledge (k=6)			
de Rotrou, 2011[126] France Psychoeducational program vs. usual care n=167 dyads	**Treatment:** Group sessions of 6-10 caregivers to deliver education on dementia, problem-solving techniques, emotion-centered coping, behavior management, communication skills, crisis management, and resources; debriefing and ecological stimulation used	***Agitation/Aggression***: NR ***General behavior***: NPI – Mean(SD) at 6 mo: 15.8(16.0) vs. 14.2(13.0); p=0.57 ***Patient Distress, QoL***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden***: ZBI – Mean (SD) at 6 mo: 23.0

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Low risk of bias	- weekly 2-hour sessions over 12 weeks - psychologists and experienced geriatric health professionals **Comparison:** Waitlist	***Nursing Home Admission***: NR ***Adverse effects***: NR	(14.6) vs. 26.5 (17.0); p=0.25 ***Caregiver QoL***: NR
Klodnicka, 2011[139] Canada Psychoeducational communication intervention vs. information pamphlet n=50 Low risk of bias	**Treatment:** Education on communication difficulties relating to cognitive limitations (concentration, attention, memory, orientation, reasoning, etc.); skill modelling and performance used - weekly 90-120 minute sessions over 5 weeks - nurse practitioner **Comparison:** Information pamphlet on memory and communication	***Agitation/Aggression***: NR ***General behavior*** RMBPC (communication difficulties) – Adjusted mean (SD) at 6 weeks: 1.74 (0.55) vs. 1.70 (0.59); F=69.1 (p<0.001) ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR ***Adverse effects***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden***: NR ***Caregiver QoL***: NR
Gallagher-Thompson, 2010[127] United States Psychoeducational skill training DVD vs. information control n=70 Low risk of bias	**Treatment:** DVD of role-playing with narrations, accompanying workbook, and home practice exercises on dementia, management of difficult behaviors, and stressful family situations (recognizing and changing stressful care recipient behaviors, effective communication with family and healthcare providers, accessing community resources, legal issues, and preparing for end-of-life care) - 2.5 hours of DVD footage used over 4 months - delivered via DVD **Comparison:** Two DVDs of information on dementia	***Agitation/Aggression***: NR ***General behavior*** RMBPC – Mean (SD) 4 months: 11.6 (5.2) vs. 11.0 (4.2); NS (p-value NR) ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR ***Adverse effects***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden***: NR ***Caregiver QoL***: NR
Gitlin, 2003[130] RCT United States Environmental skill-building vs. usual care n=190 Competence-environmental press framework Moderate risk of bias	**Treatment**: Education about dementia and impact of home environment; instruction in problem solving and developing effective approaches to manage caregiving concerns that involve manipulating physical/social environment including cognitive reframing/validation; implementation of environmental strategies tailored to caregivers context; generalization of strategies; - five 90-minute home visits and one 30-minute phone session - occupational therapist **Comparison**: Resource information at each outcome assessment point	***General Behavior*** **RMPBC no. of disruption-related behaviors** AMD (CI): -.07 (-46 to .33) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior*** **Perceived change in ability to manage caregiving** AMD (CI): .12 (-.05 to .30) Mastery AMD (CI): .11 (-.05 to .27) ***Antipsychotic Use:*** NR ***Caregiver Burden:*** NR ***Caregiver distress*** **Upset with disruptive behaviors (RMPBC subscale)** AMD (CI): -.05 (-19 to .09) ***Caregiver QoL:*** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Teri, 2000[154] RCT United States Behavioral Management Training vs. Haloperidol vs. placebo n=75 Moderate risk of bias (4 months)	**Treatment**: AD information; strategies for decreasing agitation/aggression, and structured in-/out-of-session assignments; - 8 weekly & 3 biweekly sessions - master's level therapists **Comparison 1**: Haloperidol treatment began with 0.5 mg per day and was increased at the next visit by 0.5 mg per day unless the subject had at least moderately improved behavior, significant adverse events were noted, or the maximum dose was reached (3 mg/day) Comparison 2: Placebo	***Agitation/Aggression*** **Improved score on ADCS-CGIC** RR (CI)=1.0 [0.7 to 1.4] ***Agitation*** **CMAI** MC (SD): -3.37 (11.45) vs. -7.26 (22.51) ***Agitation*-ABID Frequency** MC (SD): -3.61 (9.88) vs. -6.74 (16.22) ***General Behavior*** **BRSD** MC (SD): -3.56 (12.85) vs. -5.35 (22.41) **RMBPC Total Frequency** -0.08 (0.54) vs. -0.17 (0.65) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress*** **ABID Reaction** MC (SD): -2.41 (6.71) vs. -3.27 (9.10) ***Caregiver Burden*-SCB Subjective** MC (SD): -2.95 (7.29) vs. -1.88 (8.89) ***Caregiver Burden*-SCB Objective** MC (SD): -1.23 (3.32) vs. -0.44 (3.22) ***Caregiver QoL:*** NR
Ulstein, 2007[152] RCT United States Caregiver education vs. usual care n=180 Moderate risk of bias	**Treatment**: Education on symptoms and normal course of dementia, how to handle neuropsychiatric symptoms, available resources, and fostering care recipients' acceptance of help; pharmacological and nonpharmacological treatment; training on communication techniques and structured problem-solving; cognitive reframing - one 3-hour educational program; six 120-minute group meetings over 4.5 months - physicians (geriatricians and psychiatrists) **Comparison**: "Treatment as usual" at memory clinic not defined	***General Behavior*** **NPI-S, *4.5 month*:** MD in MC (SD)=0.8 (-3.61 to 5.28) **NPI-S, *12 month*** MD in MC (SD)=-2.2 (-2.65 to 7.06) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** **RSS, *4.5 month*:** MD in MC (SD)=-0.1 (-2.50 to 2.32) **RSS, *12 month*** MD in MC (SD)=-1.2 (-4.23 to 1.79) ***Caregiver Distress:*** NR ***Caregiver QoL:*** NR
Interventions addressing skills-behavior (k=9)			
Gonzalez, 2014[134] United States Resourcefulness training sessions vs. no treatment/information n=102	**Treatment:** Group sessions of 5-7 caregivers to identify problem behaviors and management strategies (cognitive behavioral skills: problem identification, coping, problem solving, priority setting, decisionmaking) - weekly 2-hour sessions over 6 weeks - registered nurse	***Agitation/Aggression***: NR ***General behavior*** RMBPC – Adjusted mean (SD) at 12 weeks: 1.3 (0.6) vs. 1.6 (0.6); p=0.11 ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR	***Caregiver Behavior***: NR ***Antipsychotic Use***: NR ***Caregiver Distress***: NR ***Caregiver Burden*** Caregiver Role Strain (global strain subscale) –

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Moderate risk of bias	**Comparison:** binder of information on Alzheimer's disease, community resources, and new research	***Adverse effects***: NR	Mean (SD) at 12 weeks: 1.90 (0.88) vs. 1.85 (0.88); p=0.78 ***Caregiver QoL***: NR
Huang, 2013[138] Taiwan Behavior management program + telephone support vs. attention control n=129 dyads Moderate risk of bias	**Treatment:** In-home training to enhance behavior management, self-efficacy, and preparedness; education to identify timing/frequency and causative stressors of behavior problems, and modify environment to decrease stress - visits 1 week, 2 weeks, 3 months, and 6 months after treatment initiation, and monthly phone calls over 6 months - study nurse **Comparison:** In-home, general information on dementia with written informational materials provided (written instruction + telephone support)	***Agitation/Aggression*** CMAI – n (%) at 6 mo: 9 (16.4) vs. 14 (26.4); p=0.20 ***General behavior***: NR ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR ***Adverse effects***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden***: NR ***Caregiver QoL***: NR
Gitlin, 2010a[131] RCT United States Care of Persons with Dementia in their Environments (COPE) vs. Attention Control n=209 Moderate risk of bias (4 months)	**Treatment**: Education on patient capabilities, potential effects of medications, pain, constipation, and dehydration; training to address caregiver-identified concerns and reduce stress (problem-solving, communication, engaging patients in activities, and simplifying tasks) - up to 10 sessions over 4 months with therapist, 1 face-to-face session and 1 telephone session with nurse - occupational therapists, advance practice nurse **Comparison**: Three 20-minute phone calls; education materials	***Agitation/Aggression*** **ABID** AMD (CI)[a]: -.65 (-3.05 to 1.74) ***Patient QoL-AD*** AMD (CI)[a]: 0.10 (0.00 to 0.20) ***General Behavior:*** NR ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior*** **Confidence using activities** AMD (CI)[a]: 0.81 (0.30 to 1.32) ***Antipsychotic Use:*** NR ***Caregiver Burden*** **Perceived change in wellbeing** AMD (CI)[a]: 0.22 (0.08 to 0.36)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Gitlin, 2010b[132] RCT In-home caregiver training vs. attention control n=239 at 16 weeks; n=220 at 24 weeks Low to moderate risk of bias	**Treatment**: Advancing Caregiving Training in strategies to modify triggers and reduce care recipient upset - 9 home sessions with OT, 1 home, and 1 phone nursing sessions over 16 weeks; 3 maintenance phone calls between 16 and 24 weeks - health professional **Comparison**: No contact	***General Behavior*** **Improvement in occurrence of targeted behavior**, 16 weeks 67.5% vs. 45.8%; p=.002 **Target symptoms worsened/stayed the same**, 16 weeks 18.4%/14% vs. 31.7%%/22.5%; p>.05 ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior*** **Confidence managing behavior** 16 weeks AMD (CI)[b]: 0.33 (0.08 to 0.58) 24 weeks: 71.9% vs 29.1%; χ^2=41.1; p=.001 ***Antipsychotic Use:*** NR ***Caregiver Burden*** **ZBS**, 16 weeks AMD (CI)[b]: -1.37 (-2.75 to 0.01) **ZBS**, 24 weeks AMD (CI)[b]: -1.61 (-3.13 to -0.09) **Behavior upset overall**, 16 weeks AMD (CI)[b]: -1.07 (-1.57 to -0.56) **Behavior upset overall**, 24 weeks AMD (CI)[b]: -0.82 (-1.34 to -0.29) **Caregiver Wellbeing** **Perceived Change Index,** 16 weeks AMD (CI)[b]: 0.45 (0.29 to 0.62) **Perceived Change Index**, 24 weeks AMD (CI)[b]: 0.29 (0.14 to 0.44)
Gitlin, 2008[129] RCT United States Tailored Activity Program vs. waitlist/information control	**Treatment**: One activity prescription based upon assessment with information, role-playing, direct demonstration with patient; stress management techniques - 8 sessions [6 90-minute home visits and 2 15-minute phone sessions] over 4 months - occupational therapists	***Agitation/Aggression*** **Specific Behaviors-agitated** AMD (CI)[c]: .06 (.01 to .56) **Behavioral Occurrences** AMD (CI)[c]: -.32 (-.55 to -.09) **Number of Behaviors**[d]	***Caregiver Behavior*** **Mastery** AMD (CI)[c]: .34 (.08 to .60) **Confidence using activities** AMD (CI)[c]: 1.67 (.41 to 2.94)

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
n=56 Low risk of bias	**Comparison**: Resource information at each assessment	AMD (CI)[c]: -.98 (-2.67 to .71) ***General Behavior: NR*** ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	**Strategy use** AMD (CI)[c]: 0.25; (0.04 to 0.46) ***Antipsychotic Use:*** NR ***Caregiver Burden*** **ZBS Subjective - Behavior Upset** AMD (CI) [c]: -.01 (-1.21 to 1.18) **ZBS Subjective - Burden** AMD (CI) [c]: .75 (-3.36 to 4.85) ***Caregiver Distress:*** NR ***Caregiver QoL:*** NR
Bourgeois, 2002[122] RCT United States Patient-focused skills training vs. caregiver-focused skills training vs. attention control n=63 Moderate risk of bias	**Treatment 1**: Patient-focused behavior change – in-home training to identify most frequent problem behaviors and corresponding antecedents/consequences, and formulate behavior management plans; used cues, diversion, and prompting depending on behavior type. Group session focused on antecedent-behavior-consequence relationship of dementia symptoms. **Treatment 2**: Caregiver coping skills– in-home training to increase pleasant events, improve problem solving skills, and learn relaxation techniques. Group session focused on self-change strategies. **Comparison**: In-home sessions with general information with handouts, and general suggestions for problem behaviors. Group session focused on stages of family adjustment to Alzheimer's disease. - 12 1-hour weekly in-home training sessions, one 3-hour group workshop - project staff, trained research assistants	***Agitation/Aggression***: BEHAVE-AD aggressivility/activity disturbance subscale – adjusted mean (SD) at 6 months: 5.6 (3.8) vs. 5.2 (3.6) vs. 8.4 (2.4); treatment 1 significantly lower than control (p<0.05); treatment 2 significantly lower than control (p<0.01) ***General behavior***: BEHAVE-AD total score – Adjusted mean (SD) at 6 months: 17.5 (10.4) vs. 14.8 (10.5) vs. 23.1 (11.4); treatment 2 score significantly lower than control (p<0.01) ***Patient Distress, QoL***: NR ***Nursing Home Admission***: NR ***Adverse effects***: NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Distress***: NR ***Caregiver Burden***: NR ***Caregiver QoL***: NR
Gerdner, 2002[128] PLST training program vs. attention control n=237 Moderate risk of bias	**Treatment**: Individualized care plan (structured routine with environmental modifications, engaging activities, reduced screen time); review, education, written summary of care plan - 2 sessions; 4 hours total - research associate	***General Behavior*** MBPC frequency (hierarchical linear model): Coefficient (SE) Nonspouse experimental: REF Nonspouse comparison: 0.77 (0.36);	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden:*** NR ***Caregiver distress*** MBPC reaction hierarchical linear model

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
	Comparison: Two one-hour visits of information on ADRD (Alzheimer's Disease and Related Disorders), referral to community services, local support groups, and case management; caregiver book; related information pamphlets; notebooks (content differed according to treatment - not further explained)	p<.001 Spouse experimental: 0.18 (0.26) Spouse comparison: 0.18 (0.26) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	estimate -0.39; SE 0.18; p<.01 ***Caregiver QoL:*** NR
Gormley, 2001[135] RCT United States Behavior management of aggression in dementia vs. sham treatment n=62 Moderate risk of bias	**Treatment**: Training to identify precipitating and maintaining factors; behavioral interventions suggested by behavioral analysis - 4 sessions over 8 weeks - study author **Comparison**: Equivalent number of group sessions; discussions of care-related issues with advice regarding local services (no behavior change)	***Agitation/Aggression*** ***RAGE, baseline*** Mean (SD)=9.2 (3.8) vs. 8.8 (2.9) ***RAGE, postintervention*** Mean (SD)=6.9 (3.6) vs. 8.6 (4.5) ***General Behavior*** ***BEHAVE-AD, baseline*** Mean (SD)=8.0 (3.7) vs. 8.0 (4.0) ***BEHAVE-AD, postintervention*** Mean (SD)=6.5 (2.8) vs. 7.8 (3.4) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use*** ***Taking psychotropic drugs*** **Baseline,** n/N (%) 20 (58.8) vs. 16 (57.1) **Postintervention,** n/N (%) 18 (52.9) vs. 17 (60.7) RR: 0.87 (0.56 to 1.35) ***Caregiver Burden*** **ZBS, *baseline*:** Mean (SD)=38.6 (13.9) vs. 39.5 (13.0) **ZBS, *postintervention*** Mean (SD)=36 (12.3) vs. 41.2 (12.0)
Marriott, 2000[140] RCT United States Family intervention vs. attention control vs. no treatment n=42 Moderate risk of bias	**Treatment**: Education based on assessment using knowledge about dementia interview; provided general AD information and practical advice on management; stress management; coping skills training - 14 biweekly sessions - clinical psychologist **Comparison 1**: Audiotaped semi-structured interview to assess caregiving situation and unmet needs, but no intervention **Comparison 2:** No interview or intervention	***General Behavior*** **MOUSE-PAD-Behavioral disturbance** Baseline, mean (SD): 5.1 (2.1) vs. 5.4 (2.5) vs. 5.1 (2.2) Post-treatment, mean (SD): 4.9 (0.2) vs. 5.0 (0.2) vs. 5.6 (0.2) Postintervention, mean (SD): 5.3 (2.0) vs. 5.5 (2.4) vs. 5.2 (2.0) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden:*** NR ***Caregiver Distress:*** NR ***Caregiver QoL:*** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Interventions addressing skills-affect (k=2)			
Belle, 2006[121] RCT United States Results reported by race REACH II vs. waitlist/attention control Hispanic or Latino n=168 REACH II vs. attention control White n=182 REACH II vs. attention control Black n=168 Moderate risk of bias	**Treatment:** Range of strategies tailored to needs (could include information, didactic instruction, role playing, problem solving, skills training, stress management, telephone support groups) - 12 sessions [nine 1.5 hour in-home sessions, three 30-minute telephone sessions, and five telephone support sessions] - certified college graduate interventionist **Comparison:** Two brief check-in phone calls; educational materials	**Hispanic or Latino:** ***General Behavior*** Problem behavior: Change (%) in net improvement (CI): 36.3 (13.2 to 56.7) ***Long term care admission*** RR (95% CI): 0.17 (0.02 to 1.36) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **White:** ***General Behavior*** Problem behavior: Change (%) in net improvement (CI): 13.6 (-6.3 to 35.3) ***Long term care admission*** RR (95% CI): 0.51 (0.21 to 1.22) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR **Black:** ***General Behavior*** Problem behavior: Change (%) in net improvement (CI): -3.6 (-25.2 to 16.7) ***Long term care admission*** RR (95% CI): 1.54 (0.45 to 5.31) ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	**Hispanic or Latino:** ***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** Change (%) in net improvement (CI): -4.2 (-16.9 to 25.7) ***Caregiver distress:*** NR ***Caregiver QoL:*** NR **White:** ***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** Change (%) in net improvement (CI): -4.6 (-23.7 to 15.4) ***Caregiver distress:*** NR ***Caregiver QoL:*** NR **Black:** ***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden*** Change (%) in net improvement (CI): 23.1 (0.6 to 45.7) ***Caregiver distress:*** NR ***Caregiver QoL:*** NR

