



Effective Health Care Program

Nonpharmacologic Interventions for Agitation and Aggression in Dementia

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

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at www.effectivehealthcare.ahrq.gov/reports/final.cfm.

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
	Care delivery level	Psychological	Preventing incidents	Validation therapy, reality orientation, reminiscence therapy, support groups
		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
Community Dwelling	Patient level	Environmental	Preventing incidents	Walled-in areas, wandering areas, way-finding enhancement, reduced-stimulation areas, enhanced environments
		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 education	Preventing incidents; treating incidents	Specific curriculums to educate caregivers about dementia
	Caregiver level	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

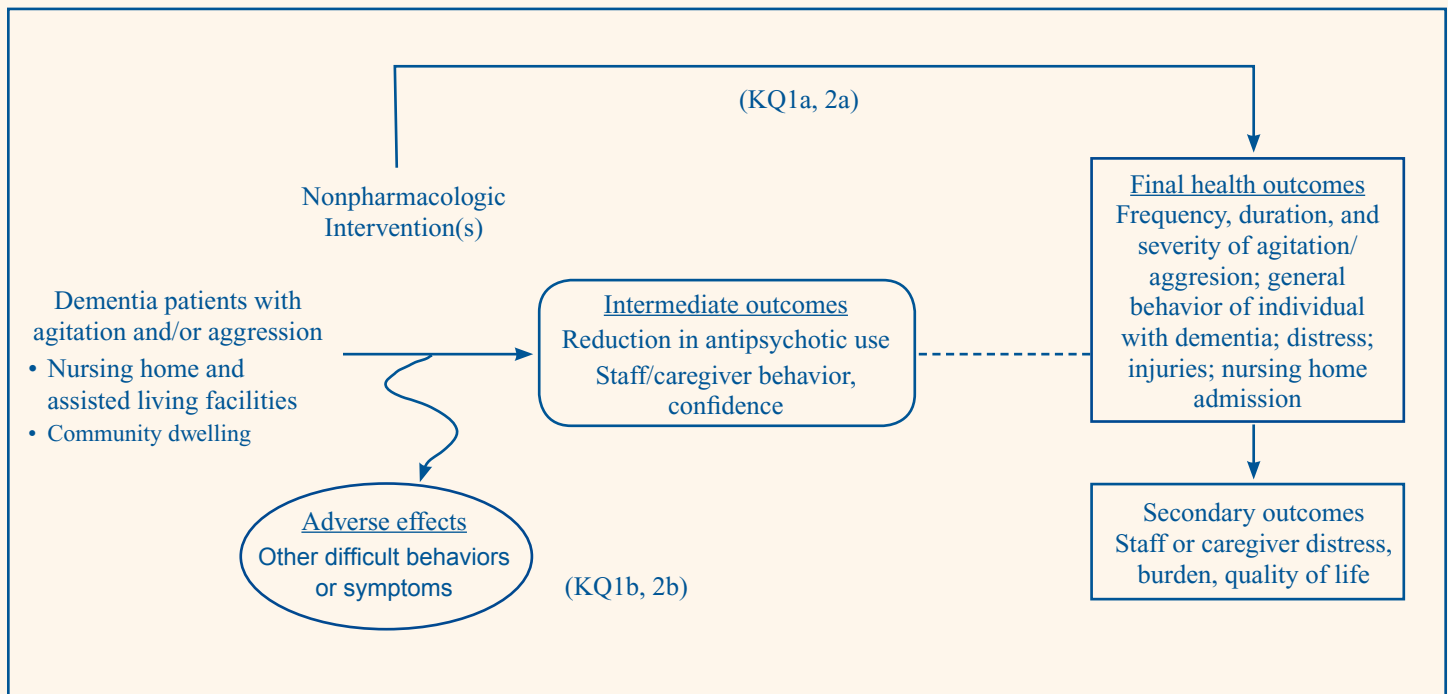
and assisted living settings?

