



Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: Nonpharmacologic Interventions for Agitation and Aggression in Dementia

Draft review available for public comment from May 12, 2015 to June 8, 2015.

Research Review Citation: Brasure M, Jutkowitz E, Fuchs E, Nelson VA, Kane RA, Shippee T, Fink HA, Sylvanus T, Ouellette J, Butler M, Kane RL. Nonpharmacologic Interventions for Agitation and Aggression in Dementia. Comparative Effectiveness Review No. 177. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2012-00016-I.) AHRQ Publication No.16-EHC019-EF. Rockville, MD: Agency for Healthcare Research and Quality; March 2016.
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Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Executive Summary	I thought executive summary was a bit too detailed and overlapping with full report.	The executive summary summarizes the results without discussion issues at the individual study level. Because this is a large report with significant heterogeneity, the details cannot be avoided. We have streamlined where we could, but would like important information available for those without time to read the full report.
Peer Reviewer #2	Executive Summary	The executive summary is quite long.	The executive summary summarizes the results without discussion issues at the individual study level. Because this is a large report with significant heterogeneity, the details cannot be avoided. We have streamlined where we could, but would like important information available for those without time to read the full report.
TEP #1	Executive Summary	Given that the key findings of the proposal is the level of evidence is 'weaker than needed for this critical topic' I would have expected the future research section to have been more extensive and explicit. The table on future research needs is perhaps the most important piece of the report but the suggestions in the table are not adequately reiterated in the text or executive summary. I think the ES should included a more strident call to organized studies in this space according to the schema adopted here, strengthen measurement in this area, and advocate for large scale multi-site trials of scalable interventions.	Our role is to identify gaps in the literature and we do not make recommendations about clinical caregiving. We have tried to enhance the research gaps section to explain why the evidence is weak and how that could be overcome with future research.
TEP #3	Executive Summary	The executive summary notes (p. ES, lines 28-29) that agitation/aggression challenges both informal and formal caregivers. In the full report (p.40, lines 27 and 28) the impact on staff in nursing homes and assisted living facilities is explicitly stated. This is an important point for all audiences. The authors should add the point explicitly in the executive summary.	We already make this point in the introduction section of the executive summary; "These behaviors challenge formal and informal caregivers and contribute to caregiver anger, resentment toward the patient, stress, and decreased psychological health."
TEP #5	Executive Summary	p. 9: How often do agitation and aggression specifically occur during the course of dementia?	Our background is based upon the most reliable data that we could find. We did not identify the specific data requested.
TEP #5	Executive Summary	p. 9: "Individuals with dementia typically reside in nursing homes or assisted-living facilities or at home in their community (community-dwelling)." Are there any other options for someone with dementia to live?	The community and institutional settings are the primary residences for dementia patients.
TEP #5	Executive Summary	p. 10: define patient-centered care here. Similarly, define "informal" family caregiver.	We have removed the term "patient-centered" from the sentence to help shorten the executive summary. In regards to informal family caregiver, the text now states: "The caregiver is typically an informal family caregiver (i.e., an unpaid family member who provides care to the person with dementia)"

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TEP #5	Executive Summary	p. 10: "Caregiver-level interventions to address agitation/aggression address the family caregiver approach to caregiving." What does that mean?	We have clarified the meaning of the sentence. The text now states: "Caregiver-level interventions to address agitation/aggression intervene on the caregiver patient relationship."
TEP #5	Executive Summary	p. 10: delete "direly." Is decisionmakers one word?	Thank you. We have deleted "direly." AHRQ considers decisionmakers to be one word.
TEP #5	Executive Summary	"While agitation/aggression is our primary outcome, we did extract 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." This is a key issue; most interventions of this type simply are not targeting aggression/agitation as a primary outcome, but behavioral issues more generally. This will likely influence any extracted/synthesized results, and require comment.	We address this in the discussion section: "Understanding that we may not find studies that reported agitation/aggression, we included studies that assessed behavioral symptoms with instruments measuring behavioral symptoms more generally. These instruments (NPI, MOSES) contain items across a wide variety of behavioral symptoms. Changes in overall scores on these instruments are not straightforward or directly related to agitation/aggression."
TEP #5	Executive Summary	"We searched for but did not find established minimum important differences for key outcomes measurement instruments in the literature." Does the NPI-Q have a clinical threshold?	This was reported in Table 2 of the full report.
TEP #5	Executive Summary	-A stronger rationale is needed for what is a fairly limited focus on agitation and aggression. Why only these two behaviors? Are they necessarily more costly or burdensome than other types of behavior problems?	<p>We believe the executive summary makes a strong case for the focus on agitation and aggression. We have revised the introduction of the main text to correspond with our rationale for focusing on agitation and aggression. For example the introduction to the main text now states:</p> <p>"Agitation and aggression are costly to manage and are associated with institutionalization among community-dwelling patients, social isolation, and other negative outcomes.⁸"</p> <p>In addition, the topic of the systematic review was nominated and vetted through a topic refinement period. During this vetting the key questions and protocol went through refinement. The end result of the topic refinement was the key questions used to address this review.</p>