Study **Design** **Country** **Comparison** **n** **Study Risk of Bias**	**Intervention Description** **[Intensity, Duration, Qualifications Interventionist]**	***Primary Outcomes-Instrument*** **Results**	***Intermediate/Secondary Outcomes-Instrument*** **Results**
Mittelman, 2004[141] RCT United States Caregiver intervention vs. usual care/attention control n=406 Moderate risk of bias	**Treatment**: Individual and family counseling sessions tailored to needs assessment; weekly support groups [beginning in month 5; indefinitely]; ad hoc counseling via phone as needed - 2 individual, 4 family sessions over 4 months - counselors **Comparison**: Informational resources, advice when requested by caregivers, support available elsewhere; requests for in-person information and counseling not refused	***General Behavior*** MBPC-frequency log growth model: Estimate for group (SE): 0.24 (1.23); p=.84 Estimate for group x time (SE): -0.03 (0.86); p=.96 ***Patient Distress, QoL:*** NR ***Nursing Home Admission:*** NR ***Adverse effects:*** NR	***Caregiver Behavior:*** NR ***Antipsychotic Use:*** NR ***Caregiver Burden:*** NR ***Caregiver distress*** MBPC-reaction: Estimate for group (SE): -2.90 (1.27) p=.02 Estimate for group x time (SE): -1.86; (0.89) p=.04 ***Caregiver QoL:*** NR

ABID = Agitated Behavior in Dementia Scale; ADCS-CGIC = Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change; AMD = adjusted mean change; ASMD = adjusted standardized mean difference; BEHAVE-AD = Behavioral Pathology in Alzheimer's disease; BRSD = CERAD Behavior Rating Scale for Dementia; CI = confidence interval; CMAI = Cohen-Mansfield Agitation Inventory; DEMQoL = Dementia Quality of Life measure; MBPC = Memory and Behavior Problem Checklist; MC = mean change NPI-Q = Neuropsychiatric Inventory Questionnaire; NPI-S = Neuropsychiatric Inventory Questionnaire Score; NR = not reported; NS = not significant; QoL = quality of life; QoL-AD = Quality of Life in Alzheimer's Disease; RAGE = Rating Scale for Aggressive Behavior in the Elderly; RCT = randomized controlled trial; RMBPC = Revised Memory and Behavior Problem Checklist; RR = risk ratio; SCB = Screen for Caregiver Burden; SD = standard deviation; SE = standard error; WHO-QoL= World Health Organization Quality of Life; WHO-QoL-Brief, Psych = World Health Organization Quality of Life, short form – psychological questions; ZBS = Zarit Burden Scale

[a] adjusted for living arrangement (alone vs. with caregiver) and baseline value of dependent variable

[b] adjusted for baseline value, caregiver gender and relationship to patient

[c] analysis adjusted for baseline value, care recipient cognitive status (MMSE) and number of ADL dependencies, caregiver age, gender, education, relationship to the care recipient

[d] Behavioral outcomes included occurrence of each of 24 behaviors (16 from ABDS and 2 from RMBPC and 2 others identified by families). For each behavior, families indicated yes if behavior occurred and how many times. Behaviors reported as constantly occurred were scored 300.

Discussion

Reducing off-label use of antipsychotic drugs for individuals with dementia is a priority. Ideally, strong evidence that nondrug treatments can effectively reduce agitation/aggression and improve patient quality of life could support this treatment change; but even in the absence of strong evidence about the effectiveness of nonpharmacological treatment, due to their potential risks and limited efficacy, efforts should continue to reduce the use of psychoactive medications in these patients. Evidence is mounting about the risks of this type of drug treatment. Patients who are overmedicated with antipsychotics and robbed of experiencing life due to sedatives experience a clear detriment. For people with dementia, psychoactive medications can cause harm and even death. The Centers for Medicare & Medicaid Services has launched an active campaign to reduce the use of psychoactive medications.[16,156] Even in clinical circumstances when psychoactive drugs are appropriate, they must be used sparingly and for a specific documented behavior, and they must also use the lowest effective dose. Ideally, nonpharmacologic approaches, which have few, if any, adverse effects, would be substituted as psychoactive medication use was reduced, creating a win-win situation. Caregivers who are confident about the efficacy of nonpharmacologic options may be more willing to reduce and forgo medications.

Unfortunately, despite the urgent need for strong evidence, the current literature on nonpharmacologic options is weak. Research on the nonpharmacologic management of aggression in dementia is not well coordinated and has some major problems. Trials are mostly small and vary widely in interventions, instruments used to measure outcomes, analysis techniques, and reporting. Each investigator seems anxious to add something new. Given the heterogeneity in comparisons and outcomes, pooling for meta-analysis was rarely possible. Wherever possible, we tried to identify patterns within groups of conceptually similar comparisons, but the evidence was insufficient to draw conclusions for a large number of comparisons and outcomes.

In some cases, low strength evidence showed that interventions were not effective in reducing agitation/aggression. For example, among patient-focused interventions in nursing home and assisted living settings, music, aromatherapy with lavender, and bright light therapy had similar effects on agitation/aggression as inactive control (placebo, attention controls, usual care). Further, among interventions implemented at the care-delivery level in nursing home and assisted living settings, dementia care mapping and patient-centered care had similar effects on agitation/aggression as usual care. Low strength evidence also showed that tailored caregiver education and training combined with a caregiver psychosocial component was similar to inactive control in managing general behavior in dementia, improved caregiver confidence, and reduced caregiver burden.

Limitations of Available Studies

Our review reflects the limitations of the available literature. We found substantial heterogeneity in interventions and outcomes across trials and methodological problems within trials. While we did identify a large number of trials that tested interventions for improving behavioral symptoms in dementia; fewer specifically measured agitation/aggression. Few groups of studies had sufficient similarity in interventions, comparisons, and outcomes to allow appropriate data pooling. When pooling was not appropriate, we attempted a qualitative synthesis of similar comparisons and outcomes. Despite these attempts, our analysis still consists of several unique comparisons, often from small studies with methodological limitations,

resulting in evidence insufficient to draw conclusions about efficacy or comparative effectiveness.

Our primary outcome was agitation/aggression. Because the research has tended to combine these two, we followed that practice. However, as noted earlier, they have different manifestations and implications. Our primary outcome was agitation/aggression. Agitation affects primarily the person with dementia (although the behaviors may be disruptive for others in his/her environment). By contrast, aggression directly involves at least one other person (the target of the aggression) and can represent a real risk to that person. As a result, one might argue that although it makes sense to identify and treat the underlying cause of agitation whenever possible, some regular manifestations of agitation may not need intervention per se; they can simply be tolerated. By contrast, aggression needs to be dealt with because of the possible risk to others.

Several different instruments were used to assess this agitation/aggression. Certain instruments are best suited to certain settings and patients. Whether each study selected the most appropriate instrument was unclear, and we found little information regarding changes in these scores associated with a clinically meaningful difference. None of the studies we analyzed used instrument-specific thresholds to assess efficacy or comparative effectiveness. Additionally, although the CMAI is a very widely used instrument in nursing home and assisted living settings and has been determined valid and reliable, many studies reported only subscales of the CMAI. Whether these subscales are valid or reliable or sensitive to changes occurring in response to treatment is unclear.

Changes in aggression and agitation will vary with the goal of the intervention. Interventions designed to respond to a behavior are different from those designed to prevent the occurrence or reduce the intensity of future behaviors. If the former case, a successful intervention ends an episode but its duration of effect is likely to be short. By contrast, a more preventive approach aims to have a longer lasting effect, marked by fewer or less severe future events. Although we attempted to classify interventions on the basis of the intent (i.e., responsive or preventive), we found that many studies failed to make the distinction clear. Future research should address this distinction more overtly in presenting their conceptual model for the effectiveness of the intervention being tested.

Understanding that we may not find studies that reported agitation/aggression per se, we included studies that assessed behavioral symptoms with more general instruments. These instruments (NPI, MOSES) contain items across a wide variety of behavioral symptoms. Changes in overall scores on these instruments are not easily interpreted nor directly related to agitation/aggression.

We found few references documenting established minimal important differences for any of the instruments used to assess agitation/aggression, general behavior, or intermediate and secondary outcomes. Without an understanding of what constitutes a clinically meaningful change, interpretation of statistically significant differences and assessment of precision was challenging.

Individual studies assessed as having a low or moderate risk of bias still presented several methodological problems. Many trials were underpowered. Underpowered studies that cannot be pooled add little value to the field and should not be conducted. Calculating sample sizes necessary for appropriately powered RCTs should incorporate the high attrition rate commonly found in this population of older adults with health problems. Sample size calculations should also take into consideration that individuals with dementia may change living status (e.g., move from the community to a facility) and face a higher risk of death compared with similarly aged individuals.

Withdrawals and dropouts created considerable loss of participants from already small sample sizes in some studies. Although attrition was predictably high in the studies we reviewed, it was not always adequately described and intention to treat analysis was rarely conducted.

Details regarding the population, setting, and methodology were often inadequately described. Few studies provided details on dementia type or severity/stage of illness. Few clearly described the control groups.

Current study designs are not well described, which is a common problem in nonpharmacologic research.[157] Control conditions are also poorly described, including the concomitant use of antipsychotic medications. This was especially a problem in older studies. Usual care was rarely described when it was used as a comparison. Often, sample selection and method of randomization were not reported. Few studies described and accounted for simultaneous treatments, especially psychoactive medications. When use of psychoactive medications was reported, trials rarely eliminated their use; at most, medications were held constant during the study and/or medication changes were recorded as an outcome. Outcome assessors were often aware of the intervention status of participants or of the research question, potentially biasing the findings. Many studies used multiple outcomes and analyzed multiple comparisons, but most failed to make statistical adjustments for the multiple comparisons.

Moreover, when studies were compared with "usual care," the usual treatment was rarely defined. People with dementia, especially in group residential settings, were typically exposed to a hodgepodge of activities and therapies designed to improve functioning and quality of life. Indeed, RCTs of one intervention were sometimes used as an attention control for another intervention. Similarly, the physical environments and rules for conduct in the residential settings of the studies were seldom described, yet could have powerful effects on reducing or ameliorating agitation/aggression. In some instances the intervention was added to this usual care; in others it was offered as an alternative. It was frequently not even clear if psychoactive medications were being given concurrently.

Many trials tended to combine aggression and agitation/aggression as an outcome, but these are not synonymous. Although aggression is a form of agitation, it differs from agitation and anxiety in a caregiving context. Agitation/aggression was rarely described other than reports of instrument scores. Further, agitation/aggression was reported in a variety of ways. Some instruments combined them; others separated them. However, when the behaviors were separately assessed with certain elements of an instrument, we could not always determine whether that instrument was designed to yield valid and reliable subsets of questions. Scales to measure agitation include elements such as restlessness or aimless pacing, repetitive requests and "verbalizations," and so forth.

Agitation may be prompted by loss of memory or it may reflect anxiety. If the anxiety is the patient's and not the caregiver's, then its underlying cause must be ascertained (e.g., pain or discomfort or some specific stimulus). Agitated verbal or physical behavior may be annoying and even frustrating to caregivers but is not necessarily a problem requiring treatment. By contrast, verbal and especially physical aggression often require treatment. At minimum, aggression may arouse fear or disturb the calm of other patients in group settings; at worst, it may cause injury to caregivers or other patients. Aggression is also likely to harm its perpetrator in the form of increased restrictions or temporary or permanent removal to another setting, resulting in increased confusion. For these reasons, aggression is likely to be treated more assertively than various forms of agitation. Ironically, the epidemiology of agitation/aggression is not well understood, from the distribution of agitated behavior to how often various behaviors

occur separately or together in the same patient and whether any discernable progression can be observed.

Agitation and aggression are typically grouped together as part of a spectrum, although they have different manifestations and implications.

These two goals may imply different strategies. Preventing or minimizing events can rely on environmental manipulation such as music or light, or activities that create a diversion or draw on strengths of remote memories. It may involve individually based approaches to identify triggers for a given person and subsequently avoid them (this is essentially the basis for dementia care mapping and for the general stance that agitation/aggression is communication that caregivers need to try to decipher and respond to). Conversely, managing events once they arise may involve distraction, calming behavior by staff, or moving individuals to a calming environment.

Given this distinction, preventive strategies should be enacted over long time periods in order to reduce the frequency and/or intensity of events. Likewise, treatments designed to prevent agitation/aggression should produce long-lasting effects, and thus longer-term followup is appropriate. Some of these treatments require staff to change their approach to dealing with individuals with dementia. Sustaining any behavior changes that follow may require additional caregiver or staff support beyond that involved in the initial intervention. Other techniques aim to squash or at least diminish agitation/aggression when they arise. Unlike preventive strategies, reactive strategies are in the moment and need to work immediately; however, their effect may not last beyond the episode. Therefore, the measures of success for preventive and reactive approaches should differ. However, we found substantial confusion in distinguishing strategies and measures.

We might expect to see interventions tested for effectiveness before being used as the basis for training, but such was not the case. Instead, the line between training studies and interventions proved hard to draw. Several interventions required that staff be trained to behave differently, but the training was sparsely described. Some studies used a combination of outside experts and trained staff to implement interventions.

Changing the behavior of caregiving staff is challenging, especially in nursing homes, where training and oversight are modest at best. Nursing home staff are notoriously overworked and may not be eager to take on new tasks, especially ones that require them to radically alter their typical behavior and routines. Although all nursing homes are required to have in-service educators and to conduct training at intervals, staff training tends to be perfunctory and brief with sparse oversight and encouragement. Maintaining a new behavior requires regular feedback to engender a sense that it is working. Staff training is even more difficult when the staffing is unstable or staff feel great pressure to complete other assigned tasks. The more that interventions require clinical judgment, the more difficult they are to implement, especially within nursing home hierarchies.

In regard to assisted living and other group residential settings and in-home care services, training requirements are even fewer, dependent largely on state rules. Furthermore, the appropriate staff to conduct interventions in such settings is harder to define. Some studies used external staff to establish the effectiveness of the behavior; and the effects of these interventions tend to have short half-lives because implementation disappears when the study ends. Relying on staff to administer the intervention increases chances of longer-term success, but doing so is far more complicated. As mentioned, staff must then be trained and supervised. Ultimately, the more an intervention depends on staff, the harder it is to separate it from a training study in research.

Many studies used multiple outcome measures; most failed to make statistical adjustments for the multiple outcomes. The large number of measures may reflect uncertainty about the goals of the intervention or the lack of a good measure.

Few studies accounted for or even described simultaneous therapies, especially psychoactive medications. Further, physical environment was rarely addressed (e.g., private or shared rooms, freedom or restrictions of movement, policies for dining, bathing, and care routines that may generate resistance). We found few studies of such environmental and practice shifts (other than the training to generate more effective staff) and the environments for these studies were rarely described. Even studies of bathing interventions did not describe usual routines for bathing. In studies of individualized activities, authors provided little sense of the spaces available for such efforts. Most of the nursing home studies took place in multiple facilities, either with facilities or units randomized or with intervention and control groups in each study site. In these cases we know little about how settings varied. Studies didn't account for potential differences in study sites in statistical analyses, but even if they had, sample size would make facility differences in effects hard to find.

Our findings are consistent with many prior reviews, but more pessimistic than others, which showed benefit for certain interventions. A recent systematic review of music therapy for a broad range of behavioral and psychological symptoms found a small effect for anxiety and behavior (broadly defined).[158] This review included a broader range of symptoms and study designs and did not specifically address agitation/aggression. Another recent review that specifically addressed agitation concluded that music therapy following protocol failed to produce a sustained benefit.[159] The same review found no evidence of efficacy for aromatherapy or light therapy.[159] In contrast, Livingston et al. concluded that the available evidence showed that dementia care mapping and person-centered care showed efficacy.[159] They included a broader range of study designs, failed to conduct a meta-analysis, and may have concluded efficacy when changes from baseline were present in the absence of differences from control group. Brodaty et al. concluded that caregiver interventions improved behavioral outcomes in community-dwelling individuals with dementia.[160] However, this study included a broad range of psychological and behavioral symptoms and the strongest effects were from studies focusing on depression.

In summary, the evidence for nonpharmacologic treatment of agitation/aggression in individuals with dementia is weak and obfuscated by an inconsistent and confusing terminology. A clearer taxonomy of interventions and more precise terms are needed to outline the variations in the problem and the links between specific interventions and problem elements. Given the variation in intervention fidelity and complexity in RCT reports and the great difficulties of addressing selection bias even in RCTs, we believed that observational studies would be difficult to interpret. Trials should be designed to adequately address treatment goals within appropriate timelines. Simultaneous treatments such as psychoactive treatments must be accounted for. Nonetheless, this line of research will continue to be difficult. The incidence of problems is unpredictable and nursing home environments are unstable.

Applicability

Our conclusions are likely relevant to the broad population of individuals with dementia. The populations described appear similar to the overall population with dementia within each setting, at least by age and sex. The ethnic composition is less representative. Nursing home residents and dementia patients are more often female, likely due to their longer life expectancy. When dementia type was described, Alzheimer's disease was typically the most prevalent, consistent

with national estimates. While the populations reflect the population of individuals with dementia, it is more challenging to assess the applicability of results of studies conducted in nursing homes and assisted living facilities. These facilities vary greatly in size, environments, and staffing models. Few studies described these characteristics, so applicability is unclear.