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 R²⁴ 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 I² 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

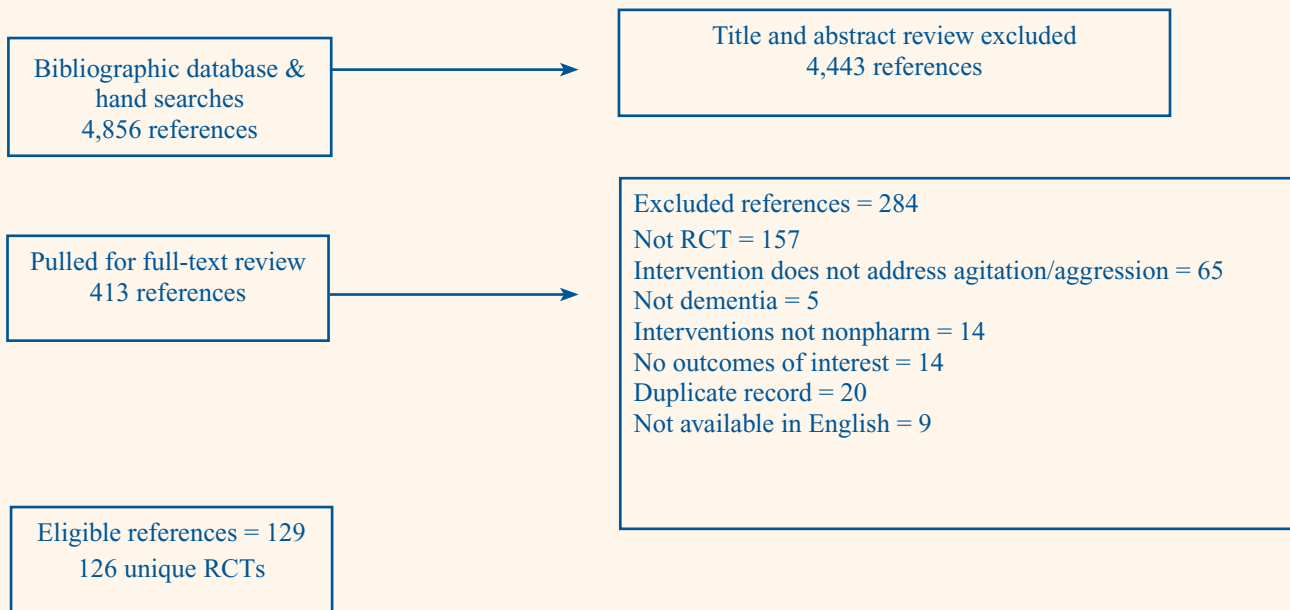
Applicability of trials was determined according to the PICOTS framework. Study characteristics affecting applicability included the population from which the trial participants were enrolled, diagnostic assessment processes, narrow eligibility criteria, and patient and intervention characteristics different 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 trial³² 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 lavender³⁶⁻³⁹ 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

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

Intervention-Comparison	Total Number of Trials (Number of Participants)	Strength of Evidence - Summary of Results
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
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; I² = 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; I² = 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; I² = 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) 2 (339) 1 (158)	Insufficient – no conclusions drawn (staff behavior) Insufficient – no conclusions drawn (staff distress) Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use)
Person-centered care vs. usual care	2 (505) 1 (159)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use) Insufficient – no conclusions drawn (staff distress)
Protocols to reduce neuroleptic use vs. usual care	3 (1,263) 1 (659)	Insufficient – no conclusions drawn (antipsychotic & psychotropic drug use) 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) 1 (180)	Insufficient – no conclusions drawn (injuries) 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
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)

Table G. Caregiver-level interventions: evidence summary (continued)

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)

Table G. Caregiver-level interventions: evidence summary (continued)

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
<p>General methodological issues</p>	<p>Agitation and aggression not consistently described, defined, or treated as separate behaviors</p>	<p>Consensus conference</p>	<p>Consensus among experts to arrive at standard definitions of specific behavioral symptoms</p>
	<p>Improvement and agreement needed on instruments to measure agitation/aggression</p>	<p>Consensus conference</p>	<p>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</p>
	<p>Few groups of studies with sufficient similarity in interventions, comparisons, and outcomes to allow appropriate data pooling</p>	<p>Consensus conference</p>	<p>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</p>
	<p>No established minimum important differences for commonly used instruments measuring agitation/aggression outcomes</p>	<p>Original research</p>	<p>Studies to determine thresholds for commonly used instruments that indicate clinically meaningful changes, which could be used in comparative effectiveness research</p>
	<p>Wide heterogeneity in interventions, comparisons, outcomes, and analysis techniques</p>	<p>Consensus conference</p>	<p>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</p>
	<p>Agitation/aggression not specifically studied; behaviors broadly addressed in many trials</p>	<p>RCTs</p>	<p>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</p>
	<p>Objectives of interventions not well specified</p>	<p>RCTs</p>	<p>Interventions designed to prevent or respond to agitation/aggression; trials designed according to objective</p>