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Anonymous Public Reviewer #1	Executive Summary	Page: ES-1 The sentence that "Agitation/aggression in individuals with dementia is associated with the use of antipsychotics (and resulting side effects)" could be read as implying that antipsychotics are causing agitation/aggression. While this is certainly possible, more commonly antipsychotics are begun with an aim to treating agitation/aggression. The parenthetical comment "(and resulting side effects)" is presumably a negative outcome of antipsychotic use that is being highlighted but this could be made more explicit. (e.g., In an effort to reduce agitation/aggression, individuals with dementia may be treated with antipsychotic medications and can experience side effects from such treatment.) Alternatively, it may be better to delete the concept of antipsychotics here since it is discussed in detail in the paragraphs below.	The revised text now states: "Agitation/aggression in individuals with dementia is associated with institutionalization among community-dwelling patients, social isolation, and other negative outcomes." ⁸
Anonymous Public Reviewer #1	Executive Summary	Page: ES-1, middle of paragraph 4 It may be preferable to change the phrase "high risk" to different wording (e.g., "significant risk...", "increased risk for serious events..."). The absolute number and absolute percent for these events is still fairly low although the relative increase in risk is clearly significant. "High risk" does not seem to give a full picture of the data, particularly if taken outside the context of a review of the medication related evidence.	The revised text now states: "Antipsychotic medications have limited efficacy and significantly increase the risk of stroke and mortality"
Anonymous Public Reviewer #1	Executive Summary	Page: ES-1, middle of paragraph 4 The sentence "These treatments are also associated with reduced quality of life..." seems like an oversimplification. Although some individuals may experience sedation, extrapyramidal effects and other adverse effects that reduce their quality of life as a result of antipsychotic treatment, this is not invariably the case. For most individuals, there is a reduced quality of life due to dementia which is further worsened by the associated behavioral/psychological symptoms. Consequently the same factors that lead to treatment with antipsychotics are also likely to be causing the reduced quality of life. It would be more accurate to say that "For some individuals, side effects of antipsychotic medications can contribute to a reduced quality of life ..."	We made the suggested change: "For some individuals with dementia, side effects of antipsychotic medications can contribute to a reduced quality of life."

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Anonymous Public Reviewer #1	Executive Summary	Page: ES-23 Paragraph 4 Some of the sentences in this paragraph would benefit from rewording to avoid painting a globally negative picture of nursing home staff. For example, the statements that staff are not eager to take on new tasks and that training tends to be perfunctory and brief with sparse oversight seems overly negative. It also seems to ignore the many "system" factors that are at work such as low reimbursements, low pay for staff, low levels of staffing required for adherence to state/federal regs, and societal stigmas about older adults and nursing facilities.	Reworded paragraph, revised text now reads: "Nursing home staff is notoriously overworked and taking on new tasks is challenging, especially those that require radical alterations in behavior and routines."
Anonymous Public Reviewer #1	Executive Summary	Page: ES-23 Paragraph 4 The statement that begins "The more complex and judgmental the intervention...." may benefit from re-wording. I think it is trying to point out that some interventions require application of clinical judgment but that is not clear from the current phrasing.	The text now states: "The more interventions require clinical judgment, the more difficult it is to implement, especially within nursing home hierarchies."
Anonymous Public Reviewer #1	Executive Summary	Page: ES-24 2 nd full paragraph I'm not sure what is meant by "a clearer map".	The text now states: "A clearer taxonomy of interventions and more precise terms are needed to outline the variations in the problem and the links between specific interventions and problem elements."
Anonymous Public Reviewer #1	Executive Summary	Page: ES-24 2 nd full paragraph The statement that begins "Simultaneous treatments..." would be better phrased as "Simultaneous treatments such as psychoactive medications must be taken into consideration." Also, since this is such a crucial point, it may be worthy of emphasis in the bullet points and abstract.	Suggested wording does not convey the same intent as current language. Our intent was in describing limitations common in available literature. No changes made.

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<p>Anonymous Public Reviewer #1</p>	<p>Executive Summary</p>	<p>Page: ES-25 2nd paragraph The need to use consistent and validated instruments is also an important point to emphasize (e.g., in bullet points, abstract) given the fact that antipsychotic treatments have limited benefit and notable harms and that other interventions (e.g., antidepressants, cholinesterase inhibitors) also have minimal effect and/or insufficient evidence. If well-standardized and validated instruments already exist, it would be helpful to list examples.</p>	<p>Revised text to emphasize complexity in selecting instruments: “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 (ABID, BARS, CMAI, DBRS, OASS, PAS, SOAPD) and four specifically measuring aggression (ABS, OAS, RAGE, and RAS).{Gitlin, 2014} Specific components of these instruments suggests a cloudy distinction between the behaviors in the identified instruments. For instance, the ABID, the CMAI, and the DBRS are classified as instruments measuring agitation when individual components ask about physical and verbal aggression; thereby treating aggression as a component of agitation. Psychometric properties of these instruments suggested that reliability (one or more types) and validity (one or more types) had been established for most instrument, but was 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 (BARS, CMAI, OASS, SOAPD).{Gitlin, 2014} As far as possible, future research should separate the intervention effects on these two behaviors. 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 comingle them making separation impossible at the review stage. A few studies attempt to analyze results using individual components of select 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.</p>

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Anonymous Public Reviewer #1	Executive Summary	Page: ES-25 last paragraph Despite the gaps in the evidence, formal and informal care-givers are left with a need to do something in the context of a patient with severe/chronic and/or dangerous agitation/aggression. In an ideal world, it is preferable to prove the effectiveness of interventions before they are implemented, but with limits on research funding and problems with the existing evidence base, this may not always be feasible.	Current recommendations suggest that nonpharmacologic interventions be first considered.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27 Future research needs table For both benefits and harms of treatments, there is a significant need for true effectiveness studies (rather than efficacy studies with multiple exclusion criteria). When clinical trials exclude individuals (or caregivers) who can not complete needed assessments due to the urgency of the situation or when they exclude subjects due to other common clinical factors, it becomes hard to use existing evidence to balance the benefits and harms of interventions.	Most trials, especially those in nursing homes, did not exclude patients with common medical conditions.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27 : In the context of medications and agitation/aggression/psychosis in dementia, an unanswered question is the way in which a pre-existing serious mental illness affects treatment risks/benefits. In developing practice guidelines for the treatment of individuals with dementia, it would be helpful to know how response rates to non-pharmacological therapies differ between individuals with serious mental illness (who would ordinarily have been treated chronically with antipsychotics) as compared to individuals with other psychiatric diagnoses (e.g, non-psychotic depression, anxiety) vs. dementia without psychiatric co-morbidity. It would also be important to know more about the use of antipsychotics and other medications in the patient subgroups being treated in the trials of non-pharmacological therapies. This is noted in the text but is worth emphasizing in the table as well.	The suggested comparison is beyond the scope of this report.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: Many studies of non-pharmacological therapies seem to be initiated cross-sectionally among individuals who have specific behavioral symptoms when the study is begun. In contrast, when making clinical decisions, one is usually attempting to address a situation in which a patient has a new onset of agitation. The clinical issue is whether one should start with a non-pharmacological or pharmacological treatment based on factors including efficacy, urgency and symptom severity. The available studies are not typically designed to address these important clinical questions.	Our review included trials testing interventions for behavioral symptoms. Many, but not all, enrolled individuals with dementia and behavioral symptoms.