Future Research Needs

This review sought to identify and synthesize RCTs testing nonpharmacologic interventions for agitation/aggression in dementia. The evidence is weak and offers no insight about promising practices. The discussion of study limitations above points to many issues that must be addressed in future work. Future research should be thoughtfully planned and rigorously conducted (Table 13). Several conceptual issues must be addressed. A clearer map of specific types of agitation/aggression and links to specific interventions may prove more valuable than addressing the general dementia population with broadly defined behavioral symptoms. Also needed are more consistent measures and clearer rationales for how the measures address treatment goals as well as appropriate timelines. A roadmap that uncouples agitation and aggression and links each of them to treatment goals may be helpful. More attention to the role of environment would help elucidate the effectiveness of interventions. If the pathway is via changing staff (or informal caregiver) behavior, evidence of that intermediate effect would be helpful.

Future research should take a more systematic approach. Variations in treatment should be tested sequentially and under more defined conditions. This type of research could move the field forward. Interventions need to be more precisely described with attention to what is done (how much, how often), under what circumstances, and by whom. Fidelity needs to be documented. Likewise the nature of "usual care" needs to be explicated and any concurrent treatment delineated. An order of procedure that would be clinically acceptable might start with adding a candidate treatment. That approach, if it produced a substantial effect, could then be tested instead of existing drug therapy.

Future RCTs should be adequately powered and power calculations should incorporate the expected high attrition rate when calculating necessary sample sizes. Given that many studies showed little or no effect for most interventions, accumulating more studies with the small sample sizes is unlikely to change the results. Future trials should adequately describe the intervention and control condition, blind outcomes assessors, and use instruments appropriate to the intervention. They should also appropriately correct for multiple comparisons and account for simultaneous treatments such as psychoactive medications. In addition, more work needs to be done on establishing minimal important differences for the major outcomes.

Table 13. Future research needs

Key Question	Results of Literature Review	Types of Studies; Needed To Answer Question	Future Research Needs
General methodological issues	Agitation and aggression not consistently described, defined, or treated as separate behaviors	Consensus conference	Consensus among experts to arrive at standard definitions of specific behavioral symptoms.
	Improvement and agreement on instruments to measure agitation/aggression.	Consensus conference	Consensus among experts to identify or develop instruments with adequate psychometric properties to measure agitation/aggression and guidance on which measures to use in select settings, populations.
	Few groups of studies with sufficient similarity in interventions, comparisons, and outcomes allowing appropriate data pooling.	Consensus conference	It would be beneficial to standardize promising practices and study those practices in RCT studies. It would also be beneficial to develop guidance to assist researchers in selecting the appropriate instruments to measure agitation/ aggression.
	No established minimum important differences for commonly used instruments measuring agitation/aggression outcomes.	Original research	It would be beneficial to conduct studies to determine thresholds for commonly used instruments that indicate clinically meaningful changes. These threshold values could be used in comparative effectiveness research.
	Wide heterogeneity in interventions, comparisons, outcomes, and analysis techniques.	Consensus conference	Consensus among experts about which interventions might be most appropriate, effective in which populations and settings. Prioritization of interventions with specific characteristics could lead to a more homogeneous set of trials that could provide sufficient evidence to draw conclusions.
	Agitation/aggression not specifically studied; many trials address behaviors broadly.	RCTs	Trials should address agitation or aggression specifically, enrolling persons with dementia with similar symptoms to better study the potential of interventions to manage these specific behaviors.
	Objectives of interventions not well-specified	RCTs	Interventions should be designed to prevent or respond to agitation/aggression; trial should be designed according to objective.
	Small, underpowered studies	RCTs	Funding/conducting RCTs with power adequate to answer the research question is necessary to avoid underpowered studies which do not strengthen available evidence. Power calculations should incorporate the expected higher rate of attrition common in this population.

Key Question	Results of Literature Review	Types of Studies; Needed To Answer Question	Future Research Needs
KQ 1a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among individuals with dementia in long-term care?	Study populations in nursing home settings often had a wide variety of agitation/aggression behaviors that might respond differently to specific treatments.	RCTs	Persons with dementia with similar symptoms could provide the population for intervention trials. Larger trials would provide more valuable information and strengthen the evidence base.
	Few trials studied particular environmental interventions	RCTs	Trials that assess environmental changes.
KQ 1b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/ aggression among individuals with dementia in long-term care settings?	Harms were rarely reported; most interventions were unlikely to have serious harms.	RCTs	It would be beneficial to record and report harms or lack thereof for each treatment group.
KQ 2a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/ aggression among community-dwelling individuals with dementia?	Tailored interventions did not demonstrate an effect on behaviors. Few trials specifically targeted agitation/aggression.	RCTs	Persons with dementia with similar symptoms could provide the population for intervention trials to determine if certain behavioral symptoms do not respond to nonpharmacologic treatment.
	Caregiver tailored education and training showed benefits to caregivers (improved confidence of managing behaviors). It is unclear if these benefits are maintained after the intervention ends.	RCTs	Long-term followup is necessary to determine if caregiver benefits are maintained after intervention ends. Testing could be conducted to determine if booster sessions or long-term psychosocial interventions help maintain intervention benefits.
KQ 2b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/ aggression among community-dwelling individuals with dementia?	Harms were rarely reported; most interventions were unlikely to have serious harms.	RCTs	It would be beneficial to record and report harms or lack thereof for each treatment group.

KQ=Key Question; RCT=randomized controlled trial

Conclusions

Research on nonpharmacologic treatment of agitation/aggression seems to have developed in a piecemeal fashion without overarching coordination. Our review found insufficient evidence to draw conclusions regarding most of the interventions that have been studied to address agitation/aggression in individuals with dementia. The few interventions with low strength evidence had null effects. Despite the urgent need for alternatives to medication for the treatment of problem behaviors, the current state of the literature provides little information useful to changing practice. Nonetheless, efforts should continue to find alternatives to psychoactive medication treatment.

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Abbreviations

ABID	Agitated Behavior in Dementia Scale
ABRS	Agitated Behavior Rating Scale
ACT	Advancing Caregiver Training
ADCS-CGIC	Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change
AHRQ	Agency for Healthcare Research and Quality
AICT	Advance Illness Care Teams
ARD	Absolute risk difference
BEHAVE-AD	Behavioral Pathology in Alzheimer's disease
BLT	Bright light therapy
BMD	Behaviour and Mood Disturbance
BPSD	Behavioral and Social Symptoms of Dementia
BRS	Behavioral Rating Scale
BRSD	Behavior Rating Scale for Dementia
CENTRAL	Cochrane-Central Register of Controlled Trials
CFI	Camberwell Family Interview
CI	Confidence interval
CMAI	Cohen-Mansfield Agitation Inventory
COPE	Care of Persons with Dementia in their Environments
DBRS	Disruptive Behavior Rating Scales
DCM	Dementia care mapping
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
ESP	Environmental Skill-Building Program
MID	Minimal important difference
MOSES	Multi-dimensional Observation Scale for Elderly Patients
NCD	Neurocognitive disorders
NPI	Neuropsychiatric Inventory
NPI-C	Neuropsychiatric Inventory Clinician
PAS	Pittsburgh Agitation Scale
PCC	Person-centered care
PICOTS	Population, Interventions, Comparators, Outcomes, Timing, Setting
QoL	Quality of life
RCT	Randomized controlled trial
REACH	Resources for Enhancing Alzheimer's Caregiver Health
REHAB	Rehabilitation Evaluation Hall and Baker
RMBPC	Revised Memory and Behavior Problem Checklist
RR	Risk ratio
RSS	Relative Stress Scale
SCB	Screen for Caregiver Burden
SMD	Standardized mean difference
TAP	Tailored Activity Program
TREA	Treatment Route for Exploring Agitation
WMD	Weighted mean difference
ZBI	Zarit Burden Index

List of Appendixes

Appendix A. Search Strategy
Appendix B. Excluded Studies
Appendix C. Patient-Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities
Appendix D. Care Delivery–Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities
Appendix E. Patient-Level Interventions for Agitation/Aggression in Community-Dwelling Individuals With Dementia
Appendix F. Caregiver-Level Interventions for Agitation/Aggression in Community-Dwelling Individuals With Dementia
Appendix G. References for Appendixes

Appendix A. Search Strategy

Database: Ovid MEDLINE(R) <1946 to November Week 1 2014>
Search Strategy:

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1 exp *Dementia/
2 dementi*.ti.
3 alzheimer*.ti.
4 1 or 2 or 3
5 neuropsych*.mp.
6 behav*.mp.
7 agitat*.mp.
8 aggress*.mp.
9 exp Behavioral Symptoms/
10 exp Psychomotor Agitation/
11 5 or 6 or 7 or 8 or 9 or 10
12 4 and 11
13 limit 12 to "therapy (maximizes sensitivity)"
14 limit 13 to (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial phase iv or clinical trial or controlled clinical trial or randomized controlled trial)
15 limit 14 to yr="1994-Current"

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Embase Search Strategy:

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1 dementia/
2 Alzheimer*.ti.
3 dementia.ti.
4 1 or 2 or 3
5 agitation/
6 neuropsych*.mp.
7 agitat*.mp.
8 behav*.mp.
9 exp behavior/
10 aggres*.mp.
11 5 or 6 or 7 or 8 or 9 or 10
12 4 and 11
13 limit 12 to "therapy (maximizes sensitivity)"
14 limit 13 to (article or journal)
15 limit 14 to (randomized controlled trial or multicenter study)
16 limit 15 to yr="1994-Current"

Appendix B. Excluded Studies

(Reason for exclusion appears in italics following each reference)

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Appendix C. Patient-Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities

Table C1. Patient-level interventions for agitation/aggression in nursing home and assisted living facilities: risk of bias assessments

Study	Risk of Bias Assessment
Ancoli- Israel, 2003[1]	Moderate - Patient blinding unclear; staff/outcome assessors not blinded, staff reported preconceptions of what each treatment group would do for the patients; analysis methods do not mention attrition, but period is short so possibly little.
Baillon, 2004[2]	High - High performance, detection, and attrition bias.
Baker, 2003[3]	Moderate - Fidelity issues, also different organizational contexts across countries, high attrition.
Ballard, 2002[4]	Moderate - Randomization at facility level but study does not account for facility differences.
Beck, 2002[5]	Moderate - Attrition not equal in groups.
Burns, 2011	Moderate - High attrition at posttreatment; not corrected for multiple comparisons.
Burns, 2009[6]	Low
Camberg, 1999[7]	Moderate - Intervention not implemented as directed; instruments not validated for agitation; staff reporting may introduce bias.
Clark, 1998[8]	High - Blinding unclear; only valid data presented in line graphs; other data combines from crossover groups; attrition and missing data unclear.
Cohen-Mansfield, 2012[9]	Moderate - Selection bias; unclear performance bias; potential detection bias.
Cohen-Mansfield, 2007[10]	High - Partial randomization; baseline characteristics not similar regarding age; no mention of blinding of participants, interventionists, manuals, power analysis, attrition, or handling of missing data; outcome assessors not blinded; co-interventions not similar.
Cooke, 2010[11]	Low
Deponte, 2007[12]	High - Selection and randomization unclear; high performance bias; blinding and fidelity unclear; incomplete data not handled appropriately; underpowered.
Dowling, 2007[13]	Moderate - Performance and detection bias unclear; high attrition.
Fu, 2013[14]	Moderate - Mid intervention they had 5 dropouts that withdrew consent because they wanted to be sure they were in experimental group--they were dropped so ITT model not completely used.
Fuji, 2008[15]	Moderate - Performance bias may be an issue; they did the aroma therapy 3 times a day, an hour after meals; no placebo control.
Garland, 2007[16]	High - Unclear randomization method and baseline characteristics; no mention of fidelity checks, manuals, outcome assessors, power and attrition; high risk of reporting bias; crossover study, unclear if patients were observed for all outcomes or only those which the patient primarily displayed; unsure if 2-day washout is appropriately long enough, assessors not completely blinded (seemed to guess which treatment the participant had); many excluded participants seemingly after randomization; not ITT analysis.
Gerdner, 2000[17]	High - Unclear randomization method, no mention of blinding of participants, interventionists, fidelity checks, manuals and outcome assessors; no mention of power analysis or handling of missing data; crossover study, unblinded outcome assessor (RA who did assessment was also there while the music was playing); possibly unbalanced groups at baseline (no demographic table, but mention 2 of 16 demographic variables significantly different); low attrition; not ITT analysis.
Hatakeyama, 2010[18]	High - Small sample size; selective recruitment unclear randomization, blinding, attrition, fidelity.
Hawranik, 2008[19]	Moderate - Selection bias, small sample size, diffusion, definition of intervention, fidelity unclear.
Hicks-Moore, 2008[20]	High - Randomization and allocation methods unclear, unblinded, power calculation not reported, attrition unclear.
Houser, 2014[21]	High - Unclear randomization method; small study sample (no power analysis); no mention of blinding of participants, interventionists, fidelity checks, manuals and outcome assessors; no mention of handling of missing data.
Hozumi, 1996[22]	Moderate - Participants seemingly blinded, unclear about outcomes assessors; attrition unclear; missing data unclear.
Hutson, 2014[23]	Moderate - Unclear if participants in control group received treatment, unblinded, underpowered at randomization.

Study	Risk of Bias Assessment
Ito, 2007[24]	Moderate - Participants and staff not blinded; high attrition and MNAR obvious from group comparisons; not ITT analysis; high possibility for bias for how data is presented for primary and secondary analysis purposes.
Janata, 2012[25]	High - Unblinded, power calculation not reported, most results reported via graphs.
Jablonski, 2005[26]	High - Selection bias; performance bias actual implementation of intervention, fidelity checks, hard to know what exactly was done for the intervention.
Kolanowski, 2001[27]	High – Randomization methods not described, patients served as their own controls, small sample size, power calculation not reported.
Kolanowski, 2005[28]	Moderate - Crossover study; outcome assessors blinded; only selected certain behaviors by patient; did not assess all behaviors; fidelity checks appropriate; study design and analysis very confusing since A, B, and C treatments are individualized; multiple comparisons correction unclear but unlikely and many comparisons were made, not ITT analysis.
Kolanowski, 2011[29]	Moderate - Baseline differences among groups.
Kovach, 2004[30]	Moderate - Performance bias; nurses sometimes didn't implement if they were too busy; had to change schedules several times, groups unequal at baseline; high attrition.
Landi, 2004[31]	High - Authors call this a case control study but mention randomization; blinding unclear; little description of intervention, no mention of attrition or missingness; bar graphs only for outcomes.
Lawton, 1998[32]	High - About 50% attrition rate, missing data not appropriately handled, outcome assessors not blinded; fidelity and power unclear.
Lichenberg, 2005[33]	Moderate -Assessor not blinded—an outside geriatric neuropsychologist; attrition not reported.
Lin, 2007[34]	Moderate - Non-random sampling, issues with design (assumes no changes in condition), staff were not blinded to outcomes.
Lin, 2009[35]	Low
Lin, 2011[36]	Moderate - Some issues with selection bias and contamination (in the same facility); blinding unclear; low attrition; likely not ITT analysis, but unclear; did not appear to correct for multiple comparisons.
Low, 2013[37]	Moderate - Theory-base unclear, unclear if manualized, outcome assessor blinding compromised.
Lyketsos, 1999[38]	Moderate - High attrition, not clear about how these patients were selected (and small sample size), whether sample was appropriate (did not report concerns with sleep/wake cycles), concerned about diffusion, not clear if staff were trained differently, etc.
Mariko, 2015[39]	High - Randomization and allocation methods not described, standardization of intervention unclear, missing data handling unclear.
Maseda, 2014	Moderate - Unblinded outcome assessor, power calculation not reported, all results reported via graphs.
McCallion, 1999a[40]	Moderate - Unclear regarding method of randomization and study may be under powered, unbalanced on two baseline measures one being length of stay which may mean there are unobserved disease severity variables impacting results.
McGilton, 2003[41]	High – Issues with selection bias, unclear intervention intensity and fidelity to treatment, small sample size.
Milev, 2008[42]	High - No ITT analysis; mostly unblinded; low attrition, but small population; unbalanced groups at baseline; selection bias, contamination, power issues, inadequate randomization. -Incomplete data not handled appropriately; lack of blinding of outcome assessors.
Moyle, 2014	Moderate - Some detection bias (underpowered, multiple comparisons not corrected for)
Narme, 2014[43]	High - Selection bias (only native French speakers, those without musical expertise, etc.); diffusion issues in same NH; attrition issues, small sample size, no usual care control group; very high attrition; assessors blinded; blinding of participants unclear; not ITT analysis.
Raglio, 2010[44]	Moderate - High attrition issues, differences across experimental and control groups, inadequate controls in statistical models.
Remington, 2002[45]	Moderate - Issues with detection bias, questions about whether this was the right sample (residents all had low scores for agitation).
Ridder, 2013[46]	High – Unblinded; some baseline differences; paired RCT; say ITT analysis, but then say they exclude missing data from main analysis.
Robichaud, 1994[47]	Moderate - Issues with selection bias, sample size, diffusion across institutions, concerns about fidelity of the program; some baseline differences between groups; second assessment unblended; participant blinding unclear; ITT analysis; low attrition.
Rodriguez-Mansilla, 2013[48]	Moderate - Self designed instruments not validated.