Table H. Future research needs (continued)

<p>General methodological issues</p>	<p>Small underpowered studies</p>	<p>RCTs</p>	<p>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</p>
<p>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?</p>	<p>Study of populations in nursing home settings with a wide variety of agitation/aggression behaviors that might respond differently to specific treatments</p>	<p>RCTs</p>	<p>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</p>
<p>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?</p>	<p>Few trials studying particular environmental interventions</p> <p>Harms rarely reported; most interventions unlikely to have serious harms</p>	<p>RCTs</p>	<p>Trials that assess environmental changes</p> <p>Recording and reporting harms or lack thereof for each treatment group</p>
<p>KQ 2a: What is the comparative effectiveness of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?</p>	<p>Tailored interventions that did not demonstrate an effect on behaviors; few trials specifically targeting agitation/aggression</p> <p>Lack of clarity about whether benefits to caregivers of tailored education and training (improved confidence in managing behaviors) are maintained after the intervention ends</p>	<p>RCTs</p>	<p>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</p> <p>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</p>
<p>KQ 2b: What are the comparative harms of nonpharmacologic interventions in preventing and responding to agitation/aggression among community-dwelling individuals with dementia?</p>	<p>Harms rarely reported; most interventions unlikely to have serious harms</p>	<p>RCTs</p>	<p>Recording and reporting harms or lack thereof for each treatment group</p>

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.