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Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In terms of the statement about the importance of funding for RCTs, an important question is what funding mechanisms are even available to finance such studies. Obviously, drug companies are unlikely to fund trials on nonpharmacological therapies and NIMH has been fairly clear in stating that they are not planning to fund traditional clinical trials. Instead, they are investing in studies of innovative therapies with underlying mechanistic "targets". Since agitation is multi-faceted and without a clearcut etiology in patients with dementia, studies of non-pharmacological interventions will be hard to do.	We agree; funding for trials will likely need to come from government or other non-profit organizations.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In terms of assisting researchers in selecting the appropriate instruments to measure agitation/aggression, was the impression of the systematic review authors that available instruments are sufficient or does a better instrument need to be developed? If so, it may be worth stating this specifically. (This was also mentioned above). If such a scale does not already exist, it would be useful to develop an instrument that is usable both for RCTs and (perhaps in a reliable/valid short version) for clinical practice. This would also allow research results to be integrated into practice more readily. Also, the effects (or lack of effects) of interventions in clinical settings could be assessed.	This is beyond the scope of our review; many instruments are available. We have revised the text to provide information about selecting instruments in future research.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In terms of the comment that it would be beneficial to conduct studies to determine thresholds for clinically meaningful changes with commonly used instruments that indicate, it would also be helpful to identify thresholds on rating scales for instituting interventions and/or shifting to different treatments (if clinical response is insufficient).	This is beyond the scope of our review; identification of a minimal important difference to assist interpretation of research results is very different than patients and providers determining the balance of benefits and harms are appropriate.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: RCTs may not be the most appropriate study design for identifying homogenous subsets of individuals based upon the characteristics of their behavior, demographics, comorbidities, etc. RCTs would ultimately be needed to test whether there was a differential treatment response among subgroups but factor analysis, latent class analysis, support vector machine classifiers or other approaches would likely be needed to actually identify the subgroups first. A related element is the need to stratify treatment effects by symptom severity. This is done in some studies but is still rather infrequent. In part this is due to small sample sizes but if results were reported in a stratified fashion, they may be more amenable to meta-analysis.	We agree, trials will provide more useful information when focused on specific symptoms.

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Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In terms of the statement (which is repeated twice in the table) that "Patients with similar symptoms could provide the population for intervention trials", this might be more clear if stated as follows (or something similar): Homogenous subgroups of patients (identified through statistical approaches to symptom classification) could be studied in intervention trials to determine whether subgroups differed in their response to treatment.	This is listed twice in the table because it is relevant to two key questions. We feel that 'similar symptoms' is sufficiently clear; no changes made.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: Another problem with the literature (discussed further on p. 1) is that "behavioral or psychological symptoms" are often lumped together and include an extremely broad set of symptoms. It is important for the response of specific signs/symptoms to a given treatment to be reported in clinical trials	We have emphasized this point in the discussion.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In terms of the comment about reporting harms by group (which is repeated twice in the table), it might be more clear to say "for each treatment group."	Made suggested edit.
Anonymous Public Reviewer #1	Executive Summary	Page: ES-26 to ES-27: In row KQ1a, where the text reads "often likely", either or both of these words may be able to be deleted.	The text now states: "Study populations in nursing home settings often had a wide variety of agitation/aggression behaviors that might respond differently to specific treatments."
Eilon Caspi PhD,	Executive Summary	The term nonpharmacological interventions belongs to the old culture of care for persons living with dementia and should be replaced with a term such as "Psychosocial Interventions." See experts' recommendation in the White Paper you cite (#3 in list of references) from the National Dementia Initiative: Dementia Care: The Quality Chasm (2013). It is ironic and very disturbing that we still use biomedical terms to describe person-directed psychosocial approaches.	We selected nonpharmacologic because it covered a broader set of interventions than 'behavioral' or 'psychosocial'; Psychosocial interventions does not adequately describe the environmental or care delivery interventions that were included in this report.
Eilon Caspi PhD	Executive Summary	Re: "Up to 90% of individuals with dementia exhibit behavioral or psychological symptoms at some point, usually in advanced stages of the disease." => This is a very problematic and inaccurate statement. Many people with dementia do not experience significant behavioral expressions when provided with adequate and timely person-directed care in a "culturally transformed" care environments (at home and in LTC settings). Large variations in "agitation" levels (0%-38%) were found in previous research across special care units for people with dementia (See study by Sloane et al. 1998). Engagement in meaningful activities and staff approaches accounted for most of the behaviors.	We have revised the text to read "Many individuals with dementia exhibit neuropsychiatric symptoms at some point, usually in advanced disease stages." ² We understand your concern about labeling behavioral expression or reactive behaviors as symptoms. However we decided to be consistent with the vast majority of the literature. Many of the treatments are considered therapies and reimbursed for by health insurance. In these cases, it may be appropriate to treat analyze them with a medical model.