Study	Risk of Bias Assessment
Rolland, 2007[49]	Moderate - Only assessor blinded; low attrition; not ITT analysis for outcomes we are interested in here.
Sakamoto, 2013[50]	Moderate - Not enough information about selection of patients, short followup, power issues; participant blinding unclear; assessors blinded; corrected for multiple comparisons; attrition unclear.
Sloane, 2004[51]	High - Group-randomized trial; participant blinding unclear; assessors blinded; analyses combined treatment groups (person-centered vs. towel were separate time periods in two groups, seemingly combined for analysis); baseline differences for important characteristics; corrected for multiple comparisons; attrition unclear.
Smallwood, 2001[52]	High - Study does not have enough power to detect a difference; the allocation of subjects is poorly described; differences between controls and intervention group; participant blinding unclear; outcome assessors and aromatherapist blinded; attrition unclear; analysis methods not described.
Staal, 2007[53]	High - Selection bias, low sample size, differences between exp. and control groups; participant blinding unclear; nurse assessors unblinded; reported significant group differences at baseline; attrition unclear.
Sung, 2006[54]	High - Low attrition, but not ITT analysis; researchers blinded, outcome assessors not blinded.
Sung, 2012[55]	High - No blinding; single facility; tool for measuring anxiety has poor validity; low attrition, but not ITT analysis; not blinded.
Svansdottir, 2006[56]	High - Authors refer to it as a case-control study, but it appears to be RCT; little information about analysis, but not ITT analysis according to tables; Attrition under 20%; outcome assessors blinded; blinding of intervention staff and patients unclear.
Telenius, 2015[57]	Moderate - Multiple comparisons not corrected for; some details of standardization and fidelity to intervention unclear.
Van de Winckel, 2004[58]	High - Practitioner not blinded; behavior assessors blinded to treatment; cognition assessor not blinded (same person who delivered intervention); low attrition.
Van der Ploegg, 2013[59]	Moderate - Control intervention same number of one-on-one therapy time; unclear if outcomes assessors blinded; underpowered; odd selection of instruments for agitation trial.
Van Haitsma, 2015[60]	Moderate – Randomization methods unclear, blinding methods unclear, unclear if outcome measures validated, power calculation not reported.
Vink, 2013[61]	Moderate - Nurses who took patients to activities were those who completed outcomes instruments; not ITT analysis; attrition okay, but excluded a lot of people from analysis.
Woods, 2005[62]	Moderate - Blinded patients and assessors, not research assistants who performed intervention; questionable assignment of research assistants to intervention and placebo groups.
Woods, 2009[63]	High – Blinded; dropped one participant from the study and analysis due to problem behaviors; did not correct for multiple comparisons, yet many time points shown; did not seem to present results for each measure collected.
Yang, 2015[64]	Moderate - Randomization and allocation methods not described, investigators not blinded, moderate level of attrition.

Patient-Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities: Description of Trials Rated High Risk of Bias

Music

Eight studies of music intervention were rated as having high risk of bias.[8,17,20,43,46,54-56] Both the Sung studies were participatory with the first involving movement, and the second involving percussion instruments;[54,55] Narme et al., was a group music therapy intervention.[43] The other five studies used individual interventions;[8,17,20,46,56] Clark et al. used pre-recorded soothing music for residents with a history of aggression during bathing; Hicks-Moore et al. used pre-recorded music participants' indicated they enjoyed paired with a hand massage; Gerdner et al. compared listening to recordings of preferred music rather than recordings of classical music; Svansdottir et al. used a music therapist to engage patients in singing and instrument-playing compared to an undefined control; and Ridder et al. tested the effects of individual in-person music therapy compared with usual care (which often included group music therapy).[46] These studies are briefly summarized below.

In a cross-over design with 18 subjects, Clark at el. examined the effects of prerecorded music on aggressive behavior among people with severe Alzheimer's type dementia during bath time in a 2-week period, compared with usual care.[8] Significant decreases were found in hitting behaviors during the intervention, and "discussions with caregivers" was associated with less agitation during the intervention.

Hicks-Moore et al., in an unblinded, repeated-measures design, reported randomizing 41 residents with mild to moderate dementia to music, hand massage, both combined, or control.[20] The actual number randomized was unclear, as was attrition. Participants in the music conditions received 10 minutes of pre-recorded music they indicated was their favorite song, artist, or type. There were no significant differences between groups for aggression at posttreatment.

Gerdner, et al., in a cross-over design, 39 residents participated in a study comparing 30 minute periods listening to recordings of relaxing classical music versus recordings of preferred music during their lives, as determined by family members completing a preferred music questionnaire on their behalf.[17] Dose was 30 minutes 2 days a week. The outcomes were measured by the Temporal Pattern in Assessment of Agitation (TPAA) scale, which was modified from the CMAI. The study compared the immediate and 30-minute residual effects of the individualized music. Positive findings are reported, but the raters of outcomes were the ones who applied the intervention.

Sung, et al. studied a 1-month study of 30-minute, twice weekly sessions of group music therapy with movement compared with usual care in a single large Taiwanese nursing home.[54] The authors reported significant decrease in episodes of agitation by week 2 and week 4 using CMAI.

Sung et al. randomized 60 residents from a Taiwanese residential care facility to the intervention (active participation in music therapy with percussion instruments and exercise for 30 minutes twice-weekly for a month versus usual care).[55] Authors reported no differences in agitation but significantly less anxiety on the RAID measure in the music group compared with the control group.

Narme, et al. randomized 48 residents with dementia in a single nursing home in France to music therapy or a cooking group;[43] 37 remained in the study for analysis. Groups lasted for an hour, and were conducted twice weekly for 4 weeks. They found no differences in reduction of agitation between the new groups measured by CMAI and by NPI.

Svansdottir et al. randomized 38 residents with moderate to severe Alzheimer's disease in four locations in Iceland to small-group music therapy or an undefined control. Residents in the intervention were either engaged in singing and instrument-playing with a certified music therapist or sat listening for 30 minutes thrice weekly for 6 weeks. The authors reported significant decreases in activity disturbances during the intervention, but no lasting effects.

Ridder et al. conducted a cross-over trial in 14 nursing homes in Denmark and Norway.[46] Forty-two paired participants were randomized to 6 weeks of individualized music therapy or 6 weeks of usual care, which could include group music therapy. In this nonblinded study, the experimental group experienced a significant reduction in agitation while the control group was reported to have had a significant increase in psychoactive medication prescriptions.

Massage

Hicks-Moore et al., in an unblinded, repeated-measures design, reported randomizing 41 residents with mild to moderate dementia to hand massage, music, both combined, or control.[20] However, the actual number randomized was unclear, as was attrition. Based on a previously-developed protocol, participants in the hand massage group slow, light pressure applied to each hand for five minutes. There were no significant differences between groups for aggression at posttreatment.

Aromatherapy

Smallwood et al. randomized 21 district general hospital ward patients into three groups: aromatherapy and massage, conversation and aromatherapy, and massage only (seven per group).[52] The intervention is not well explained, but it appears that the aromatic oil was used for massage in the combined group, conversation occurred during aromatherapy for the second group, and ordinary oil was used for massage in the last group. Each individual received treatment twice weekly, after which the patients' behavior was recorded. Treatment time of day was rotated in each period so that over the course of the study each person received treatment twice in each period of the day. The study used a single-blind design. Frequency of behaviors was based on daily recordings. Findings showed no overall difference in frequency of behavior across groups. Aromatherapy and massage showed a reduction in the frequency of excessive motor behavior (one of the domain on the scale) of all three conditions which reached statistical significance between 3 p.m. to 4 p.m. ($P<0.05$).

Acupoint

Mariko et al., randomized 23 residents with moderate to severe dementia to either acupoint touch twice daily for four weeks, a or control.[39] Randomization, blinding, and analysis methods were not reported. Antipsychotics were prescribed as needed, but unclear for which groups. General behavior symptoms decreased significantly from baseline in the intervention condition, but not in control. Comparisons were not reported between groups.

Tailored Interventions

Three studies involving individual assessments and tailored activity interventions to reduce agitation were identified but rated as having a high risk of bias. One is an earlier study of the TREAS model;[10] a later study of TREAS was rated as having lesser risk of bias and is included in our analysis.[9] The second selected activities tailored towards patients' skill level, personality, and interests.[27] The third is a study which tailored an intervention to optimize a mix of simulation and withdrawal.[32] The three studies are briefly described below.

Cohen-Mansfield et al. tested the efficacy of an algorithm for providing individualized nonpharmacological approaches to reduce agitation tailored to individual profiles of each resident's unmet needs, physical, cognitive, and sensory abilities; and with interventions based on residents' lifelong habits and roles as well as abilities: TREA (Treatment Routes for Exploring Agitation).[10] Interventions were applied for 10 days during the 4 hours of the individual's greatest agitation. The study was conducted in 12 Maryland nursing homes, 6 used as experimental and 6 used as controls. The implementation of personalized, nonpharmacological interventions resulted in statistically significant decreases in overall agitation in the intervention group relative to the control group from baseline to treatment and implementation of individualized interventions for agitation resulted in statistically significant increases in pleasure and interest.

Kolanowski et al. tested the efficacy of intervention activities based on validated cognitive and personality assessments versus control activities (domestic activities such as sewing cards, hanging laundry) to a random order by having 10 residents with dementia in one nursing home serve as their own control.[27] Activities were performed at least 15 minutes a day for one week. The authors reported fewer dementia behaviors observed on intervention days compared to control days, although this was not significant.

Lawton et al. randomized residents from two Dementia Special Care Units in the same nursing home to the condition of receiving a package of care according to individually assessed needs for stimulation or release from stimulation (retreat).[32] The study was conducted over 2 years, with considerable difficulty in implementation because of noncooperation of care teams and interference of prescribed the stimulation-retreat cycle with staff duties and resident schedules. Over time most functions worsened for both groups, agitated behavior did not decline more in the experimental unit, and there was marginal improvement in external engagement and lesser declines in positive affect and greater increases in negative affect in the experimental group.

Family Involvement in Care

Jablonski et al. tested family involvement in care using contracts to identify the type, frequency, and duration of involvement and activity that the family agreed to have.[26] The intervention is the Family Involvement in Care (FIC) protocol, whereby a primary family member is oriented to the facility, educated on potential involvement in resident care, and contracts to participate in a specified number of care activities in nine possible areas of care) for a specified amount of time. The dosage is calculated across all types and amount of activities. The experimental group exhibited less global deterioration but inappropriate behavior remained the same.

Creative Activity Program (TimeSlips)

Houser et al. tested a creative story telling intervention called TimeSlips.[21] This small pilot study evaluated the creative story-telling activity known as TimeSlips (wherein residents react to a picture with story ideas that are recorded and then read back to participants as their collective story) for its effect on behavioral symptoms and mood. The intervention group of 10 residents received two 1-hour TimeSlips sessions for 6 weeks and the comparison group of 10 residents received standard activity programming for 6 weeks. In this pilot study no statistically significant differences in mood or behavior were found.

Validation Versus Sensorial Reminiscence Versus No Treatment

Deponte et al. compared validation therapy to sensorial reminiscence to no control and measured outcomes with the NPI.[12]

Simulated Presence

Garland et al. tested simulated family presence (15-minute audiotapes by a family member about a positive experience from the past), music preferred by the resident in earlier life, and a placebo condition of reading from a horticultural text, to usual care.[16] The tapes were applied once a day for 3 days a week for 3 weeks. Family presence and preferred music both led to reduced counts of physically agitated behavior, and simulated presence (but not music) resulted in significantly reduced counts of verbally agitated behaviors. The placebo tape also was associated with benefits over usual care.

Hatakeyama et al. tested an intervention consisting of modified television watching by screening a person's home-made DVD with favorite pictures and greetings of family members.[18] Patients in a large Japanese long-term care setting who had a dementia diagnosis participated and were assigned to a homemade or comparable length commercial DVD for 2 hours each afternoon, for 4 weeks. Positive results in agitation are reported on the NPI.

Multisensory Stimulation

Staal et al. compared multisensory behavior therapy with a structured activity session.[53] The study took place on a geriatric psychiatric unit using a single-blinded, between-group study design. Twenty-four participants were randomized to MSBT or structured activity. Outcomes included the Pittsburgh Agitation Scale and the Scale for the Assessment of Negative Symptoms in Alzheimer's disease. Combination treatment of MSBT and standard psychiatric care reduced agitation and apathy more than standard psychiatric inpatient care alone ($P = 0.05$). Multiple regression analysis predicted that within the multisensory group, apathy and agitation were reduced ($R2 = 0.42$; $p = 0.03$).

Milev et al. used multisensory stimulation (MSS) study (using a Snoezelen room), in this case a dimly lit room that included many objects pertaining to the five senses: fiber-optic cables, aroma therapy, different music/sounds, water columns of different colors, textured balls to touch, and screen projectors, among others.[42] Subjects were assigned to one of three groups. The control group received no experimental treatment for the entire duration of the study and had only care as usual. The first experimental group had one Snoezelen session per week, and the other experimental group had three Snoezelen sessions per week for 12 weeks. Each session lasted for 30 minutes on a 1:1 basis with a qualified Snoezelen facilitator. At the end of the 12 weeks, all participants received no Snoezelen treatment for another 12 weeks. The 21

participants were randomly assigned to one of three groups. Outcomes included DOS mean scores. Patients who received one and three Snoezelen treatments per week had a consistently lower DOS mean score (i.e., they improved), without much fluctuation when compared with the control group. The effect was sustained even 12 weeks after the cessation of intervention.

Bathing

Sloane et al. randomized residents with dementia and a history of agitation during bathing to person-centered showering, a towel bath (i.e., a person-centered, in-bed, bag-bath with no-rinse soap), or usual care bathing.[51] The study was done in nine Oregon and six North Carolina facilities using a cross-over design between the two experimental conditions with randomization at the facility level. The Care Recipient Behavior Assessment (CAREBA), a modification of the CMAI, was used to rate behaviors for the videotaped bathing experience. All measures of agitation and aggression declined significantly in both treatment groups but not in the control group, with aggressive incidents declining 53 percent in the person-centered shower group ($P<.001$) and 60 percent in the towel-bath group ($P <.001$). Discomfort scores also declined significantly in both intervention groups ($P <.001$) but not in the control group. The two interventions did not differ in agitation/aggression reduction.

Multisensory Stimulation Versus Reminiscence

Baillon, et al. used Snoezelen versus reminiscence sessions as an attention control.[2] Each subject was allocated one of three research staff with whom they had all their intervention sessions. This staff member spent time with the resident prior to commencing the interventions. Sessions lasted up to 40 minutes every day for 2 weeks. The study was done at the Bennion Centre, Glenfield General Hospital, at Foxton Grange, which is a charity-run nursing home for older people, and at the Evington Centre, Leicester General Hospital. Subjects were randomized to one of two groups using a sealed envelope technique. Outcomes included the ABMI with reference to 3-minute samples before, immediately after, 15 minutes after, and 30 minutes after each therapy session. No statistically significant differences were seen between Snoezelen and Reminiscence sessions in terms of the change in level of agitation from pre-session to immediately post-session (CI -4.3 to 2.0) or from pre-session to 15 minutes post-session (CI -2.0 to 3.4).

Exercise

Landi et al. studied and exercise program in nursing homes in managing dementia residents' behaviors and use of antipsychotic drugs.[31]

Therapeutic Touch

Woods et al. studied therapeutic touch on behavior of nursing home residents with dementia.[63]

Table C2. Patient-level interventions for agitation/aggression in nursing home and assisted living facilities: strength of evidence assessments

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Music vs. No treatment/ Attention Control (for sustained reduction in agitation/ aggression)	Patient Agitation/ Aggression k=4; n=233	**Standardized Mean Difference**[36,50] -0.18 95% CI:-2.41 to 2.05 **NPI Agitation Subscale,** mean (SD)[44] Baseline: 3.13 (NR) vs. 3.87 (NR) End of treatment: 1.36 (NR) vs. 3.00 (NR) 4 week followup: 1.57 (NR) vs. 2.92 (NR)	Moderate	Direct	Imprecise	Consistent	Undetected	Low
	Patient General Behavior k=2; n=99	**Behave-AD** Global mean (SD)[50] Baseline: 0.9 (0.5) vs. 1.5 (0.7) vs. 1.3 (0.7) Post: 0.8 (0.4) vs. 0.7 (1.0) vs. 1.5 (0.8) 3 weeks follow-up: 1.1 (0.5) vs. 1.2 (0.6) vs. 2.2 (0.9) **NPI:**[44] results presented graphically; authors report lower scores post-intervention (F1,51=4.84, p<0.05); difference likely not significant at followup	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient
Music vs. No treatment/ Attention Control (for immediate reduction in agitation/ aggression)	Patient Agitation/ Aggression k=1; n=34	**CMAI** mean (SD)[45] Baseline: 18.41 (11.19) vs. 21.76 (9.09) Immediately post: 9.18 (11.11) vs. 21.88 (10.38) 10 min. post: 7.76 (9.55) vs. 20.88 (8.66) 20 min. post: 3.06 (5.44) vs. 20.47 (10.90)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Music vs. interactive control	Patient Agitation/ Aggression k=4; n=218	***Behave-AD Aggressiveness,*** mean (SD)[50] Baseline: 1.5 (1.8) vs. 2.5 (2.4) Post-intervention: 1.5 (0.9) vs. 0.7 (1.0) 3 weeks followup: 1.3 (2.0) vs. 2.5 (2.2) ***CMAI***[61] means– shown in figures; adjusted mean difference NS(F=2.89; p=0.09) **CMAI,** mean (95% CI)[11] Baseline: 1.66 (1.42-1.91) vs. 1.54 (1.32-1.77) After first arm:1.67 (1.49-1.85) vs. 1.66 (1.37-1.96) Post crossover:1.65 (1.38-1.91) vs. 1.70 (1.44-1.97)	Low to Moderate	Direct	Imprecise	Consistent	Undetected	Low