References

1. American Psychiatric Association. Neurocognitive disorders. In: Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: American Psychiatric Association; 2013.
2. Trivedi D, Goodman C, Dickinson A, et al. A protocol for a systematic review of research on managing behavioural and psychological symptoms in dementia for community-dwelling older people: evidence mapping and syntheses. *Syst Rev*. 2013;2(1):1-9. PMID: 23985083.
3. Gitlin L, Marx K, Stanley I, et al. Assessing neuropsychiatric symptoms in people with dementia: a systematic review of measures. *Int Psychogeriatr*. 2014;26(11):1805-48. PMID: 25096416.
4. Desai AK, Schwartz L, Grossberg GT. Behavioral disturbance in dementia. *Curr Psychiatry Rep*. 2012;14(4):298-309. PMID: 22644311.
5. Black W, Almeida OP. A systematic review of the association between the Behavioral and Psychological Symptoms of Dementia and burden of care. *Int Psychogeriatr*. 2004 Sep;16(3):295-315. PMID: 15559754.
6. Ornstein K, Gaugler JE. The problem with “problem behaviors”: a systematic review of the association between individual patient behavioral and psychological symptoms and caregiver depression and burden within the dementia patient-caregiver dyad. *Int Psychogeriatr*. 2012 Oct;24(10):1536-52. PMID: 22612881.
7. Pinquart M, Sorensen S. Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci*. 2003 Mar;58(2):P112-28. PMID: 12646594.
8. Volicer L. Toward better terminology of behavioral symptoms of dementia. *J Am Med Dir Assoc*. 2012 Jan;13(1):3-4. PMID: 21450232.
9. Mitka M. CMS seeks to reduce antipsychotic use in nursing home residents with dementia. *JAMA*. 2012;308(2):119-21. PMID: 22782393.
10. Salzman C, Jeste DV, Meyer RE, et al. Elderly patients with dementia-related symptoms of severe agitation and aggression: consensus statement on treatment options, clinical trials methodology, and policy. *J Clin Psychiatry*. 2008 Jun;69(6):889-98. PMID: 18494535.
11. APA Work Group on Alzheimer’s Disease and other Dementias, Rabins PV, Blacker D, et al. American Psychiatric Association practice guideline for the treatment of patients with Alzheimer’s disease and other dementias. Second edition. *Am J Psychiatry*. 2007 Dec;164(12 Suppl):5-56. PMID: 18340692.
12. Lyketsos CG, Colenda CC, Beck C, et al. Position statement of the American Association for Geriatric Psychiatry regarding principles of care for patients with dementia resulting from Alzheimer disease. [Erratum appears in *Am J Geriatr Psychiatry*. 2006 Sep;14(9):808]. *Am J Geriatr Psychiatry*. 2006 Jul;14(7):561-72. PMID: 16816009.
13. Gill SS, Bronskill SE, Normand SL, et al. Antipsychotic drug use and mortality in older adults with dementia. [Summary for patients in *Ann Intern Med*. 2007 Jun 5;146(11):I52; PMID: 17548405]. *Ann Intern Med*. 2007 Jun 5;146(11):775-86. PMID: 17548409.
14. Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA*. 2005 Oct 19;294(15):1934-43. PMID: 16234500.
15. Schneider LS, Tariot PN, Dagerman KS, et al. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer’s disease. *N Engl J Med*. 2006 Oct 12;355(15):1525-38. PMID: 17035647.
16. Moniz Cook ED, Swift K, James I, et al. Functional analysis-based interventions for challenging behaviour in dementia. *Cochrane Database Syst Rev*. 2012;2:CD006929. PMID: 22336826.
17. Kales HC, Gitlin LN, Lyketsos CG, et al. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. *J Am Geriatr Soc*. 2014 Apr;62(4):762-9. PMID 24635665.
18. Cohen-Mansfield J. Nonpharmacologic treatment of behavioral disorders in dementia. *Curr Treat Options Neurol*. 2013 Dec;15(6):765-85. PMID: 24136714.
19. Bogner JA, Corrigan JD, Stange M, et al. Reliability of the Agitated Behavior Scale. *J Head Trauma Rehabil*. 1999;14(1):91-6. PMID: 9949251.
20. Cohen-Mansfield J. Conceptualization of agitation: results based on the Cohen-Mansfield Agitation Inventory and the Agitation Behavior Mapping Instrument. *Int Psychogeriatr*. 1996;8 Suppl 3:309-15; discussion 51-4. PMID: 9154580.
21. Rosen J, Burgio L, Kollar M, et al. A user friendly instrument for rating agitation in dementia patients. *Am J Geriatr Psychiatry*. 1994 Winter;2(1):52-9. PMID: 21629007.
22. Berkman ND, Lohr KN, Ansari M, et al. Grading the Strength of a Body of Evidence When Assessing Health Care Interventions-AHRQ and the Effective Health Care Program: An Update; 2012. In: *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. AHRQ Publication No. 10(14)-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality. January 2014. Chapters available at www.effectivehealthcare.ahrq.gov.