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Ellon Caspi PhD	Executive Summary	<p>The term “behavioral and psychological symptoms” in dementia (BPSD) and “behavior symptoms: should be replaced with person-directed terms such as Behavioral Expressions, Expressive Behaviors, Reactive Behaviors, Responsive Behaviors.</p> <p>See my letter to the editor of JAMDA on this issue:</p> <p>Caspi, E. (2013). Time for change: Persons with dementia and “behavioral expressions,” not “behavior symptoms.” [Letter to the Editor]. Journal of the American Medical Directors Association, 14(10), 768-769.</p> <p>See also Dr. Allen Power’s piece Medicalization of Feelings: BPSD or BPSOD?</p> <p>http://changingaging.org/blog/medicalization-of-feelings-bpsd-or-bpsod/</p>	<p>We understand your concern about labeling behavioral expression or reactive behaviors as symptoms. However we decided to be consistent with the vast majority of the literature. Many of the treatments are considered therapies and reimbursed for by health insurance. In these cases, it may be appropriate to treat analyze them with a medical model.</p>
Ellon Caspi PhD	Executive Summary	<p>The term “Agitation” which is used extensively in the literature should be replaced as it is too vague. It doesn’t tell us what the person with dementia actually experiences. While as you note it consist of a various forms of behavioral expressions (i.e. Cohen-Mansfield’s long line of extremely informative line of research studies), using this term inadvertently puts a label on the person. Once labeled, care partners are less likely to seek to identify the underlying unmet human need that often underlie and leads to these behaviors</p>	<p>Thank you for your comment. We have decided to continue using the term agitation. While it is vague, our review is a review of the existing literature and our terminology should be consistent with that literature, current guidelines, and the instruments that aim to measure these behaviors.</p>
Ellon Caspi PhD	Executive Summary	<p>Depression is not a “symptom” of dementia. It is a natural human reaction to dementia, which is a terminal illness (exacerbated by lack of awareness to what can be done to preserve the person’s hope, sense of purpose and meaning in life, despite the disabilities caused by the disease).</p>	<p>We have rephrased the text to read “Many individuals with dementia exhibit neuropsychiatric symptoms at some point, usually in advanced disease stages.² While there is a wide range of neuropsychiatric symptoms, they tend to cluster into five domains (depression, agitation, aggression, apathy, and psychosis).”{Gitlin, 2014}</p>
Ellon Caspi PhD	Executive Summary	<p>The term “wandering” should not be used. It is labeling. When you look closely (as I did in my 10-month direct observation study in 2 dementia units) what you see is that the person is either bored, seeks to be with people she/he trusts, to feel secure, to feel that she/he is doing something useful and purposeful. The person may experience pain but she/he may not be able to express it verbally. The person may simply need to use the bathroom or be outside to decompress and enjoy the outdoors but he is unable to reach these destinations due to visuospatial disorientation combined with non dementia-friendly physical environments.</p>	<p>We have removed the term “wandering” when appropriate.</p>

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Ellon Caspi PhD	Executive Summary	<p>Re: "Individuals with dementia typically reside in nursing homes or assisted living facilities or at home in their community." => About 80% of people with dementia live in the community. The rest live in LTC residences. Studies at home/in the community are sorely needed!</p>	We mentioned this in our research gaps section.
Ellon Caspi PhD	Executive Summary	<p>Please consider avoiding using the term "patient." This term belongs to the old culture of dementia care. See groundbreaking book by the late Prof. Tom Kitwood: Dementia Reconsidered: The Person Comes First (1997).</p> <p>We need to move away from biomedical terms to person-directed care terms. Suggestions include: "People living with dementia"; clients; residents; etc.</p>	We use the term 'person with dementia'.
Ellon Caspi PhD	Executive Summary	<p>Re: "Person-centered." Please consider using the term: "Person-directed care." As explained by Dr. Allen Power, author of the two excellent books Dementia Beyond Drugs and Dementia Beyond Disease, in person-centered care we assume what's good for the person. In person-directed care, we seek the input directly from the person with dementia (through their verbal and non-verbal expressions and, in the later stages of dementia through their close care partners, either family members and care staff members).</p>	We use the term "person-centered" as this is what is used by the studies included in our review.
Ellon Caspi PhD	Executive Summary	<p>Re: The term "Caregiver." Please consider using the term "Care Partner." The term "Caregiver" implies a unidirectional interaction, relationship, and care. It suggests that the person with dementia is a passive recipient of care without any ability to contribute to the people around her. In reality, many persons with dementia have various remaining abilities and have a lot to give to those who care for them well into the disease progression. The term "Care Partner" reflects a more reciprocal relationship. It reflects a true collaboration and partnership with the person with dementia. The first time I heard this wonderful term was in 2003 in Joanne Koenig Coste's excellent book Learning to Speak Alzheimer's.</p> <p>I know several people with dementia who are personally offended when they hear the term "caregiver."</p>	The terms used in this report reflect those used by researchers, regulatory bodies, and by policy makers. As such we have opted to keep the term caregiver.

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Ellon Caspi PhD	Executive Summary	<p>Section on instruments. Prof. Jeanne Teresi and her colleagues recently developed and evaluated the 1st instrument to measure resident-to-resident altercations:</p> <p>Teresi, J.A., Ocepek-Welikson, K., Ramirez, M., Eimicke, J.P. Silver, S., Van Haitsma, K., Lachs, M.S., & Pillemer, K. (2013b). Development of an instrument to measure staff-reported resident-to-resident elder mistreatment (R-REM) using item response theory and other latent variable models. <i>The Gerontologist</i>, [Advance Access published February 28, 2013]</p> <p>It is very important to recognize the prevalent, concerning, but under-recognized public health problem of resident-to-resident aggressive behavioral expressions in dementia in LTC residences.</p> <p>One of the reasons that these behaviors were basically ignored in research until the groundbreaking study by Shinoda-Tagawa et al. (2004) has to do with the fact that the MDS 3.0 (Behavior E. Section) does not enable to identify the target of aggressive behaviors. See my letter to the editor of JAMDA:</p> <p>Caspi, E. (2013). M.D.S. 3.0 – A giant step forward but what about items on resident-to-resident aggression? [Letter to the Editor]. <i>Journal of the American Medical Directors Association</i>, 14(8), 624-625.</p> <p>Shinoda-Tagawa, T., Leonard, R., Pontikas, J., McDonough, J.E., Allen, D., & Dreyer, P.I. (2004). Resident-to-resident violent incidents in nursing homes. <i>Journal of the American Medical Association</i>, 291(5), 591-598.</p>	Thank you for the information. We did not identify any trials using this instrument.
Ellon Caspi PhD	Executive Summary	<p>Prof. Jeanne Teresi and colleagues also developed and evaluated the first staff training program on resident-to-resident “aggression.” The intervention demonstrated ~5-fold increase in the number of episodes of resident-to-resident “aggression” recognized by staff (compared to prior to the training).</p> <p>Teresi, J.A., Ramirez, M., Ellis, J., Silver, S., Boratgis, G., Kong, J., Eimicke, J.P., Pillemer, K., & Lachs, M. (2013a). A staff intervention targeting resident-to-resident elder mistreatment (R-REM) in long-term care increased staff knowledge, recognition, and reporting: Results from a cluster randomized trial. <i>International Journal of Nursing Studies</i>, 50, 644-656</p>	This trial does not meet eligibility criteria because it does not specifically address persons with dementia or report their behavioral outcomes.