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		CMAI-SF, mean (SD)[45] Baseline: 18.41 (11.19) vs. 16.47 (9.94) vs. 22.00 (11.94) Imm post: 9.18 (11.11) vs. 10.35 (11.20) vs. 8.59 (7.87) 10 min post: 7.76 (9.55) vs. 7.76 (9.55) vs. 7.06 (7.08) 20 min post: 3.06 (5.44) vs. 3.06 (5.44) vs. 3.76 (4.40)						
	Patient General Behavior k=1; n=26	**Behave-AD Global,** mean (SD)[50] Baseline: 0.9 (0.5) vs. 1.5 (0.7) Post-intervention: 0.8 (0.4) vs. 0.7 (1.0) 3 weeks followup: 1.1 (0.5) vs. 1.2 (0.6)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Aromatherapy (lavender) vs. no treatment/ attention control	Patient Agitation/ Aggression k=3; n=245	**CMAI,** mean (SD)[64] Posttreatment: 41.08 (8.24) vs. 41.72 (5.08) 3 week followup: 39.80 (7.27) vs. 42.13 (5.53) **CMAI** – aggressive behaviors[14] No overall results reported; no statistically significant difference between groups on individual behaviors reported. **C-CMAI,** mean (SD)[34] Baseline: 63.17 (17.81) vs. 63.94 (SD 17.67) Post: 58.77 (16.74) vs. 63.90 (17.73)	Moderate	Direct	Imprecise	Consistent	Undetected	Low
	Patient General Behavior k=2; n=98	**NPI**, mean (SD)[15] Baseline: 31 (10) vs. 32 (11) 4 weeks: 18 (12) vs. 27 (12) **CNPI**, mean (SD)[34] Baseline: 24.68 (10.54) vs. 24.33 (10.08) Post: 17.77 (7.52) vs. 24.41 (10.24)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Aromatherapy (melissa) vs. no treatment/ attention control	Neuroleptic Use k=1; n=72	**Prescribed additional psychotropic drugs during the study:**[4] 6% vs. 8% (SDs not reported)	Moderate	Indirect	Unclear	Unknown	Undetected	Insufficient
	Patient Agitation/ Aggression k=1; n=72	**CMAI**[4] Proportion making 30% decrease in score: (60% vs. 14%, $\chi 2$=16.3; p<.0001) CMAI, median change[4] -22.0 vs. -6.5 Z=4.1; p<.0001	Moderate	Direct	Unclear	Unknown	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Aromatherapy (melissa) vs. active control	Patient Agitation/ Aggression k=1; n=77	**PAS**[65] median (95% CI) change from baseline 12 week followup: -0.7 (-1.7, 0) vs. -0.7(-1.7, 0)	Moderate	Direct	Unclear	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=77	**NPI,** mean (95% CI) change from baseline 12 week followup: : –7.2 (–12.6, –1.7) vs. –10.0 (–17.2, –3.0)	Moderate	Direct	Unclear	Unknown	Undetected	Insufficient
	Patient Quality of Life k=1; n=77	**Blau QoL,** mean (95% CI) change from baseline 12 week followup: 17 (–13, 47) vs. –2 (–34, 30)	Moderate	Indirect	Unclear	Unknown	Undetected	Insufficient
Bright Light vs. no treatment/ attention control k=4; n=225	Patient Agitation/ Aggression k=4; n=225	Standardized Mean Difference, 95% CI[1,6] 0.09 (-0.32 to 0.50) **NPI Agitation/aggression**, mean (SD)[13] Morning bright light vs. evening bright light vs. standard light Baseline: 5.3 (3.5) vs. 3.7 (2.4) vs. 5.8 (3.4) Post-intervention mean: 5.5 (3.3) vs. 4.8 (2.6) vs. 4.3 (2.5) ***Agitation – Behave-AD Aggression subscale***[38] No significant differences, did not present data (p>0.05)	Low to Moderate	Direct	Imprecise	Consistent	Undetected	Low
	Patient General Behavior k=3; n=133	**Crichton Royal Behavior Rating,** mean (SD)[6] Baseline: 34.2 (6.5) vs. 35.6 (7.6) Week 4: 41.3 (2.9) vs. 42.8 (1.4) Week 8: 43.8 (3.4) vs. 44.2 (2.5) **MOUSEPAD**, mean (SD)[6] Baseline: 13.5 (11.6) vs. 13.4 (8.8) Week 4: 7.8 (7.9) vs. 7.8 (SD 4.3) Week 8: 8.0 (7.8) vs. 7.7 (3.7) **NPI**, mean (SD)[13] Baseline: 29.4 (20.7) vs. 27.0 (15.7) vs. 24.1 (15.8) Post-intervention: 26.3 (13.9) vs. 27.5 (16.5) vs. 19.6 (10.8) **Behave-AD, mean (SD)**[38] Baseline: 14.9 (3.83) vs. 13.7 (3.49) Week 4: 12.6 (SD 4.79) vs. 10.7 (4.85)	Low to Moderate	Indirect	Imprecise	Consistent	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Therapeutic Touch vs. no treatment/ attention control	Patient Agitation/ Aggression k=1; n=51	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=2; n=108	See Report Text Table 4	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient
Massage therapy vs. no treatment/ attention control K=2; n=105	Patient Agitation/ Aggression k=1; n=34	Baseline: 16.47 (9.94) vs. 21.76 (SD 9.09) Post:10.35 (SD 11.20) vs. 21.88 (SD 10.38) 10 min. post: 7.76 (SD 9.55) vs. 20.88 (SD 8.66) 20 min. post: 3.06 (SD 5.44) vs. 20.47 (SD 10.90)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=71	**Behavior alterations improvement** 3 months: 34/36 vs. 0/35 5 months: 28/35 vs. 32/36	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Massage therapy vs. interactive control	Patient Agitation/ Aggression k=1; n=55	**CMAI**[66] mean (SD) Posttreatment Total: 27.76 (9.63) vs. 36.07 (9.72) Physical non-aggression: 10.08 (5.01) vs. 12.25 (4.52) Physical aggression: 5.36 (3.07) vs. 6.43 (3.50) Verbal nonaggression: 6.40 (3.44) vs. 9.57 (3.82) Verbal aggression: 5.92 (2.81) vs. 7.82 (3.76)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Tailored Activities vs. Nontailored Activities k=4; n=334	Patient Agitation/ Aggression k=4; n=334	**Mean (SD)**[59] Baseline: 16.7 (9.9) vs. 17.1 (9.8) During intervention: 8.4 (9.9) vs.10.0 (10.4) After intervention: 17.6 (10.3) vs. 17.0 (9.4) **ABMI, mean (SD)**[9] Baseline: 8.76 (5.61)vs. 7.16 (7.61) Post: 2.08 (2.68) vs. 7.92 (9.09) **Visual Analog Scale (0 to 100 based upon observation),** mean (SD)[30] Baseline: 38.97 (20.54) vs. 32.59 (21.66)	Moderate	Direct	Imprecise	Inconsistent	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Posttest mean (SD): 30.54 (15.31) vs. 32.25 (20.16) (Pretest to Posttest * group: $F_{1,69}$=4.26; p=0.43) **Nonverbal Behavior Observations – Aggression**[60] mean (SE) Posttreatment: 0.016 (0.04) vs. 0.117 (0.04)						
	Patient General Behavior[60] k=1; n=87	**Nonverbal Behavior Observations – General restlessness**, mean (SE) Posttreatment: 6.50 (5.66) vs. 5.28 (5.56)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Tailored Activities vs. Tailored Activities K=2; n=158	Patient Agitation/ Aggression k=2; n=158	**CMAI,** Least Square means (95%CI)[29] Baseline: 1.62 (0.9-2.4) vs. 2.46 (1.7-3.2) vs. 1.86 (1.1-2.6) vs. 1.88 (1.1-2.6) Post: 1.2 (0.3-2.0) vs.1.7 (0.9-2.5) vs.1.5 (0.6-2.3) vs.1.10 (0.3-1.9) **CMAI, mean (CI)**[28] Baseline: 2.85 (2.0-3.7) vs. 2.85 (2.0-3.7) vs. 2.85 (2.0-3.7) Post: 1.35 (0.5-2.2) vs. 1.09 (0.3-1.9) vs. 1.14 (0.2-4.0)	Moderate	Direct	Imprecise	Unknown	Undetected	Low
Aroma-acupressure vs. no treatment/ attention control	Patient Agitation/ Aggression k=1; n=113	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Exercise vs. interactive control k=1; n=170[57]	Patient General Behavior k=1; n=170	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Multisensory room + massage + exercise vs. no treatment/ attention control k=1; n=39[23]	General Patient Behavior k=1; n=39	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient Distress, QoL k=1; n=39	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Multisensory room vs. no treatment/ attention control k=1; n=32[67]	Patient Agitation/ Aggression k=1; n=32	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=32	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Multisensory room vs. interactive control k=1; n=32[67]	Patient Agitation/ Aggression k=1; n=32	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=32	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Humor therapy vs. no treatment/ attention control k=1; n=398[37]	Patient Agitation/ Aggression k=1; n=398	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=398	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient Distress, QoL k=1; n=398	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Acupuncture k=1; n=76	Patient General Behavior k=1; n=76	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Massage vs. Ear Acupuncture k=1; n=75	Patient General Behavior k=1; n=75	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Acupressure K=1; n=133	Patient Agitation/ Aggression k=1; n=133	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Structured Activities K=1; n=133	Patient Agitation/ Aggression k=1; n=133	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Acupressure vs. Structured Activities K=1; n=133	Patient Agitation/ Aggression k=1; n=133	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Reminiscence K=1; n=40	Patient General Behavior k=1; n=40	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Exercise K=1; n=134	Patient General Behavior k=1; n=40	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Adverse Effects	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Pleasant Experiences K=1; n=20	Patient General Behavior k=1; n=20	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Multisensory stimulation vs. Recreation K=1; n=40	Patient General Behavior k=1; n=40	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Activities of Daily Living vs. Psychosocial Activity k=1; n=127	Patient General Behavior k=1; n=127	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Simulated presence K=1; n=54	Patient Agitation/ Aggression k=1; n=54	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Enhancing Family Visits k=1; n=66	Patient Agitation/ Aggression k=1; n=66	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Comparison	Outcome (Instrument) # Trials (n)	Summary Statistics	Study Limitations	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
	Patient General Behavior k=1; n=66	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Electro stimulation K=1; n=27	Patient Agitation/ Aggression k=1; n=27	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Group Multistimu-lation vs. Leisure Activities k=1; n=40	Patient Agitation/ Aggression k=1; n=40	See Report Text Table 4	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior k=1; n=40	See Report Text Table 4	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

Appendix D. Care Delivery–Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities

Table D1. Care delivery–level interventions for agitation/aggression in nursing home and assisted living facilities: risk of bias assessments

Study	Risk of Bias Assessment
Chapman, 2007[68]	Moderate - Risk of contamination across groups; crossover design with incomplete reporting; attrition unclear.
Chenoweth, 2009[69]	Moderate - Unclear: not balanced on several facility and patient level variables; low attrition, attrition higher than 20% in the control group at followup.
Clare, 2013[70]	Low - Slightly underpowered in terms of patients but provided power calculation.
Davison, 2007[71]	High - Intervention has been described elsewhere in greater detail; as a standalone article difficult to fully understand implementation; no power calculation, small sample, assessors not blinded; high attrition of staff; high detection bias.
Deudon, 2009[72]	Moderate - Randomization unclear, groups unbalanced on key outcomes; even through no power calculation there was a relatively large number of observations in treatment and control.
Finnema, 2005[73]	Low - Assessors not blinded but used a validation method to determine if this impacted results and found it did not; patient attrition >20% and staff attrition = 20%.
Fossey, 2006[74]	Moderate - The unit of analysis is the NH but patients were not stable in the study and both groups experienced a large amount of turnover in terms of residents.
Galik, 2015[75] (Assisted Living)	High - Unclear randomization method, attrition unclear.
Galik, 2014[76] (Nursing Homes)	Moderate - Potential risk of bias due to detection bias (assessors could easily determine group assignment), attrition bias, and bias in the reporting of outcomes by group assignment).
Gozolo, 2014[77]	High - Potential risk of bias due to detection bias (assessors could easily determine group assignment), attrition bias, and bias in the reporting of outcomes by group assignment).
Kovach, 2006[78]	Moderate - Potential selection bias (method of randomization not clear) and detection bias (assessors not blinded).
Magai, 2002[79]	Moderate - Reporting of outcomes is unclear and method of randomization was not adequately explained, unbalanced on race; method of randomization unclear, not balanced on race; unclear if reported CMAI or Behavioral Pathology in Alzheimer Disease Rating Scale; no power calculation.
McCabe, 2015[80]	High - Adequacy of randomization unclear; intervention not adequately defined; no fidelity checks; blinding unclear, no ITT analysis, no group comparisons.
McCallion, 1999[81]	Moderate – Unclear; method of randomization not clear, not balanced on some baseline variables including overall disease severity; no power calculation; only provided attrition info on staff; in control group attrition greater than 20% for staff; unclear regarding selection, detection, and attrition bias.
McGilton, 2003[41]	Moderate - No ITT analysis; unclear if participants blinded; 15% attrition; groups similar at baseline on demographic characteristics, possibly different on agitation; intervention dose, fidelity issues, small sample size.
Proctor, 1999[82]	Moderate - Unclear method of randomization; unclear performance bias; unclear blinding.
Rapp, 2013[83]	Moderate - Performance bias (unclear application of the intervention) and detection bias (not blinding assessors).
Rokstad, 2013[84]	Moderate - Not balanced on secondary outcomes; high attrition but no difference in groups in terms of attrition or reasons for attrition; unbalanced on some baseline measures.
Schrijneamaekers, 2002[85]	Moderate - Facility selection unclear; different sources for reporting, risk of contamination; unclear (use of staff for reporting of outcomes); problems with missing data; paired group-randomized trial; unblinded assessors; participant blinding unclear; appropriate analysis; low attrition except at 12 months due to deaths.
Teri, 2005[86]	Moderate - Unbalanced on baseline data, no info on attrition, focus on paper is really on implementation and development of intervention not testing it; method of randomization not clear and not balanced on baseline variables; no power calculation and small sample size; no information regarding attrition.

Study	Risk of Bias Assessment
Testad, 2005[87]	High - Not balanced on key baseline variables; unbalanced at baseline and high attrition; attrition in both groups at 6 months and 12 months higher than 20%; very high staff turnover; no power calculation and high attrition led to smaller sample sizes.
Testad, 2010[88]	High - Attrition in both groups at 6 months and 12 months higher than 20%; also very high staff turnover.
van de Ven, 2013[89]	Moderate - Unclear regarding performance and detection bias; unit of analysis is patient and NH but patients lost to followup were replaced with new patients but imputed missing data for resident questionnaires not completed; unclear if assessors blinded to the intervention; unclear if fidelity checks conducted.
Visser, 2008[90]	High - Unclear regarding method of randomization and high detection bias; high attrition in one group but this group excluded from analysis; no power calculation and had small sample size, outcome assessors not blinded; not clear regarding fidelity; method of randomization unclear.
Wells, 2000[91]	High – Randomization methods unclear, no power calculation, and high attrition; unclear: no power calculation; attrition was 28.5%, complete reasons for attrition not given, not clear how handled missing or incomplete data.
Wenborn, 2013[92]	Moderate - Issues related to fidelity and high dropout; not clear if protocol followed exactly some residents could have received more activity; attrition >20% but similar in both groups, also say use ITT but clear how handled drop outs.
Zwijsen, 2014[93]	Moderate - Bias in randomization and analysis unclear; complex cross-over design; fidelity checks not reported; unclear blinding of outcomes assessors.

Care Delivery–Level Interventions for Agitation/Aggression in Nursing Home and Assisted Living Facilities: Description of Trials Rated High Risk of Bias

Eight studies were assessed as having a high risk of bias.[71,75,77,80,87,88,90,91] These studies were not included in our narrative analysis but are described below.

Testad et al. compared a staff-training program designed to reduce restraint use (n = 55) and a control group (n = 96).[87] The 7-month intervention consisted of educating staff on dementia-related behaviors and alternatives to the use of restraints. Intervention staff members were also provided with an hour of monthly guidance for 6 months. Treatment effects were tested with the Mann-Whitney U-test and Wilcoxon matched pairs signed rank test. At followup, use of restraints was significantly lower in the intervention group than in the control (p = 0.017). The intervention and control groups did not statistically significantly differ on the measure of agitation or use of psychotropic drugs. This study had a high risk of bias due to high detection bias (potentially underpowered given no power calculation [resident N = 151] and unclear if assessor were blinded) and high attrition bias.

Visser et al. compared two interventions, staff education only (n = 21) and staff education with peer support (n = 23), to a control group over a 3-month period (n = 32).[90] The education-only program trained staff members to manage behaviors with individualized approaches. The education and peer support intervention combined training in individualized approaches to behavior management with support to staff members. Treatment effects were evaluated with a mixed analysis of variance. Neither intervention group nor the control group differed significantly on measures of agitation on the CMAI or CMAI subscales. This study had a high risk of bias due to possible selection bias (unclear method of randomization), high detection bias (potentially underpowered given no power calculation and small sample size), and high performance bias (fidelity inadequately explained).

Wells et al. compared a staff-training program (n = 20) with a control group (n = 20).[91] Over a 3-month period staff members in the intervention group attended five sessions on providing abilities-focused care. Treatment effects were estimated with repeated measures analysis of variance. Residents in the intervention group improved significantly in agitated behavior (measured by the agitation subscale of the MIBM) compared with the control group (p = 0.021). On the PAS, the intervention group exhibited nonsignificant improvements compared with the control (p = 0.19). Staff outcomes of stress and ease of caregiving did not differ between intervention and control. This study had a high risk of bias due to potential selection bias (unclear regarding method of randomization), potential detection bias (potentially underpowered given no power calculation and small sample size [resident N = 44] and failure to adjust for multiple comparisons), and high attrition bias.