23. Viswanathan M, Ansari MT, Berkman ND, Chang S, Hartling L, McPheeters LM, Santaguida PL, Shamliyan T, Singh K, Tsertsvadze A, Treadwell JR. Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. Agency for Healthcare Research and Quality Methods Guide for Comparative Effectiveness Reviews. March 2012. AHRQ Publication No. 12-EHC047-EF. Available at: www.effectivehealthcare.ahrq.gov/
24. R Development Core Team. The R Project for Statistical Computing. R Foundation for Statistical Computing; 2008. www.R-project.org.
25. StataCorp. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP; 2013.
26. Fu R, Gartlehner G, Grant M, et al. Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. *J Clin Epidemiol*. 2011 Nov;64(11):1187-97. PMID: 21477993.
27. Berkman ND, Lohr KN, Morgan LC, et al. Interrater reliability of grading strength of evidence varies with the complexity of the evidence in systematic reviews. *J Clin Epidemiol*. 2013 Oct;66(10):1105-17.e1. PMID: 23993312.
28. Atkins D, Chang SM, Gartlehner G, et al. Assessing applicability when comparing medical interventions: AHRQ and the Effective Health Care Program. *J Clin Epidemiol*. 2011 Nov;64(11):1198-207. PMID: 21463926.
29. Sakamoto M, Ando H, Tsutou A. Comparing the effects of different individualized music interventions for elderly individuals with severe dementia. *Int Psychogeriatr*. 2013 May;25(5):775-84. PMID: 23298693.
30. Lin Y, Chu H, Yang CY, et al. Effectiveness of group music intervention against agitated behavior in elderly persons with dementia. *Int J Geriatr Psychiatry*. 2011 Jul;26(7):670-8. PMID: 20672256.
31. Raglio A, Bellelli G, Traficante D, et al. Efficacy of music therapy treatment based on cycles of sessions: a randomised controlled trial. *Aging Ment Health*. 2010 Nov;14(8):900-4. PMID: 21069596.
32. Remington R. Calming music and hand massage with agitated elderly. *Nurs Res*. 2002 Sep-Oct;51(5):317-23. PMID: 12352780.
33. Cooke ML, Moyle W, Shum DH, et al. A randomized controlled trial exploring the effect of music on agitated behaviours and anxiety in older people with dementia. *Aging Ment Health*. 2010 Nov;14(8):905-16. PMID: 20635236.
34. Vink AC, Zuidersma M, Boersma F, et al. The effect of music therapy compared with general recreational activities in reducing agitation in people with dementia: a randomised controlled trial. *Int J Geriatr Psychiatry*. 2013 Oct;28(10):1031-8. PMID: 23280604.
35. Ballard CG, O'Brien JT, Reichelt K, et al. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: the results of a double-blind, placebo-controlled trial with Melissa. *J Clin Psychiatry*. 2002;63(7):553-8. PMID: 12143909.
36. Fu CY, Moyle W, Cooke M. A randomised controlled trial of the use of aromatherapy and hand massage to reduce disruptive behaviour in people with dementia. *BMC Altern Med*. 2013;13:165. PMID: 23837414.
37. Fujii M, Hatakeyama R, Fukuoka Y, et al. Lavender aroma therapy for behavioral and psychological symptoms in dementia patients. *Geriatr Gerontol Int*. 2008 Jun;8(2):136-8. PMID: 18713168.
38. Lin PW, Chan WC, Ng BF, et al. Efficacy of aromatherapy (*Lavandula angustifolia*) as an intervention for agitated behaviours in Chinese older persons with dementia: a cross-over randomized trial. *Int J Geriatr Psychiatry*. 2007 May;22(5):405-10. PMID: 17342790.
39. Yang MH, Lin LC, Wu SC, et al. Comparison of the efficacy of aroma-acupressure and aromatherapy for the treatment of dementia-associated agitation. *BMC Altern Med*. 2015;15:93. PMID: 25880034.
40. Burns A, Perry E, Holmes C, et al. A double-blind placebo-controlled randomized trial of Melissa officinalis oil and donepezil for the treatment of agitation in Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2011;31(2):158-64. PMID: 21335973.
41. Ancoli-Israel S, Martin JL, Gehrman P, et al. Effect of light on agitation in institutionalized patients with severe Alzheimer disease. *Am J Geriatr Psychiatry*. 2003 Mar-Apr;11(2):194-203. PMID: 12611749.
42. Burns A, Allen H, Tomenson B, et al. Bright light therapy for agitation in dementia: a randomized controlled trial. *Int Psychogeriatr*. 2009 Aug;21(4):711-21. PMID: 19323872.
43. Dowling GA, Graf CL, Hubbard EM, et al. Light treatment for neuropsychiatric behaviors in Alzheimer's disease. *West J Nurs Res*. 2007 Dec;29(8):961-75. PMID: 17596638.
44. Lyketsos CG, Veiel LL, Baker A, et al. A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *Int J Geriatr Psychiatry*. 1999 Jul;14(7):520-5. PMID: 10440971.
45. Hawranik P, Johnston P, Deatrich J. Therapeutic touch and agitation in individuals with Alzheimer's disease. *West J Nurs Res*. 2008 Jun;30(4):417-34. PMID: 18272750.
46. Woods DL, Craven RF, Whitney J. The effect of therapeutic touch on behavioral symptoms of persons with dementia. *Altern Ther Health Med*. 2005 Jan-Feb;11(1):66-74. PMID: 15712768.
47. Rodriguez-Mansilla J, Gonzalez-Lopez-Arza MV, Varela-Donoso E, et al. Ear therapy and massage therapy in the elderly with dementia: a pilot study. *J Tradit Chin Med*. 2013 Aug;33(4):461-7. PMID: 24187866.
48. Moyle W, Cooke ML, Beattie E, et al. Foot massage versus quiet presence on agitation and mood in people with dementia: a randomised controlled trial. *Int J Nurs Stud*. 2014 Jun;51(6):856-64. PMID: 24216598.
49. Van Haitsma KS, Curyto K, Abbott KM, et al. A randomized controlled trial for an individualized positive psychosocial intervention for the affective and behavioral symptoms of dementia in nursing home residents. *J Gerontol B Psychol Sci Soc Sci*. 2015 Jan;70(1):35-45. PMID: 24304555.