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Ellon Caspi PhD	Executive Summary	<p>One major limitation in most instruments for measuring behaviors in persons with dementia has to do with the fact that they are not designed to capture the circumstances, sequence of events, and situational triggers leading to these behaviors. This, when we know that in the majority of behavioral expressions in this population it is possible to identify unmet needs and negative contributing factors in the social and physical environment. The result of this omission is that the behavioral expressions are decontextualized, leading us to label the person as the source of these expressions of unmet needs. We need to develop instruments that capture the situational circumstances leading to and causing the behaviors.</p> <p>Prof. Cohen Mansfield wrote, “the most important principle in treating the aggressive person is the effort to understand the meaning of the sequence that led to the aggressive behavior.”</p> <p>Direct observation is the gold standard in research on behavioral expressions in dementia. However, a major limitation of observational schedules is the fact that significant number of them use time-sampling approaches for data collection. These “rigorous” approaches prevent us from capturing the naturally occurring sequence of events leading and causing these behaviors. Findings from studies using these approaches should be interpreted with this fact in mind and a shift towards clinically relevant observational schedules should be encouraged.</p> <p>In his book <i>The Stream of Behavior</i> Barker (1963:19) explains, “Methods that divide the behavior continuum into arbitrary time intervals dismantle the behavior stream. The destructive effect of these methods is automatic when they involve bits of behavior stream that are shorter than the units of the behavior phenomenon with which one is concerned.”</p>	<p>An understanding of causes and contexts of behaviors is important, especially when designing interventions within this theoretical framework; many studies analyzed the context as part of their initial assessment of the persons with dementia. These were often used to design interventions. We used the reported results with these instruments; it is not clear how additional components assessing the context of the behavior would change our interpretation of the difference between treatment groups in an RCT.</p>
Ellon Caspi PhD	Executive Summary	<p>As strongly advocated by Dr. Allen Power in his book <i>Dementia Beyond Disease</i>, we need to put much more emphasis on studying and measuring positive aspects of living with dementia and outcomes (such as psychological well-being). If Dr. Power’s ideas (as described in his book) were systematically implemented, the majority of behavioral expressions in dementia would discontinue and the need for psychotropic meds would be dramatically reduced (beyond current successful efforts to reduce the use of this meds nationwide).</p>	<p>Positive aspects of living with dementia was not one of our outcomes; we did include outcomes such as quality of life and measures of distress. These were not often reported in the available literature.</p>

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Commentator & Affiliation	Section	Comment	Response
Ellon Caspi PhD	Executive Summary	<p>Re: “Environmental” interventions. See excellent study/article by Dr. John Zeisel et al. on the effects of various aspects of the physical environment on behavioral expressions in LTC residents with dementia.</p> <p>Zeisel J, Silverstein NM, Hyde J, Levkoff S, Lawton MP, Holmes W. Environmental correlates to behavioral health outcomes in Alzheimer’s special care units. <i>The Gerontologist</i>. 2003;43(5):697-711.</p> <p>Also, it is important to consult with national experts such as Steve Orfield (Orfield Labs, Minneapolis) about high-quality measurement methods and effects of the physical environment on older adults in general and those with dementia in particular.</p> <p>Email: steve@orfieldlabs.com</p>	<p>We identified few trials that studied environmental interventions. The study mentioned is an observational study correlating environmental characteristics with a broad range of outcomes measures. If well-done, these types of studies are useful for generating hypothesis that should be tested with a more rigorous study design.</p>
Ellon Caspi PhD	Executive Summary	<p>Page ES-5: “Dementia patients.” Please refrain from using this biomedical term. A term recommended by experts in the field including by several people with dementia is: “Persons living with dementia.” The focus here is first on the whole person and only then on her/his dementia.</p>	<p>We have replaced dementia patients with ‘persons with dementia’.</p>
Ellon Caspi PhD	Executive Summary	<p>Page ES-12: “Evidence was insufficient to conclude whether music interventions reduce agitation/aggression immediately after participation.”</p> <p>=> This is a classic example of why RCTs should not be the standard for capturing highly effective interventions such as music therapy on people with dementia. Every person who works in a LTC residence with a good music therapy program knows that music therapy (delivered by a qualified and skilled music therapist) substantially reduces various forms of behavioral expressions in this population (including “aggressive” behaviors). It is about time to consider using inclusion criteria for this and other reviews that are not determined by biomedical parameters. See below examples of studies on the effects of music-based interventions.</p> <p>One only needs to either visit high quality LTC settings or watch the film <i>Alive Inside</i> to appreciate the highly therapeutic value of music therapy and music-based activities for this population. It is very concerning that this conclusion is made as it creates the misleading impression that music therapy is ineffective.</p>	<p>Observational studies have significant risk of bias issues (i.e., selection bias) that often explain the study results. This is especially a problem for behavioral interventions, subjective outcomes, and interventions for which there is a high placebo effect. Inclusion of observational studies is unlikely to enhance the strength of evidence for this intervention.</p>

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Ellon Caspi PhD	Executive Summary	Aromatherapy. This intervention can have tremendous positive effects on many individuals living with dementia. I've seen it many times in various nursing homes. Aromatherapy is much more than the description used in the review. The description oversimplifies this holistic, multidimensional, and enriching activity.	The specific interventions used in each eligible trial are described in more detail in the full report.
Sonya Barsness, Sonya Barsness Consulting LLC	Executive Summary	In the Executive Summary of the report the understanding of behaviors as symptoms of dementia is clearly stated. This reflects a purely medical lens that does not more broadly consider an alternative person-centered paradigm in which what has often been described as "symptoms" could also be the reactions of persons with dementia to their environment or caregiver, a form of communication, and an expression of need.	The focus of our review was on symptoms that are problematic and require treatment; symptoms are typically treating by determining the cause and addressing that or by directly treating the symptoms. Both of these approaches are used in the literature that we analyzed. Appropriate reactions to situations do not necessarily require treatment.