Galik et al. compared function-focused care (n = 40) with attention control (n = 41). Assisted living facilities were randomized to treatment conditions and eligible residents within facilities were identified for participation.[75] The intervention consisted for four components: 1) evaluation of person-fit within the environment; 2) staff education; 3) establish resident care plan and goals; and 4) provide support to staff. Treatment effects were evaluated using repeated measures regression. There was no significant difference in agitation (CMAI) between treatment and control group. There was no significant difference in staff outcomes (job satisfaction or observed performance) between groups. This study had a high risk of bias due to detection bias (assessors

could easily determine group assignment), attrition bias, and bias in the reporting of outcomes by group assignment).

Gozalo et al. compared an intervention designed to reduce agitation during bathing (n = 134) with a wait-list control (n = 106).[77] Up to five staff members from each intervention home attended a 2-day training session focused on effective communication strategies and interpreting behaviors as an unmet need. These five staff then trained other staff at their home institution. Fixed-effects regressions were estimated to evaluate treatment effects. We could not determine the effect of the intervention compared with the wait-list control group from the results presented. This study had a high risk of bias due to detection bias (assessors could easily determine group assignment), attrition bias, and bias in the reporting of outcomes by group assignment).

McCabe et al. compared a staff educational workshop with structured clinical protocol (n = 53), staff educational workshop with clinical support visits (n = 49), staff training in use of structured clinical protocol (n = 48), and usual care (n = 37).[80] Staff in treatment groups with an educational workshop received an overview of the epidemiology of dementia and person-centered care strategies. Clinical support consisted of a trained mental health professional providing person-centered care strategies and support to staff. A mental health professional also helped to implement a clinical protocol. No details were provided regarding usual care. Treatment effects were evaluated using analysis of covariance. There was no significant difference in agitation (CMAI) between treatment groups. Staff in the training/support condition had lower stress than staff in the support only condition ($p < 0.05$). There was no difference between groups on measures of staff disruption. This study had a high risk of bias due selection bias (unclear method of randomization) and performance bias (unclear if assessors blinded, poor fidelity, and poor description of intervention).

Davison et al. compared a staff-training program only (n = 46), a staff training combined with a peer-support program (n = 35), and usual care (n = 32).[71] Staff training consisted of eight 60 to 90 minute sessions on care for dementia-related behaviors. The peer-support program consisted of facilitated informal group session among staff members to discuss challenging behaviors of residents. Analysis of covariance was used to evaluate treatment effects. Treatment and control groups did not differ significantly on staff emotional exhaustion or resident agitation as measured by CMAI. This study had a high risk of bias due to high performance bias (intervention not adequately described), high detection bias (potentially underpowered given no power calculation and small sample size [resident N = 113] and assessors not blinded), and high attrition bias.

Testad et al. compared a staff-training program designed to reduce the use of restraints (n = 75) with usual care (n = 70).[88] All staff in intervention nursing homes were provided a 2-day seminar. In addition, study investigators led six monthly group guidance meetings. Repeated measures analysis of variance was used to evaluate treatment effects. At 6 months the proportion of residents who started, remained unchanged, or stopped interactional restrain differed between the intervention and control (Mann-Whitney test, $p = 0.021$). However, whether this difference favored the intervention or control is not clear. At 12 months (6 months post intervention) no evidence of treatment effect was observed. The intervention group improved significantly in CMAI scores relative to the control group over a 12-month period (mean difference -5.6 95% CI -10.2 – 1.0). Use of antipsychotic drugs over time did not differ significantly between intervention and control. This study had a high risk of bias due to high selection bias (not balanced on key baseline variables), high detection bias (potentially underpowered given no power calculation (resident n = 145) and attrition bias.

Table D2. Care delivery–level interventions for agitation/aggression in nursing home and assisted living facilities: strength of evidence assessments

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
Dementia Care Mapping K=3; n=643	Staff Behavior K=1; n=180	**QEAW emotion reactions, baseline** Mean (SE)=13.69 (1.51) vs. 9.48 (1.40) **QEAW emotion reactions, 4 months postintervention** Mean (SE)=23.38 (1.67) vs. 25.97 (1.59) **QEAW emotion reactions, 8 months postintervention** Mean (SE)=53.28 (1.20) vs. 53.09 (1.12) **Linear mixed-effect model** *p*-value for group: 0.719	Moderate	Direct	Precise	Unknown	Undetected	Insufficient
	Neuroleptic Drug Use K=1; n=159	**Antipsychotic use adjusted proportion, baseline** 0.15% vs. 0.19% **Antipsychotic use adjusted proportion, 4 months postintervention** 0.19% vs. 0.14% **Antipsychotic adjusted proportion, 8 months postintervention** Adjusted Proportion=0.15% vs. 0.14% **Hierarchical linear model:** p-value for group: 0.01	Low	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Patient Agitation/Aggression K=3; n=643	SMD: -0.12 (-0.66 to 0.42)	Moderate	Direct	Imprecise	Consistent	Undetected	Low
	Patient General Behavior K=3; n=643	**NPI, baseline**[69] Adjusted Mean (SE)=12.7 (5.1) vs. 16.9 (5.3) **NPI, 4 months postintervention**[69] Adjusted Mean (SE)=16.8 (5.1) vs. 20.2 (5.4)	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		NPI, 8 months postintervention[69] Adjusted Mean (SE)=12.7 (5.1) vs. 16.9 (5.3) **Hierarchical linear model:**[69] p-value for group: 0.68 **NPI-Q**[84] MC(p-value between group) -0.2 vs. 1.4 (<0.01) **NPI-Q**[84] Multivariate regression Coefficient (CI)= -2.7 (-4.6 to -0.7) **NPI-NH, baseline**[89] Mean (SE)=5.35 (0.94) vs. 6.28 (0.88) **NPI-NH, 4 months postintervention**[89] Mean (SE)=7.19 (0.95) vs. 4.45 (0.88) **NPI-NH, 8 months postintervention**[89] Mean (SE)=6.28 (0.92) vs. 4.13 (0.86) **Linear mixed-effect model**[89] p-value for group: 0.23						
	Injuries K=1; n=159	**Falls, injuries, drug errors, behavioral events, baseline** Adjusted Proportion=0.40% vs. 0.25% **Falls, injuries, drug errors, behavioral events, 4 months postintervention** Adjusted Proportion=0.49% vs. 0.37% **Falls, injuries, drug errors, behavioral events, 8 months postintervention)** Adjusted Proportion=0.46% vs. 0.37% **Hierarchical linear model:** p-value for group: 0.15	Moderate	Indirect	Unclear	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
	Staff Distress, Burden, QoL K=1; n=180	**GHQ 12, baseline** Mean (SE)=17.48 (0.33) vs. 16.67 (0.29) **GHQ 12, 4 months postintervention** Mean (SE)=15.72 (0.38) vs. 14.89 (0.34) **GHQ 12, 8 months postintervention** Mean (SE)=14.57 (0.37) vs. 14.42 (0.32) **Linear mixed-effect model**: p-value for group: 0.122 **Linear mixed-effect model** p-value for group * time: 0.43 **MJSS-HC, baseline** Mean (SE)=76.98 (1.36) vs. 77.29 (1.44) **MJSS-HC, 4 months postintervention** Mean (SE) =76.40 (1.34) vs. 75.10 (1.43) **MJSS-HC, 8 months postintervention** Mean (SE)=78.08 (1.40) vs. 75.58 (1.46) **Linear mixed-effect model** p-value for group: 0.56 **Linear mixed-effect model** p-value for group * time: 0.069	Moderate	Indirect	Precise	Unknown	Undetected	Insufficient
Person Centered Care K=3; n=775	Neuroleptic Drug Use K=2; n=487	**Adjusted proportion, baseline**[69] 0.42% vs. 0.19% **Adjusted proportion, 4 months postintervention**[69] 0.30% vs. 0.14% **Adjusted proportion, 8 months postintervention**[69] 0.34% vs. 0.14% **Hierarchical linear model Chenoweth 2009)** p-value for group: 0.01	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Proportion taking neuroleptics[74] MD (CI) = -19.5% (-47.1% to 3.0%) **Dose of neuroleptics**[74] AMD (CI) = -4.0% (-29.9% to 22.0%)						
	Patient Agitation/Aggression K=2; n=487	Standardized Mean Difference, 95% CI: -0.15 (-0.67 to 0.38)	Moderate	Direct	imprecise	Consistent	Undetected	Low
	Patient General Behavior K=2; n=429	**NPI, baseline**[69] Adjusted Mean (SE)=21.3(6.8) vs. 16.9 (5.3) **NPI, 4 months postintervention**[69] Adjusted Mean (SE)=16.8(5.1) vs. 20.2 (5.4) ***General Behavior*** **NPI, 8 months postintervention**[69] Adjusted Mean (SE)=13.5 (5.1) vs. 15.3 (5.3) **Hierarchical linear model**[69] p-value for group: 0.68 **Hierarchical linear model**[69] p-value for group x time: p = 0.30 **NPI-Q**[84] MC (p-value between group)=-0.7 vs. 1.4 (<0.01) **Multivariate regression**[84] Coefficient (CI)= -2.4 (-4.1 to -0.6)	Low to Moderate	Indirect	Imprecise	inconsistent	Undetected	Insufficient
	Injuries K=1; n=141	**Falls, injuries, drug errors, behavioral events, baseline** Adjusted Proportion=0.43% vs. 0.25% **Falls, injuries, drug errors, behavioral events, 4 months postintervention** Adjusted Proportion=0.53% vs.	Moderate	Indirect	Unclear	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		0.37% **Falls, injuries, drug errors, behavioral events, 8 months postintervention** Adjusted Proportion=0.44% vs. 0.37% **Hierarchical linear model**: p-value for group: 0.15						
Protocols to reduce Neuroleptic Use K=3; n=1,263	Neuroleptic Drug Use K=3; n=1,263	Daily Dose SMD postintervention: -0.28 (-3.50 to 2.94) pooled	Low to Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient
	Patient Agitation/Aggression K=2; n=604	CMAI postintervention MD: -4.50 (-38.83 to 29.83) pooled	Low to Moderate	Direct	Imprecise	Inconsistent	Undetected	Insufficient
Emotion Oriented Care K=2; n=297	Neuroleptic Drug Use K=1; n=151	**Psychotropic use ward unit caregivers linear multilevel model** adjusted MD per month (p-value): 0.00 (NS) **Psychotropic use 3-month ward unit caregivers linear multilevel model** adjusted MD per month (p-value): 0.00 (NS) **Psychotropic use 6-month ward unit caregivers linear multilevel model** adjusted MD per month (p-value): 0.07 (NS) **Psychotropic use 12-month ward unit caregivers linear multilevel model** adjusted MD per month (p-value): 0.02 (NS)	Moderate	Indirect	Unclear	Unknown	Undetected	Insufficient
	Patient Agitation/Aggression K=2; n=297	**Combined CMAI, CMAI-physically aggressive, CMAI-verbally aggressive, BIP10-resltess behavior**[73] Multivariate Analysis of Variance Adjusted Means (F-test, p-	Low to Moderate	Direct	Imprecise	Consistent	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		value): 3.34 vs. 3.63 (0.43, 0.51) **CMAI-verbal aggression Day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.04 (NS) **CMAI-verbal aggression 3-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 1.54 (NS) **CMAI-verbal aggression 6-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.78 (NS) **CMAI-verbal aggression 12-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.41 (NS) **CMAI-verbal aggression Ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.14 (NS) **CMAI-verbal aggression 3-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.07 (NS) **CMAI-verbal aggression 6-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -1.10 (NS) **CMAI-verbal aggression 12-month ward unit**						

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		caregivers linear multilevel model[85] adjusted MD per month (p-value): -1.41 (NS) **CMAI aggression Day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.04 (NS) **CMAI aggression 3-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.59 (NS) **CMAI aggression 6-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.12 (NS) **CMAI aggression 12-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.67 (NS **CMAI aggression Ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.13 (NS) **CMAI aggression 3-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.87 (NS) **CMAI aggression 6-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.83 (NS) **CMAI aggression 12-month ward unit caregivers linear multilevel model**[85]						

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		adjusted MD per month (p-value): -1.18 (NS) **CMAI physical nonaggression Day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.03 (NS) **CMAI physical nonaggression 3-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.70 (NS) **CMAI physical nonaggression 6-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.85 (NS) **CMAI physical nonaggression 12-month day-care unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): 0.97 (NS **CMAI physical nonaggression Ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.14 (NS) **CMAI physical nonaggression 3-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -0.28 (NS) **CMAI physical nonaggression 6-month ward unit caregivers linear multilevel model**[85] adjusted MD per month (p-value): -2.26 (<0.01) in favor of control **CMAI physical nonaggression**						

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		12-month ward unit caregivers linear multilevel model[85] adjusted MD per month (p-value): -1.27 (NS)						
	Staff Distress, Burden, QoL K=1; n=146	**GHQ 12** Multivariate Analysis of Variance Adjusted Means improved and not improved (F-test, p-value): treatment 15.42 and 20.47 and control 19.14 and 14.19 (9.11, 0.003). **QOS** Multivariate Analysis of Variance Adjusted Means improved and not improved (F-test, p-value): treatment 23.02 and 24.73 and control 22.59 and 23.70 (1.51, 0.54)	Low	Indirect	Imprecise	Unknown	Undetected	Insufficient
Miscellaneous Deudon 2009)[72] K=1; n=306	Patient Agitation/Aggression K=1; n=306	**CMAI** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.26 (0.05) vs. 0.02 (0.06) [0.001] **CMAI physically nonaggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.02 (0.002) vs. -0.003 (0.03) [<0.0001] **CMAI verbally nonaggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.02 (0.003) vs. 0.001 (0.004)	Low to Moderate	Direct	Precise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		[<0.001] **CMAI physically aggressive behavior** Linear mixed effect model coefficient for MC (SD) [p-value for difference between intervention and control]: -0.001 (0.002) vs. 0.004 (0.002) [0.142] **CMAI verbally aggressive behavior** Linear mixed effect model coefficient for MC for MC(SD) [p-value for difference between intervention and control]: -0.01 (0.004) vs. -0.001 (0.004) [0.571]						
Miscellaneous Proctor 1999[82] K=1; n=120	Patient General Behavior K=1; n=120	**CRB** AMD (CI)= -0.7 (-3.0 to 1.6)	Low to Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Miscellaneous Clare 2013[70] K=1; n=65	Staff Behavior K=1; n=65	**MBI Depersonalization** Analysis of Covariance Adjusted Means (SE): 1.32 (0.04) vs. 0.53 (0.07) Analysis of Covariance F-test (p-value) of group * time: 2.55 (0.12)	Low	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior K=1; n=65	**PRS** Analysis of Covariance Adjusted Means (SE): 37.39 (2.32) vs. 34.71 (2.17) Analysis of Covariance F-test (p-value) of group * time: 0.25 (0.62)	Low	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Staff Distress, Burden, QoL K=1; n=65	**GHQ** Analysis of Covariance Adjusted Means(SE): 6.63 (0.82) vs. 7.12(1.05) Analysis of Covariance F-test (p-value) of group * time: 0.22 (0.64)	Low	Indirect	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Emotional Exhaustion Analysis of Covariance Adjusted Means (SE):12.36(0.07) vs. 12.38 (0.07) Analysis of Covariance F-test (p-value) of group * time: 0.00 (0.99)						
Miscellaneous Wenborn 2013[92] K=1; n=159	Neuroleptic Drug Use K=1; n=159	**Total Medications** 4-week MD (CI)= 0.10 (-0.53 to 0.34, 0.66) 12-week AMD (CI)= -0.15 (-0.55 to 0.24	Low to Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Patient Agitation/Aggression K=1; n=159	**CBS** 4-week MD (CI)= 1.15 (-9.23 to 11.52) 12-week AMD (CI)= 4.13 (-21.10 to 29.36)	Low to Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior K=1; n=159	**CAPE BRS** 4-week MD (CI)= 1.08 (-0.18 to 2.34) 12-week AMD (CI)= 0.52 (-1.63 to 2.67)	Low to Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Miscellaneous Kovach 2006[78] K=1; n=114	Patient General Behavior K=1; n=144	**BEHAVE AD, baseline** Mean (SD)=7.43 (6.75) vs. 6.80 (5.47) **BEHAVE AD, 2 weeks postintervention** Mean (SD)=5.56 (5.64) vs. 6.15 (5.55) **BEHAVE AD, 4 weeks postintervention** Mean (SD)=4.68 (4.06) vs. 4.96 (4.39) Repeated Measures Analysis of Variance F-test (p-value) group x time: 0.70 (0.5)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Miscellaneous Magai 2002[79] K=1; n=95	Patient Agitation/Aggression K=1; n=95	**Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD, baseline** Mean (SD)=83.7 (51.2) vs. 25.2	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		(5.2) vs. 40.6 (7.8) **Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD, 3 weeks postintervention** Mean (SD)=69.1 (36.1) vs. 49.6 (27.2) vs. 75.4 (41.4) **Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD, 6 weeks postintervention** Mean (SD)=69.1 (36.1) vs. 49.6 (27.2) vs. 75.4 (41.4) **Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD, 9 weeks postintervention** Mean (SD)=71.8 (37.6) vs. 44.6 (23.7) vs. 63.1 (42.0) **Aggregate measure incorporating CDS, CMAI, and BEHAVE-AD, 12 weeks postintervention** Mean (SD)=65.5 (37.7) vs. 39.2 (15.2) vs. 61.6 (31.1) Repeated Measures Analysis of Variance F-test (p-value) for group: 2.28 (NS) Repeated Measures Analysis of Variance F-test (p-value) for group x interaction: 1.15 (NS)						
Miscellaneous McCallion 1999[81] K=1; n=95	Staff Behavior K=1; n=105	**Restraints use, baseline** Mean (SD)=1.20 (1.34) vs. 1.82 (1.62) **Restraints use, 3 months postintervention** Mean (SD)=1.53 (1.56) vs. 2.04 (1.78) Random effects regression F-test (p-value) 3-month group: 43.99 (NS) F-test (p-value) 3-month group	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		x interaction: 0.00 (NS) **Restraints use, 6 months postintervention** Mean (SD)=1.88 (1.82) vs. 1.75 (1.42) F-test (p-value) 6-month group: 7.20 (NS) F-test (p-value) 6-month group x interaction: 9.54 (<0.01)						
	Neuroleptic Drug Use K=1; n=105	**Psychotropic use, baseline** Mean (SD)=0.98 (1.41) vs. 1.62(1.70) **Psychotropic use, 3 months postintervention** Mean (SD)=0.93 (1.39) vs. 1.7(1.82) Random effects regression F-test (p-value) 3-month group: 37.48 (NS) F-test (p-value) 3-month group x interaction: 1.78 (NS) **Psychotropic use, 6 months postintervention** Mean (SD)=1.30 (2.15) vs. 1.57 (1.71) F-test (p-value) 6-month group: 4.99 (NS) F-test (p-value) 6-month group x interaction: 1.61 (NS)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Patient Agitation/Aggression K=1; n=105	**CSDD behavioral disturbance, baseline** Mean (SD)=2.00 (1.58) vs. 1.13 (1.06) **CSDD behavioral disturbance, 3 months postintervention** Mean (SD)=1.32 (1.40) vs. 0.98 (1.13) Random effects regression F-test (p-value) 3-month group: 49.20 (NS)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Random effects regression F-test (p-value) 3-month group x interaction: 7.76 (<0.01) **CSDD behavioral disturbance, 6 months postintervention** Mean (SD)=1.26 (1.17) vs. 1.29 (1.29) F-test (p-value) 6-month group: 23.46 (NS) F-test (p-value) 6-month group x interaction: 18.64 (<0.001) **CMAI aggressive behavior, Baseline** Mean (SD)=15.16 (9.81) vs. 13.25(7.52) **CMAI aggressive behavior, 3 months postintervention** Mean (SD)=11.00 (5.35) vs. 12.46 (6.82) Random effects regression F-test (p-value) 3-month group: 0.23 (NS) Random effects regression F-test (p-value) 3-month group x interaction: 8.67 (NS) **CMAI aggressive behavior, 6 months postintervention** Mean (SD)=12.21 (8.31) vs. 12.02 (6.22) F-test (p-value) 6-month group: 6.02 (NS) F-test (p-value) 6-month group x interaction: 0.92 (NS) **CMAI physically nonaggressive behavior, baseline** Mean (SD)=12.49 (6.34) vs. 11.09 (5.47) **CMAI physically nonaggressive behavior, 3 months postintervention**						