50. Van der Ploeg ES, Eppingstall B, Camp CJ, et al. A randomized crossover trial to study the effect of personalized, one-to-one interaction using Montessori-based activities on agitation, affect, and engagement in nursing home residents with dementia. *Int Psychogeriatr*. 2013 Apr;25(4):565-75. PMID: 23237211.
51. Cohen-Mansfield J, Thein K, Marx MS, et al. Efficacy of nonpharmacologic interventions for agitation in advanced dementia: a randomized, placebo-controlled trial. *J Clin Psychiatry*. 2012 Sep;73(9):1255-61. PMID: 23059151.
52. Kovach CR, Taneli Y, Dohearty P, et al. Effect of the BACE intervention on agitation of people with dementia. *Gerontologist*. 2004 Dec;44(6):797-806. PMID: 15611216.
53. Kolanowski A, Litaker M, Buettner L, et al. A randomized clinical trial of theory-based activities for the behavioral symptoms of dementia in nursing home residents. *J Am Geriatr Soc*. 2011 Jun;59(6):1032-41. PMID: 21649633.
54. Kolanowski AM, Litaker M, Buettner L. Efficacy of theory-based activities for behavioral symptoms of dementia. *Nurs Res*. 2005 Jul-Aug;54(4):219-28. PMID: 16027564.
55. Agency for Healthcare Research and Quality, Effective Health Care Program. www.effectivehealthcare.ahrq.gov/.
56. Chenoweth L, King MT, Jeon YH, et al. Caring for Aged Dementia Care Resident Study (CADRES) of person-centred care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. [Erratum appears in *Lancet Neurol*. 2009 May;8(5):419]. *Lancet Neurol*. 2009 Apr;8(4):317-25. PMID: 19282246.
57. Rokstad AM, Rosvik J, Kirkevold O, et al. The effect of person-centred dementia care to prevent agitation and other neuropsychiatric symptoms and enhance quality of life in nursing home patients: a 10-month randomized controlled trial. *Dement Geriatr Cogn Disord*. 2013;36(5-6):340-53. PMID: 24022375.
58. Van de Ven G, Draskovic I, Adang EM, et al. Effects of dementia-care mapping on residents and staff of care homes: a pragmatic cluster-randomised controlled trial. *PLoS ONE*. 2013;8(7):e67325. PMID: 23844003.
59. Fossey J, Ballard C, Juszczak E, et al. Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. *BMJ*. 2006 Apr 1;332(7544):756-8A. PMID: 16543297.
60. Rapp MA, Mell T, Majic T, et al. Agitation in nursing home residents with dementia (VIDEANT trial): effects of a cluster-randomized, controlled, guideline implementation trial. *J Am Med Dir Assoc*. 2013 Sep;14(9):690-5. PMID: 23827658.
61. Zwijsen SA, Smalbrugge M, Eefsting JA, et al. Coming to grips with challenging behavior: a cluster randomized controlled trial on the effects of a multidisciplinary care program for challenging behavior in dementia. *J Am Med Dir Assoc*. 2014 Jul;15(7):531.e1-10. PMID: 24878214.
62. Finnema E, Droes RM, Ettema T, et al. The effect of integrated emotion-oriented care versus usual care on elderly persons with dementia in the nursing home and on nursing assistants: a randomized clinical trial. *Int J Geriatr Psychiatry*. 2005 Apr;20(4):330-43. PMID: 15799079.