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Commentator & Affiliation	Section	Comment	Response
<p>Sonya Barsness, Sonya Barsness Consulting LLC</p>	<p>Executive Summary</p>	<p>There are prevalent and in my opinion, flawed, underlying assumptions about the use of non-pharmacological “interventions”, which is in itself a medical term and can limit our broader and deeper understanding of people with dementia. Perhaps these assumptions should be addressed in the review. The common assumption has been that non-pharmacological interventions can “replace” the use of antipsychotics so that people with dementia are given a “prescription” of a non-pharmacological intervention just as they would be given a prescription of medication. This assumption reflects a purely medical model of dementia care and does not acknowledge that in order to respond to the behavioral expressions of people with dementia, one might see behavior as a form of communication, and understand the reasons behind those expressions and how that person’s needs can be met. The response to that person is then about meeting their needs (particularly emotional needs) and addressing the underlying reasons behind their behavioral expressions. Providing non-pharmacological interventions without this consideration will be ineffective because it does not address the underlying reasons why the person is acting that way and does not necessarily address their needs. Related to this point, studies do not often include consideration of or analyze the circumstances in which people with dementia are showing anger, frustration, etc., such as when it is happening, with whom, etc. They might not include the variables around which a person is given non-pharmacological interventions and how this impacts success. If a person is upset because she or he does not want to take a bath, this person’s caregiver moves forward with giving them a bath, and his or her anger continues to grow as a result of a reaction to what is happening to him or her, unmet needs, etc., it is safe to assume that a non-pharmacological intervention given for this situation and at this time of increased frustration and anger will not be able to bring a person down from that level of frustration and anger. Similarly, a music therapy class given a couple of times a week might not provide a timely response to a person who is in distress at that moment.</p>	<p>Many of the interventions studied conducted assessments of the person with dementia and often designed the intervention to address the root cause of the agitation/aggression. This detail is provided in the full report.</p>

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Sonya Barsness, Sonya Barsness Consulting LLC		In interpreting and discussing these findings there needs to be consideration of the possibility that these studies show little effectiveness because they are based on one paradigm (medical) of dementia care. If anything, the studies actually support the need for an alternative paradigm. Many of the “interventions” noted in the studies can be effective ways of responding to people with dementia, when used in a way that meets the individual needs of that person and responds to what they are communicating to us through their “behaviors”. However, we need to acknowledge that perhaps this is dependent on a change in paradigm for dementia care to reflect a broader person-centered perspective.	Many interventions were tailored to the person with dementia; some trials tailored the interventions based upon an unmet needs theory. The evidence was still insufficient to draw conclusions.
Sonya Barsness, Sonya Barsness Consulting LLC	Executive Summary	ES-1: it should be noted that the great majority of people with dementia live at home (versus nursing homes and assisted living communities), while the estimates of nursing homes and assisted living residents with dementia are quite high.	Our introduction describes both settings.
Sonya Barsness, Sonya Barsness Consulting LLC	Executive Summary	ES-13: To make my points above only the trial tailoring interventions to unmet need showed decreases in agitation/aggression. Although this is only one study it does support the possibility of the need for a different paradigm.	Several trials provided tailored interventions; results were not consistent across the studies. Evidence was insufficient to conclude effectiveness for either comparison studied.
Sonya Barsness, Sonya Barsness Consulting LLC	Executive Summary	ES-15: A more detailed description of person-centered care is needed. This summary suggests that person-centered care (which is a philosophy and practice) is comparable to a process (Dementia Care Mapping).	We use the term “person-centered” as this is what is used by the studies included in our review. A more detailed description of the interventions are available in the full report.
Sonya Barsness, Sonya Barsness Consulting LLC	Executive Summary	ES-22: The last paragraph does not clearly describe the basis for dementia care mapping and agitation/aggression as a form of communication. It is more than identifying triggers but trying to understand the meaning of the behaviors and the needs that are being expressed by them (not just avoiding the triggers, although this is sometimes the case)	A more detailed description of the interventions are available in the full report.
Peer Reviewer #1	Introduction	Introduction is well-done. It is of appropriate length a provides good rationale for need for study and methodology.	Thank you.

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TEP #1	Introduction	In addition to the challenges associated with defining, combining, and measuring 'agitation/aggression', it would be helpful for the report to acknowledge that the same behavior may arise in broadly different contexts. Physical aggression that arises in an incontinent patient that is having his or her diaper changed may have a different phenomenology and root cause than aggression arising when a dementia patient targets another resident on the false belief that he or she is stealing things.	We have enhanced the description of agitation/aggression in the introduction.
TEP #1	Introduction	page 2, line 35-36 has a typo on 'instrumnets'	Thank you. We have corrected the typo.
TEP #2	Introduction	The issues with vague and differing definitions of "agitation" and "aggression" are discussed at various points - the authors should make the point early on about the lack of definitional clarity and conceptual clarity around these terms. There is also the issue of the relationship between them - do highly agitated residents go on to aggression? How often? Is that reported in the literature? There is a nice discussion of which behaviors require treatment - some of it could be moved earlier in the report.	We have enhanced the description of agitation/aggression in the introduction and discussion.
TEP #2	Introduction	The entire body of literature hinges on defining these terms consistently. Therefore one recommendation could be to convene an expert group of researchers and clinicians to decide on definitions and taxonomy, as well as the recommendation made by the authors to decide on measurement tools and outcome measures. This is the most fundamental issue and this work needs to be done before additional RCTs and meta-analyses can be integrated into practice.	We have added this suggestion to the future research needs table.
Anonymous Public Reviewer #1	Introduction	Page: 1 paragraph 2 The sentence "Behavioral and psychological symptoms cause considerable patient distress and are associated with accelerated functional and cognitive decline." might be better phrased "Behavioral and psychological symptoms are distressing to patients and often presage accelerated functional and cognitive decline." This would avoid implying that these symptoms cause decline.	We agree that behavioral symptoms do not cause cognitive decline. However, we believe the current statement as written does not imply a casual relationship. We use the term "association" to mean that cognitive decline and behavioral symptoms are correlated and not that behaviors cause cognitive decline.
Anonymous Public Reviewer #1	Introduction	Page: 1 paragraph 3 May wish to insert e.g., just after the parenthesis and before "disruptive, problem, difficult, challenging"	We have included "e.g.," as suggested.