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Mean (SD)=10.36 (4.72) vs. 11.86 (6.54) Random effects regression F-test (p-value) 3-month group: 0.56 (NS) F-test (p-value) 3-month group x interaction: 17.59 (<0.001) **CMAI physically nonaggressive behavior, 6 months postintervention** Mean (SD)=11.38 (5.99) vs. 10.38 (6.32) F-test (p-value) 6-month group: 7.78 (NS) F-test (p-value) 6-month group x interaction: 0.26 (NS) **CMAI verbally aggressive behavior, baseline** Mean (SD)=16.22 (10.31) vs. 10.44 (6.21) **CMAI verbally aggressive behavior, 3 months postintervention** Mean (SD)=11.38 (7.13) vs. 11.52 (6.71) Random effects regression F-test (p-value) 3-month group: 38.65 (NS) F-test (p-value) 3-month group x interaction: 32.97 (<0.001) **CMAI verbally aggressive behavior, 6 months postintervention** Mean (SD)=12.88 (8.39) vs. 12.05 (6.86) F-test (p-value) 6-month group: 38.82 (NS) F-test (p-value) 6-month group x interaction: 14.23 (<0.001)						
Miscellaneous Teri 2005[86] K=1; n=31	Patient Agitation/Aggression K=1; n=31	**ABID** AMC (SD)=-3.8 (4.0) vs. -0.5 (6.7)	Moderate	Direct	Precise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
	Patient General Behavior K=1; n=31	**NPI** AMC (SD)= -3.5 (8.1) vs. 2.7 (10.0) **RMBPC Total Score Frequency** AMC (SD)= -1.1 (1.0) vs. 0.2 (0.8) **RMBPC Disruption Frequency** AMC (SD)= -0.2 (0.2) vs. 0.0 (0.3)	Moderate	Indirect	Precise	Unknown	Undetected	Insufficient
	Staff Distress, Burden, QoL K=1; n=31	**NPI (staff impact)** AMC (SD)= -1.2 (5.3) vs. 1.6 (4.2) **RMBPC (reaction)** AMC (SD)= -0.7 (1.0) vs. 0.2 (0.8) **RMBPC-disruption (reaction)** AMC (SD)= -0.1 (0.3) vs. 0.0 (0.0) **Job Satisfaction** AMC (SD)= 0.2 (0.4) vs. 0.00 (0.05)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Miscellaneous Galik 2014[76] K=1; n=103	Patient Agitation/Aggression K=1; n=103	**CMAI baseline** Control M (SE): 19.06 (1.05) Treatment M (SE): 16.57 (0.69) p-value difference between control and treatment: 0.08 **CMAI 3-months** Control M (SE): 3.18.95 (1.21) Treatment M (SE): 17.04 (0.69) p-value difference between control and treatment: 0.01 **CMAI 6-months** Control M (SE): 19.48 (1.46) Treatment M (SE): 17.83 (0.89) p-value difference between control and treatment: 0.36	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Staff Distress, Burden, QoL K=1; n=103	***Staff QoL*** **Job Satisfaction (Job Attitude Scale) baseline** Control M (SE): 35.00 (1.02)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		Treatment M (SE): 39.37 (0.93) p-value difference between control and treatment: 0.002 **Job Satisfaction (Job Attitude Scale) 3-months** Control M (SE): 33.35 (1.19) Treatment M (SE): 37.85 (0.93) p-value difference between control and treatment: 0.003 **Job Satisfaction (Job Attitude Scale) 6-months** Control M (SE): 35.13 (1.24) Treatment M (SE): 36.89 (1.00) p-value difference between control and treatment: 0.280						
	Staff Behavior K=1; n=103	**The Restorative Care Behavior Checklist baseline** Control M (SE): 0.55 (0.04) Treatment M (SE): 0.63 (0.04) p-value difference between control and treatment: 0.18 **Function Focused Activities - The Restorative Care Behavior Checklist 3-months** Control M (SE): 0.61 (0.04) Treatment M (SE): 0.71 (0.04) p-value difference between control and treatment: 0.12 **Function Focused Activities - The Restorative Care Behavior Checklist 6-months** Control M (SE): 0.40 (0.06) Treatment M (SE): 0.66 (0.05) p-value difference between control and treatment: 0.001	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Harms K=1; n=103	**Falls 6-months** Control N (%): 25 (50) Treatment N (%): 15 (28) p-value difference between control and treatment: 0.02 **Emergency room visits for**	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

Intervention vs. Comparison	Outcome (Instrument)	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Reporting Bias	Strength of Evidence
		falls 6-months: Control N (%): 5 (10) Treatment N (%): 1 (2) p-value difference between control and treatment: 0.08 **Injuries post falls 6-months** Control N (%): 5 (10) Treatment N (%): 5 (9) p-value difference between control and treatment: 0.92 **Deaths 6-months** Control N (%): 3 (6) Treatment N (%): 5 (9) p-value difference between control and treatment: 0.45						

MD=mean difference; NA=not applicable; NR=not reported; RR=risk ratio

Appendix E. Patient-Level Interventions for Agitation/Aggression in Community-Dwelling Individuals With Dementia

Table E1. Patient-level interventions for agitation/aggression in community-dwelling individuals with dementia: risk of bias assessments

Study	Risk of Bias Assessment
Baker, 2001[94]	Moderate - Patient blinding unclear; assessor not blinded; attrition was low; ITT analyses attempted.
Fitsimmons, 2002[95]	High - Results not presented in a way consistent with how we will need to analyze it. Pre-/post-test design with participants included in both groups in analyses likely to increase sample size.
Hattori, 2011[96]	Moderate - Unblinded, standardization and fidelity to intervention unclear, multiple comparisons not corrected.
Steinberg, 2009[97]	High - Not based on theory, randomization and allocation methods not described, standardization and fidelity to intervention unclear, very high attrition.
Tibaldi, 2004[98]	High - Selection and detection bias; attrition and blinding unclear.

Patient-Level Interventions for Agitation/Aggression in Community-Dwelling Individuals With Dementia: Descriptions of Trials Rated High Risk of Bias

Fitzsimmons et al. studied an at-home recreational therapy for community dwelling individuals with dementia and disturbing behaviors.[95] Agitation was measured after 2 weeks of daily, individualized recreational therapy interventions.

Steinberg et al. reported randomizing 27 participants to an exercise program delivered by their caregivers, or control (home-safety assessment).[97] Randomization and allocation methods were not described. The exercise program, which was not manualized or theory-based, incorporated aerobic exercises, strength training, and balance and flexibility training to be performed every day. A random effects model showed no effects of treatment on NPI scores.

Tibaldi et al. randomized 109 patients with severe dementia who were admitted to a hospital emergency room in Italy to either home hospitalization service or general medical ward control.[98] The intervention was a service providing interactive treatment in patients' homes via geriatric health specialists. Significantly fewer behavioral disturbances were reported at posttreatment (discharge) in the intervention compared to regular in-patient care. However, there were issues with selection and detection bias, and pre-test scores were not available for all results.

Table E2. Patient-level interventions for agitation/aggression in community-dwelling individuals with dementia: strength of evidence assessments

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
Multisensory Stimulation vs. attention control[94]	Patient Agitation/Aggression K=1; n=50	**REHAB deviant behavior** AMD (CI)[c]: -.32 (-.55 to -.09) **BRS social disturbance** AMD (CI)[c]: -.32 (-.55 to -.09)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patients General Behavior K=1; n=50	**REHAB general behavior** MD (CI): ND **BMD** MD in MC: ND	Moderate	Direct	Unclear	Unknown	Undetected	Insufficient
Art therapy vs. activity vs. specialized activity[96]	Patients General Behavior K=1; n=43	**Dementia Behavior Disturbance Scale**, Mean (SD) Posttreatment: 16.8 (12.9) vs. 14.5 (12.7)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patients Distress/QoL K=1; n=43	**SF-8, mental subscale** Posttreatment mean (SD) 53.4 (3.3) vs. 52.9 (6.7)	Moderate	Indirect	Precise	Unknown	Undetected	Insufficient
	Caregiver Burden K=1; n=43	**ZBI** Posttreatment, Mean (SD) 1 6.9 (9.1) vs. 16.5 (10.5)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient

ABID=Agitated Behavior in Dementia; BARS=Brief Agitation Rating Scale; BEHAVE-AD=Behavioral Pathology in Alzheimer's disease; BMD=Behavior and Mood Disturbance; BRSD=Behavior Rating Scale for Dementia; CMAI=Cohen-Mansfield Agitation Inventory; DBRS=Disruptive Behavior Rating Scale; MBPC=Memory and Behavior Problem Checklist; MD=mean difference; MOSES=Multi-dimensional Observation Scale for Elderly Patients; NPI=Neuropsychiatric Inventory; PAS=Pittsburgh Agitation Scale; REHAB=Rehabilitation Evaluation Hall and Baker; RMBPC=Revised Memory and Behavior Problem Checklist; RR=risk ratio

Appendix F. Caregiver-Level Interventions for Agitation/Aggression in Community-Dwelling Individuals With Dementia

Table F1. Caregiver-level interventions for agitation/aggression in community-dwelling individuals with dementia: risk of bias assessments

Study	Risk of Bias Assessment
Belle, 2006[99]	Moderate - Assessors blinded, unsure about participants; attention control; minor missing data issues as they used only available data.
Bourgeois, 2002[100]	Moderate - Manualized and good fidelity, but statistical power unclear.
Burgener, 1998[101]	High - Random assignment only mentioned in abstract; randomization method unclear; blinding unclear; no methods section.
Burgio, 2003[102]	High - Minimization randomization technique used; staff not blinded, unsure about participants. Handling of missing data unclear, possibly used only complete data.
Chien, 2008[103]	Moderate - Appropriate statistics, some key intervention details unclear, attrition unclear.
De Rotrou, 2011[104]	Moderate - Adequate randomization, manualized protocol, waitlist controls; appropriate analysis methods.
Gallagher-Thompson, 2010[105]	Moderate - Adequate randomization, manualized intervention with high fidelity likely, information control; low attrition.
Gerdner, 2002[106]	Moderate - Not a crossover study; extremely high attrition; outcome assessors blinded; participant blinding unclearly only included outcomes from one measure, did not include from another scale used. Nearly ITT analysis (excluded 4 people, only about 1.5% of this study).Unclear randomization method, no mention of blinding of participants, interventionists and fidelity checks. Outcome assessors blinded. No mention of power analysis, high attrition.
Gitlin, 2003[107]	Moderate - Blinding unclear; not corrected for multiple comparisons; high attrition.
Gitlin, 2008[108]	Moderate - Blinding unclear; not ITT analysis, waitlist control, low attrition.
Gitlin, 2010a[109]	Moderate - Attrition at 9 months (over 20%), though okay at 4 months. Blinding unclear. Unsure where .5 SD clinical significance comes from (cites Belle, but only says it's consistent with this article, not a reason why it matters). Not ITT analysis. Does not report 9 month results adequately.
Gitlin, 2010b[110]	Moderate - Blinding unclear. Differential attrition approaching 20% in one group. Call it an ITT analysis, but they do not include those lost to followup in analyses.
Gonyea, 2006[111]	High - Participant blinding unclear; assessors not blinded; not ITT analysis.
Gonzalez, 2014[112]	Moderate - Lack of important study design and analysis details, unclear if monthly fidelity checks adequate.
Gormley, 2001[113]	Moderate - Participant blinding unclear; assessor blinded; no attrition.
Guerra, 2011[114]	Low - Participant blinding unclear, but staff and outcomes assessors blinded; very low attrition.
Hebert, 1994[115]	High - Moderate attrition, lack of intervention and study design detail.
Huang, 2013[116]	Moderate - Intervention manualized and theory-based, likely good fidelity, but randomization and outcome assessment methods unclear.
Klodnicka, 2011[117]	Moderate - Manualized, fidelity adequate, information control; low attrition.
Marriott, 2000[118]	Moderate - Single-blind (assessors); very low attrition (only one dyad).
Mittelman, 2004[119]	Moderate - Blinding unclear; extremely high attrition after 4 month followup; ITT analysis.
Moniz-Cook, 2008[120]	High - Poor randomization method. Extremely high attrition. Blinding unclear. Not ITT analysis, but data were analyzed unless patients died or were institutionalized.
Nobili, 2004[121]	High - Blinding unclear; extremely high attrition; last observation carried forward used for missing data, poor method.
Ostwald, 1999[122]	Moderate - Blinding unclear; 19.7% attrition; not ITT analysis.

Study	Risk of Bias Assessment
Teri, 2000[123]	Moderate - Very high attrition at 6 months. Outcome assessors blinded, unclear about participants and caregivers. ITT analyses, though using last value carried forward is a biased method.
Ulstein, 2007[124]	Moderate - Staff and outcomes assessors not blinded. ITT analyses, though using last value carried forward is a based method. Moderate attrition at 12 months, but lower before that.
Weiner, 2002[125]	High - Secondary data analysis; very high attrition; possibly not eligible due to no valid control group (placebo pill or medications with behavior therapy only); most study information unclear; original study was Teri 2000.
Wright, 2001[126]	High - Difference in minority group representation and severity of dementia despite randomization; outcome assessors not blinded, same providers who delivered intervention; ITT analysis.

Descriptions of Community-Level Intervention Trials Rated High Risk of Bias

The Geriatric Home Hospitalization Service in Torino conducted a randomized controlled trial on 109 elderly, demented patients requiring admission for acute illnesses.[98] They compared home hospital care to a general medical ward care in reducing behavioral disturbances in elderly individuals with dementia.

Burgener et al. randomized 54 home-dwelling patients with dementia and their caregivers to educational and behavioral intervention or a control group.[101] There were no group differences in outcomes relevant to our review.

Burgio et al. developed and studied manual-guided, replicable interventions based on common needs and cultural preferences of White and African American family caregivers of community-dwelling individuals with dementia.[102] Caregivers (70 White and 48 African American) were randomized to either a skills training condition or a minimal support control condition. Both interventions were delivered. according to protocol and well received by caregivers. Both groups reported decreasing levels of problem behavior and appraisals of behavioral bother.

Gonyea et al. reported on Project CARE, a randomized controlled trial designed to test the effectiveness of a caregiver-based multicomponent behavioral intervention aimed to reduce caregiver burden/distress associated with behavioral symptoms and reduce behavioral symptom severity among individuals with Alzheimer's disease.[111] The behavioral intervention involved five weekly sessions designed to teach caregivers specific techniques for managing patient behavioral symptoms in the home environment. Eighty caregivers were assigned to either the behavioral intervention group or a psychoeducational control group. Caregivers in the intervention group displayed greater reductions in caregiver distress ($p=.005$). Global caregiver burden, however, did not decrease significantly for caregivers in either group ($p>.05$). Although it was not statistically significant, there was a trend toward greater reductions in care recipients' neuropsychiatric symptom severity in the intervention group ($p=.10$).