63. Schrijnemaekers V, van Rossum E, Candel M, et al. Effects of emotion-oriented care on elderly people with cognitive impairment and behavioral problems. *Int J Geriatr Psychiatry*. 2002 Oct;17(10):926-37. PMID: 12325052.
64. Hattori H, Hattori C, Hokao C, et al. Controlled study on the cognitive and psychological effect of coloring and drawing in mild Alzheimer's disease patients. *Geriatr Gerontol Int*. 2011 Oct;11(4):431-7. PMID: 21518170.
65. Steinberg M, Leoutsakos J-MS, Podewils LJ, et al. Evaluation of home-based exercise program in the treatment of Alzheimer's disease: the Maximizing Independence in Dementia (MIND) Study. *Int J Geriatr Psychiatry*. 2009 Jul;24(7):680-5. PMID: 19089875.
66. Baker R, Bell S, Baker E, et al. A randomized controlled trial of the effects of multi-sensory stimulation (MSS) for people with dementia. *Br J Clin Psychol*. 2001 Mar;40:81-96. PMID: 11317951.
67. Fitzsimmons S, Buettner LL. Therapeutic recreation interventions for need-driven dementia-compromised behaviors in community-dwelling elders. *Am J Alzheimers Dis Other Dement*. 2002;17(6):367-81. PMID: 12501484.
68. Tibaldi V, Aimonino N, Ponzetto M, et al. A randomized controlled trial of a home hospital intervention for frail elderly demented patients: behavioral disturbances and caregiver's stress. *Arch Gerontol Geriatr Suppl*. 2004;(9):431-6. PMID: 15207444.
69. Czaja SJ, Gitlin LN, Schulz R, et al. Development of the risk appraisal measure: a brief screen to identify risk areas and guide interventions for dementia caregivers. *J Am Geriatr Soc*. 2009 Jun;57(6):1064-72. PMID: 19453305.
70. Guerra M, Ferri CP, Fonseca M, et al. Helping carers to care: the 10/66 dementia research group's randomized control trial of a caregiver intervention in Peru. *Rev Bras Psiquiatr*. 2011 Mar;33(1):47-54. PMID: 20602013.
71. Chien WT, Lee YM. A disease management program for families of persons in Hong Kong with dementia. *Psychiatr Serv*. 2008 Apr;59(4):433-6. PMID: 18378844.
72. Klodnicka Kouri K, Ducharme FC, Giroux F. A psycho-educational intervention focused on communication for caregivers of a family member in the early stage of Alzheimer's disease: results of an experimental study. *Dementia Int J Soc Res Pract*. 2011 Aug;10(3):435-53.
73. De Rotrou J, Cantegreil I, Fauconau V, et al. Do patients diagnosed with Alzheimer's disease benefit from a psycho-educational programme for family caregivers? A randomised controlled study. *Int J Geriatr Psychiatry*. 2011 Aug;26(8):833-42. PMID: 20922772.
74. Gallagher-Thompson D, Wang P-C, Liu W, et al. Effectiveness of a psychoeducational skill training DVD program to reduce stress in Chinese American dementia caregivers: results of a preliminary study. *Aging Ment Health*. 2010 Apr;14(3):263-73. PMID: 20425645.
75. Ulstein ID, Sandvik L, Wyller TB, et al. A one-year randomized controlled psychosocial intervention study among family carers of dementia patients--effects on patients and carers. *Dement Geriatr Cogn Disord*. 2007;24(6):469-75. PMID: 17986818.