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Anonymous Public Reviewer #1	Introduction	Page: 1 paragraph 3 In the sentences "consisting of overt harmful actions (physical or verbal) to others that are clearly not accidental", it may be clearer to state "consisting of physical or verbal actions that are overt, harmful, intentional and directed towards others." Since aggression can be self-directed, the phrase "to others" may be able to be deleted.	Deleted 'to others' in sentence as suggested.
Anonymous Public Reviewer #1	Introduction	Page: 1 paragraph 4 See previous comments about the phrase "high risk for adverse effects". Although there is clearly an elevated risk in terms of odds ratio, the absolute percentage at risk is still relatively low. "Increased", "Elevated" or "Significant" may be better descriptors.	We have revised the text to use the term "increased" instead of "high."
Anonymous Public Reviewer #1	Introduction	Page: 1 paragraph 5 The paragraph suggest that underuse of non-pharmacological interventions is "because clinicians lack knowledge regarding their efficacy and possible risks." However, it may also be because clinicians' experience suggests that these interventions are often ineffective. Given the limited evidence of efficacy in the available studies, this perception might not be inaccurate, particularly for patients with emergent, severe and/or potentially dangerous symptoms. Another potential reason is a lack of availability of trained staff to implement non-pharmacological interventions.	We begin the sentence with the phrase "in part" to highlight some of the reasons nonpharmacologic approaches may not be used in clinical practice. This is not intended to be an exhaustive list of reasons. Thank you for highlighting other potential reasons that these interventions maybe under-utilized. We did not identify data on the prevalence of these issues.
Soo Borson University of Washington	Introduction	I would like to see key questions include appraisal of major problems in the field thresholds for treatment prespecified indicators of successful outcome etc etc some of which I have mentioned in sections below. I understand why you organized your review around where people with dementia live community or residential facility and the type of recipient designated in each trial patient caregiver care system. Those distinctions make it easier to organize your review but miss key issues.	Thank you for your concern. Key questions are established much earlier in the comparative effectiveness review and cannot be changed at this point. We have addressed this issue in the future research needs section. It is not clear what key issues are missed by analyzing data from long term residential settings and community settings separately. The populations and interventions vary considerably and combining these would be inappropriate.
Soo Borson University of Washington	Introduction	Its not clear that isolating agitation and aggression from psychosis and other behavioral problems pain and other known provocative features will tell the story adequately. I understand that you had to limit the scope of work. But perhaps you thinned it out too much. Since many pharmacotherapeutic agents are used in efforts to reduce agitation and aggression please make it clear that the scope of this review included did not address those agents and that it is specifically the class of antipsychotics not all psychotropic medications that is the target for reduction.	The scope of our review was nonpharmacologic interventions to address agitation/aggression. We did not include interventions from any drug class.
Peer Reviewer #1	Methods	Key questions are appropriate and explicitly stated.	Thank you.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Methods	More consideration should have been made for expanding outcomes beyond agitation/aggression. The authors rightly point out that agitation/aggression are poorly defined constructs, however, given this why not include studies that look at behavioral problems more generally. The overlap of agitation/aggression and behaviors measured by scales such as NPI and RMBPC, Behave-AD, BRSD is great.	Our review does include and analyze general behavior outcomes.
Peer Reviewer #3	Methods	<p>The authors start by eliminating any study that is not a randomized control trial (RCT). The assumption is that an RCT is both necessary and sufficient to provide “hard” evidence of the efficacy of an intervention. This “gold” standard, of course, is the prototype pharmacologic study where double-blind experiments can be conducted using a drug treatment and a placebo which looks exactly like the drug treatment. Effects are produced by a drug entering the blood stream, with the expectation being that the drug will continue to produce its effects as long as a clinically significant level of the drug remains in the system. While this model is admirable for examining many medical conditions, it is a horrible way to conduct research on the efficacy of treatment for agitation or aggression in dementia. It is like comparing apples to aardvarks.</p> <p>For example, let us say that when listening to music or engaging in a meaningful activity, a person with dementia in a nursing home does not show agitation or aggression. Once the treatment stops being administered and the resident is placed back into the environment which causes or accentuates their aggressive/agitated behavior, this behavior returns. Does this mean that the treatment was not effective? Obviously not. If you want to compare this to drug treatment, consider that the effect of the nonpharmacologic intervention is dose dependent. It has a short half-life, and so must be administered through the day to produce long-term effective results. Since it may not be stored easily internally, it must be administered and maintained on a regular basis externally. This is the essence of person-centered care. In addition, it is important to provide a variety of such nonpharmacologic treatments throughout the day as no one want only to listen to music or do one specific activity all day long. Apples to aardvarks.</p> <p>In addition, many disciplines recognize alternative methods of showing efficacy (as well as effectiveness) for treatment, including well-controlled small-n or single-subject research.</p>	<p>We agree that conducting randomized controlled trials (RCT) for nonpharmacologic interventions is challenging. However, it is not impossible and studies included in our review provide examples of successful implementation of RCT study designs. A main discussion point of this report is to challenge researchers and funders to improve the evidence base through creative RCTs.</p> <p>If nonpharmacologics are to be used in clinical practice and touted as a viable alternative to pharmacologic interventions then they must be held to the evidence standards of the medical community. To evaluate the level of evidence we used globally accepted and validated measures for our risk of bias assessment.</p>