Hebert et al., in an unblinded design, randomized 41 caregivers to a support group or waitlist control.[115] Randomization and allocation methods were not reported. The support group consisted of eight weekly 2-hour sessions to discuss behavioral problems, develop stress management skills, and provide support. It was unclear if the intervention was manualized or theory-based. There was no effect of treatment on patients' behavior as measured by RMBPC at posttreatment.

Moniz-Cook et al. evaluated the effects of training community health nurses in a systematic psychosocial intervention to help family carers manage behavioural changes in individuals with dementia.[120] One hundred and thirteen family carers received the intervention or a 'usual practice'. Problem behaviour reduced with intervention with some but not all community health nurses. Carer management and mood improved with PSI support. In contrast, by 18 months, families supported by the intervention reported reduced coping resources, increased problem behaviour and their level of depression worsened.

Nobili et al. assessed the effects of a structured intervention on caregiver stress and the institutionalization rate among individuals with dementia and problem behaviors.[121] Caregivers were recruited through the Federazione Alzheimer Italia. Eligible caregiver-patient dyads were randomized to intervention or usual care. Mean problem behavior score in the 39 families completed the 12-month followup was significantly lower with intervention than control ($p <0.03$).

Weiner et al. randomized caregivers to behavior management techniques, trazodone, and haloperidol for the treatment of agitated behaviors in individuals with dementia.[125] This study reports on the 12-month outcomes, 4 month outcomes were reported in another publication. After 4 months, treatment was allowed with any agent. Nearly half of the individuals with dementia received additional psychotropics between 4 and 12 months. The relative risk of being prescribed any psychotropic drug was similar across groups.

Wright et al. evaluated a 1-year long course education and counseling program with 93 family caregivers of individuals with dementia.[126] Individuals with dementia received treatment for agitation in an inpatient setting and were subsequently discharged. Caregivers were randomly assigned to intevention (n = 68) or control (n = 25). There were no significant treatment effects for care recipient agitation, caregiver stress and no significant differences between groups in rates of institutionalization. Longitudinal data revealed several important trends. Agitation in individuals with dementia rose steadily with control but declined for intervention.

Table F2. Caregiver-level interventions: strength of evidence assessments

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
Knowledge-skills vs. no treatment Guerra, 2012 Ostwald, 1999	Patient General Behavior K=2; n=140	**NPI-Q severity score**[114] ASMD (CI): -0.10 (-0.66 to 0.48) **RMBPC, disruptive behavior subscale**[122] Baseline, mean (SD): 6.75 (5.55) vs. 5.32 (4.10) 3-months, mean (SD): 6.16 (5.26) vs. 4.87 (3.54) 5-months, mean (SD): 6.35 (5.20) vs. 6.68 (4.50)	Moderate	Direct	Imprecise	Consistent	Undetected	Insufficient
	Patient distress/QoL k=1; n=56	***DEMQOL***[114] ASMD (CI): 0.32 (-0.84 to 1.48)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Burden K=2; n=140bars	**ZBS**[114] **ASMD (CI): -1.02 (-0.53 to 0.51)** **ZBS**[122] Baseline, mean (SD): 56.18 (13.29) vs. 56.54 (15.97) 3-months, mean (SD): 56.82 (11.83) vs. 55.43 (15.91) 5-months, mean (SD): 54.13 (11.29) vs. 59.81 (15.23)	Moderate	Indirect	Imprecise	Consistent	Undetected	Insufficient
	Caregiver QoL k=1; n=88	**WHO-QoL-Bref, Psych**[114] **ASMD (CI): 0.10 (-0.47 to 0.68)**	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Behavior k=1; n=84	**RMBPC, caregiver response to disruptive behavior subscale**[122] Baseline, mean (SD): 6.76 (6.27) vs. 5.20 (5.10) 3-months, mean (SD): 5.00 (5.38) vs. 4.42 (4.23) 5-months, mean (SD): 4.08 (4.44) vs. 5.73 (4.42)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Knowledge-affect vs. attention control Chein, 2008[103]	Patient General Behavior K=1; n=88	**NPI**[103] Mean(SD) posttreatment (6 mo) 68.1 (10.2) vs. 84.5 (9.8)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
		Mean (SD) at 12 mo followup: 64.2(11.8) vs. 85.1(12.1)						
	Caregiver Burden K=1; n=88	**Family Caregiver Burden Inventory**[103] Mean (SD) posttreatment (6 mo) 56.7 (15.7) vs. 63.0 (15.1) Mean (SD) at 12 mo followup: 48.3 (13.9) vs. 65.9 (16.3)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver QoL k=1; n=88	**WHO**-QoL[103] Mean (SD) posttreatment (6 mo) 75.1 (16.8) vs. 69.8 (16.7) Mean (SD) at 12 mo followup: 81.4 (16.0) vs. 65.2(17.5)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Skills-Knowledge vs. waitlist, usual care, or info control De Rotrou, 2011 Klondnica, 2011 Gallagher-Thompson, 2010 Ulstein, 2007 Gitlin, 2003	Patient General Behavior K=5; n=657	**NPI**[104] Mean (SD) posttreatment (3 mo): 16.56 (17.20) vs. 16.29 (13.78) Mean (SD) at 6 mo followup: 15.8 (16.0) vs. 14.2 (13.0); p=0.57 **RMBPC (communication difficulties)** – Adjusted mean (SD) at 6 wk[117] 1.74 (0.55) vs. 1.70 (0.59); F=69.1 (p<0.001) RMBPC – Mean (SD) 4 months[105] 11.6 (5.2) vs. 11.0 (4.2) **RMPBC no. of disruption-related behaviors** AMD (CI)[107] -.07 (-46 to .33) **NPI-S, *4.5 month*** MD in MC (SD)[124] 0.8 (-3.61 to 5.28) **NPI-S, *12 month*** MD in MC (SD)[124] -2.2 (-2.65 to 7.06)	Moderate	Direct	Imprecise	Consistent	Undetected	Low

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
	Caregiver Burden K=2; n=337	**ZBI**[104] Mean (SD) posttreatment (3 mo): 22.18 (12.49) vs. 23.56 (16.99); Mean (SD) at 6 mo followup: 23.0 (14.6) vs. 26.5 (17.0); p=0.25 **RSS, *4.5 month*,** MD in MC (SD)[124] -0.1 (-2.50 to 2.32) **RSS, *12 month*** MD in MC (SD)[124] -1.2 (-4.23 to 1.79)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Behavior k=1; n=190	**Perceived change in ability to manage caregiving** AMD (CI)[107] .12 (-.05 to .30) **Mastery** AMD (CI)[107] .11 (-.05 to .27)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
Skills-Knowledge vs Haloperidol Teri, 2000	Patient Agitation/Aggression K=1; n=75	**Improved score on ADCS-CGIC,** RR (CI)[123] 1.0 [0.7 to 1.4] **CMAI,** MC (SD)[123] -3.37 (11.45) vs. -7.26 (22.51) **ABID Frequency** MC(SD)[123] -3.61 (9.88) vs. -6.74 (16.22)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior K=1; n=75	**BRSD,** MC (SD)[123] -3.56 (12.85) vs. -5.35 (22.41) **RMBPC Total Frequency**[123] -0.08 (0.54) vs. -0.17 (0.65)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	CG Distress K=1; n=75	**ABID Reaction,** MC (SD)[123] -2.41 (6.71) vs. -3.27 (9.10)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	CG Burden K=1; n=75	**SCB Subjective,** MC (SD)[123] -2.95 (7.29) vs. -1.88 (8.89) **SCB Objective,** MC (SD)[123] -1.23 (3.32) vs. -0.44 (3.22)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Skills-Knowledge vs placebo	Patient Agitation/Aggression	**Improved score on ADCS-CGIC,** RR(CI)[123] 1.0 [0.7 to 1.4]	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
Teri, 2000	K=1; n=75	**CMAI,** MC (SD)[123] -3.37 (11.45) vs. -5.94 (18.50) **ABID Frequency** MC (SD)[123] -3.61 (9.88) vs. -3.94 (15.44)						
	Patient General Behavior K=1; n=75	**BRSD,** MC (SD)[123] -3.56 (12.85) vs. -5.28 (24.36) **RMBPC Total Frequency**[123] -0.08 (0.54) vs. -0.10 (0.52)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	CG Distress K=1; n=75	**ABID Reaction,** MC (SD)[123] -2.41 (6.71) vs. -2.58 (10.28)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	CG Burden K=1; n=75	**SCB Subjective,** MC (SD)[123] -2.95 (7.29) vs. -2.58 (9.67) **SCB Objective,** MC (SD)[123] -1.23 (3.32) vs. -1.25 (4.02)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Skills-behavior vs. waitlist/information control 2[108,112, 118] Gonzalez, 2014 Gitlin, 2008 Marriot, 2000	Patient Agitation/Aggression K=1; n=56	**Specific Behaviors-agitated**[108] AMD (CI)[c]: .06 (.01 to .56) **Behavioral Occurrences**[108] AMD (CI)[c]: -.32 (-.55 to -.09) **Number of Behaviors**[108] AMD (CI)[c]: -.98 (-2.67 to .71)	Moderate	Direct	Imprecise	Unknown	Undetected	Insufficient
	Patient General Behavior K=2; n=144	**RMBPC**[112] Adjusted mean (SD) posttreatment: 1.31 (.64) vs. 1.34 (.64); p=0.83 Adjusted mean(SD) at 12 wk followup: 1.3 (0.6) vs. 1.6 (0.6); p=0.11 **MOUSE-PAD-Behavioral disturbance**[118] Baseline, mean (SD) 5.1 (2.1) vs. 5.1 (2.2) Post-treatment, mean (SD): 4.9 (0.2) vs. 5.6 (0.2) Followup, mean (SD): 5.3 (2.0) vs. vs. 5.2 (2.0)	Moderate	Direct	Imprecise	Inconsistent	Undetected	Insufficient
	Caregiver Behavior k=1; n=56	**Mastery**[108] AMD (CI)[c]: .34 (.08 to .60) **Confidence using activities**[108]	Moderate	Direct	Precise	Unknown	Undetected	Insufficient

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
		AMD (CI)[c]: 1.67 (.41 to 2.94) **Strategy use**[108] AMD (CI)[c]: 0.25; (0.04 to 0.46)						
	Caregiver Burden K=2; n=158	**ZBS Subjective - Burden** AMD (CI) [c108] .75 (-3.36 to 4.85) **Caregiver Role Strain (global strain subscale)** [112] Mean (SD) posttreatment: 1.94 (.83) vs. 1.84 (.83); p=0.43 Mean (SD) at 12 wk followup: 1.90 (0.88) vs. 1.85 (0.88); p=0.78	Moderate	Indirect	Precise	Consistent	Undetected	Low
	Caregiver Distress K=1; n=56	**ZBS Subjective - Behavior Upse**t, AMD (CI) [c 108] -.01 (-1.21 to 1.18)	Moderate	Indirect	Precise	Unknown	Undetected	Insufficient
Skills-behavior vs. attention control 5[106,109, 110,116, 118] Huang, 2013 Gitlin, 2010a Gitlin, 2010b Gerdner, 2002 Marriot, 2000	Patient Agitation/Aggression K=3; n=575	**CMAI – n(%) at 6 mo**[116] 9 (16.4) vs. 14 (26.4); p=0.20 **ABID**[109] AMD (CI)[a]: -.65 (-3.05 to 1.74) **MBPC frequency (hierarchical linear model): Coefficient (SE)** [106] Non-spouse experimental: REF Non-spouse comparison: 0.77 (0.36); p<.001 Spouse experimental: 0.18 (0.26) Spouse comparison: 0.18 (0.26)	Moderate	Direct	Imprecise	Consistent	Undetected	Low
	Patient General Behavior K=2; n=281	**Improvement in occurrence of targeted behavior**, 16 weeks[110] 67.5% vs. 45.8%; p=.002 **Target symptoms worsened/stayed the same**, 16 weeks[110]	Moderate	Direct	Imprecise	Inconsistent	Undetected	Insufficient

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
		18.4%/14% vs. 31.7%%/22.5%; p>.05 **MOUSE-PAD-Behavioral disturbance**[118] Baseline, mean (SD): 5.1 (2.1) vs. 5.4 (2.5) Post-treatment, mean (SD): 4.9 (0.2) vs. 5.0 (0.2) Followup, mean (SD): 5.3 (2.0) vs. 5.5 (2.4)						
	Patient Quality of Life K=1; n=209	***Patient QoL-AD***[109] AMD (CI)[a]: 0.10 (0.00 to 0.20)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Behavior K=2; n=448	**Confidence using activities** AMD (CI)[a] [109] 0.81 (0.30 to 1.32) **Confidence managing behavior,** 16 weeks AMD (CI)[b] [110] 0.33 (0.08 to 0.58) 24 weeks: 71.9% vs 29.1%; χ^2=41.1; p=.001	Moderate	Direct	Precise	Consistent	Undetected	Moderate
	Caregiver Burden K=2; n=448	***Caregiver Burden*** **ZBS**, 16 weeks[110] AMD (CI) [b]: -1.37 (-2.75 to 0.01) **ZBS**, 24 weeks[110] AMD (CI) [b]: -1.61 (-3.13 to -0.09)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Distress K=3; n=685	**MBPC reaction hierarchical linear model estimate**[106] -0.39; SE 0.18; p<.01 **Perceived change in well-being** Gitlin,[109] AMD (CI)[a]: 0.22 (0.08 to 0.36) **Perceived Change Index,** 16 weeks[110] AMD (CI) [b]: 0.45 (0.29 to 0.62)	Moderate	Indirect	Precise	Consistent	Undetected	Moderate

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
		Perceived Change Index, 24 weeks[110] AMD (CI) [b]: 0.29 (0.14 to 0.44)						
Skills-behavior vs. sham treatment K=2 [100,113] (125)	Patient Agitation/Aggression K=2; n=125	**BEHAVE-AD aggressivility/activity disturbance subscale**[100] – Adjusted mean, (SD) posttreatment: 5.4 (4.2) vs. 5.3 (3.4) vs. 6.9 (3.3); NS adjusted mean(SD) at 6 mo followup: 5.6(3.8) vs. 5.2(3.6) vs. 8.4(2.4); treatments 1 &2 significantly lower than control (p<0.05) **RAGE, postintervention mean(SD)**[113] 6.9 (3.6) vs. 8.6 (4.5)	Moderate	Direct	Imprecise	Consistent	Undetected	Insufficient
	Patient General Behavior K=2; n=125	**BEHAVE-AD total score**[100] Adjusted mean, (SD) posttreatment: 15.2 (10.1) vs. 13.5 (6.3) vs. 18.4 (10.8); only self-change sig lower than control (p<0.05) Adjusted mean(SD) at 6 mo followup: 17.5(10.4) vs. 14.8(10.5) vs. 23.1(11.4); treatment 2 score significantly lower than control (p<0.01) ***BEHAVE-AD, postintervention***[113] Mean (SD)=6.5 (2.8) vs. 7.8 (3.4)	Moderate	Direct	Imprecise	Consistent	Undetected	Insufficient
	Taking psychotropic drugs K=1; n=62	**Postintervention,** n/N (%)[113] 18 (52.9) vs. 17 (60.7) RR: 0.87 (0.56 to 1.35)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
	Caregiver Burden K=1; n=62	**ZBS, *postintervention***[113] Mean (SD)=36 (12.3) vs. 41.2 (12.0)	Moderate	Indirect	Imprecise	Unknown	Undetected	Insufficient
Skills-affect Belle, 2006	Patient General Behavior	**Problem behavior** Change (%) in net improvement (CI)[99]	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient

Setting **Intervention vs. Comparison**	**Outcome**	**Summary Statistics**	**Risk of Bias**	**Directness**	**Precision**	**Consistency**	**Reporting Bias**	**Strength of Evidence**
Mittleman, 2004	K=2; n=924	Hispanic-Latino: 36.3 (13.2 to 56.7) Caucasian: 13.6 (-6.3 to 35.3) African-American: -3.6 (-25.2 to 16.7) **MBPC-frequency log growth model**[119] Estimate for group (SE): 0.24 (1.23); p=.84 Estimate for group x time (SE): -0.03 (0.86); p=.96						
	NH Admission K=1; n=518	**NH Admission** Change (%) in net improvement (CI)[99] Hispanic-Latino: -4.2 (-16.9 to 25.7) Caucasian: 0.51 (0.21 to 1.22) African-American: 1.54 (0.45 to 5.31)	Moderate	Indirect	Imprecise	Inconsistent	Undetected	Insufficient
	Caregiver Burden K=1; n=518	**Burden** Change (%) in net improvement (CI)[99] Hispanic-Latino: -4.6 (-23.7 to 15.4) Caucasian: 0.51 (0.21 to 1.22) African-American: 23.1 (0.6 to 45.7)	Moderate	Direct	Imprecise	Inconsistent	Undetected	Insufficient
	Caregiver Distress K=1; n=406	MBPC-reaction: Estimate for group (SE): -2.90 (1.27) p=.02 Estimate for group x time (SE): -1.86; (0.89) p=.04	Moderate	Direct	Precise	Unknown	Undetected	Insufficient

ABID=Agitated Behavior in Dementia; BEHAVE-AD=Behavioral Pathology in Alzheimer's disease; BRSD=Behavior Rating Scale for Dementia; CMAI=Cohen-Mansfield Agitation Inventory; NPI=Neuropsychiatric Inventory; RMBPC=Revised Memory and Behavior Problem Checklist

Appendix G. References for Appendixes

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