76. Gitlin LN, Winter L, Corcoran M, et al. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. *Gerontologist*. 2003 Aug;43(4):532-46. PMID: 12937332.
77. Teri L, Logsdon RG, Peskind E, et al. Treatment of agitation in AD: a randomized, placebo-controlled clinical trial. [Erratum appears in *Neurology*. 2001 Feb 13;56(3):426]. *Neurology*. 2000 Nov 14;55(9):1271-8. PMID: 11087767.
78. Gonzalez EW, Polansky M, Lippa CF, et al. Enhancing resourcefulness to improve outcomes in family caregivers and persons with Alzheimer's disease: a pilot randomized trial. *Int J Alzheimer Dis*. 2014;2014:323478. Epub 2014 Sep 29. PMID: 25328754.
79. Huang H-L, Kuo L-M, Chen Y-S, et al. A home-based training program improves caregivers' skills and dementia patients' aggressive behaviors: a randomized controlled trial. *Am J Geriatr Psychiatry*. 2013 Nov;21(11):1060-70. PMID: 23933422.
80. Gitlin LN, Winter L, Dennis MP, et al. Targeting and managing behavioral symptoms in individuals with dementia: a randomized trial of a nonpharmacological intervention. *J Am Geriatr Soc*. 2010 Aug;58(8):1465-74. PMID: 20662955.
81. Gitlin LN, Winter L, Dennis MP, et al. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010 Sep 1;304(9):983-91. PMID: 20810376.
82. Gitlin LN, Winter L, Burke J, et al. Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a randomized pilot study. *Am J Geriatr Psychiatry*. 2008 Mar;16(3):229-39. PMID: 18310553.
83. Gerdner LA, Buckwalter KC, Reed D. Impact of a psychoeducational intervention on caregiver response to behavioral problems. *Nurs Res*. 2002 Nov-Dec;51(6):363-74. PMID: 12464756.
84. Bourgeois MS, Schulz R, Burgio LD, et al. Skills training for spouses of patients with Alzheimer's disease: outcomes of an intervention study. *J Clin Geropsychology*. 2002 Jan;8(1):53-73.
85. Gormley N, Lyons D, Howard R. Behavioural management of aggression in dementia: a randomized controlled trial. *Age Ageing*. 2001 Mar;30(2):141-5. PMID: 11395344.
86. Marriott A, Donaldson C, Tarrier N, et al. Effectiveness of cognitive-behavioural family intervention in reducing the burden of care in carers of patients with Alzheimer's disease. *Br J Psychiatry*. 2000 Jun;176:557-62. PMID: 10974962.
87. Belle SH, Burgio L, Burns R, et al. Enhancing the quality of life of dementia caregivers from different ethnic or racial groups: a randomized, controlled trial. [Summary for patients in *Ann Intern Med*. 2006 Nov 21;145(10):I39; PMID: 17116914]. *Ann Intern Med*. 2006 Nov 21;145(10):727-38. PMID: 17116917.
88. Mittelman MS, Roth DL, Haley WE, et al. Effects of a caregiver intervention on negative caregiver appraisals of behavior problems in patients with Alzheimer's disease: results of a randomized trial. *J Gerontol B Psychol Sci Soc Sci*. 2004 Jan;59(1):P27-34. PMID: 14722336.
89. Ostwald SK, Hepburn KW, Caron W, et al. Reducing caregiver burden: a randomized psychoeducational intervention for caregivers of persons with dementia. *Gerontologist*. 1999 Jun;39(3):299-309. PMID: 10396888.
90. Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of atypical antipsychotics for dementia: Meta-analysis of randomized, placebo-controlled trials. *American Journal of Geriatric Psychiatry*. 2006 Mar;14(3):191-210.
91. Brandt NJ, Pythtala J. Psychopharmacological medication use among older adults with dementia in nursing homes. *J Gerontol Nurs*. 2013 Apr;39(4):8-14. PMID: 23616986.
92. Hoffmann TC, Eerueti C, Glasziou PP. Poor description of non-pharmacological interventions: analysis of consecutive sample of randomised trials. *BMJ*. 2013;347. PMID: 24021722.
93. Ueda T, Suzukamo Y, Sato M, et al. Effects of music therapy on behavioral and psychological symptoms of dementia: a systematic review and meta-analysis. *Ageing Res Rev*. 2013 March;12(2):628-41. PMID: 23511664.
94. Livingston G, Kelly L, Lewis-Holmes E, et al. A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia. *Health Technol Assess*. 2014 Jun;18(39):1-226, v-vi. PMID: 24947468.
95. Brodaty H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. *Am J Psychiatry*. 2012;169(9):946-53. PMID: 22952073.

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