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Methods	<p>That being said, let us review other criteria used by these authors to determine inclusion in the paper. They eliminate studies which they view as demonstrating too much “bias.” This statement on page 16 is quite telling:</p> <p>Two investigators independently assessed risk of bias of eligible trials using instruments developed for the project based upon AHRQ guidance.²⁸ Overall 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 are believable given the study’s limitations.</p> <p>Thus, the authors decide which results (published in a peer-reviewed journal – the authors’ criterion) are “believable.” One must assume that most or all “unbelievable” outcomes are those which produced effective treatment.</p>	<p>Risk of bias (RoB) assessment is a structured and established methodological step in conducting systematic reviews. For a discussion of RoB methods and the AHRQ guidance please see citations mentioned in the full report. In addition, high risk of bias studies are described in the appendices. Readers are welcome to review studies we determined to be high risk of bias and formulate their own conclusions.</p> <p>Even peer-reviewed published articles are subject to major flaws and biases (e.g., selection bias, and attrition bias). We use the RoB procedures as outlined by AHRQ to evaluate the bias of each included article.</p> <p>We have added text to the methods section of the executive summary and full report to clarify the RoB process.</p>

Commentator & Affiliation	Section	Comment	Response
<p>Peer Reviewer #3</p>	<p>Methods</p>	<p>Then there is the criterion for determining if a study which survives to get into the review produced significant results. I will give an example: Tailored versus Nontailored Interventions We identified three trials with acceptable risk of bias comparing tailored interventions to nontailored interventions.⁵⁰⁻⁵² Trials enrolled a total of 247 nursing home residents. The interventions used various resident characteristics for tailoring. One tailored the intervention based on an assessment for unmet needs,⁵⁰ another on the Montessori model,⁵² and the third on balancing arousal throughout the day according to the patients' response to different activities.⁵¹ Delivery of the interventions varied. Only the trial tailoring interventions to unmet needs found a decrease in the level of agitation/aggression with tailored activities compared with nontailored activities.⁵⁰ All three trials had methodological limitations and imprecise estimates. Evidence was insufficient to draw conclusions regarding the effectiveness of tailored activities compared with nontailored activities.</p> <p>So, if there is a "decrease in level of agitation/aggression" why do the authors conclude that evidence is "insufficient?"</p>	<p>Evidence regarding the effect of interventions is based on the strength of the body of evidence (SoE). SoE is a validated method and recommended by AHRQ. In SoE the collected effect of all interventions within a grouping are evaluated (e.g., tailored interventions). This means that even if one of the interventions produces a significant effect the entire body of evidence may not be sufficient due to results from the other studies in the group.</p>

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Commentator & Affiliation	Section	Comment	Response
		<p>Here is text from the abstract of a study (52) which (according the authors of this review) did not produce a decrease in the level of agitation/aggression in residents with dementia:</p> <p>Background: Increasingly more attention has been paid to non-pharmacological interventions as treatment of agitated behaviors that accompany dementia. The aim of the current study is to test if personalized one-to-one interaction activities based on Montessori principles will improve agitation, affect, and engagement more than a relevant control condition.</p> <p>Methods: We conducted a randomized crossover trial in nine residential facilities in metropolitan Melbourne, Australia (n = 44). Personalized one-to-one activities that were delivered using Montessori principles were compared with a non-personalized activity to control for the non-specific benefits of one-to-one interaction. Participants were observed 30 minutes before, during, and after the sessions. The presence or absence of a selected physically non-aggressive behavior was noted in every minute, together with the predominant type of affect and engagement.</p> <p>Results: Behavior counts fell considerably during both the Montessori and control sessions relative to beforehand. During Montessori activities, the amount of time spend actively engaged was double compared to during the control condition and participants displayed more positive affect and interest as well. Participants with no fluency in English (all from non-English speaking backgrounds) showed a significantly larger reduction in agitation during the Montessori than control sessions.</p> <p>Conclusion: Our results show that even non-personalized social contact can assist in settling agitated residents.</p> <p>Tailoring activities to residents' needs and capabilities elicit more positive interactions and are especially suitable for people who have lost fluency in the language spoken predominantly in their residential facility. Future studies could explore implementation by family members and volunteers to avoid demands on facilities' resources.</p> <p>Trial Registration: Australian New Zealand Clinical Trials Registry – ACTRN12609000564257.</p> <p>How did they reach their conclusion based on what was written in this peer-reviewed journal?</p> <p>This is but one of many examples in which the conclusions reached by the authors might differ from the conclusions reached by other readers of the same research studies.</p>	<p>The abstract mentioned by the reviewer describes results consistent with our review. The abstract states “Behavior counts fell considerably during both the Montessori and control sessions relative to beforehand.” The behavioral symptoms changed in both groups, but there was no evidence that the Montessori intervention improved symptoms more than the control condition. It appears from the abstract that the Montessori intervention may have improved another outcome, (time spent actively engaged), It is not clear without the statistical data that there was truly a difference. However, this outcome was not one we gathered during our systematic review. While an intervention may have improved an outcome, it may not have been an outcome that was relevant to our review. Additionally, in some cases, authors inappropriately conclude differences exist when the differences are not statistically significant. We also found that authors sometimes inappropriately concluded effectiveness when there are statistical differences from baseline in an intervention group when there was no statistical difference from the control group. These issues likely explain the nonspecific inconsistencies the reviewer mentions between our findings and abstracts concluding effectiveness.</p>

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Commentator & Affiliation	Section	Comment	Response
TEP #1	Methods	While is understood that current indexing systems have substantial overlap, this report may receive some criticism for not including or at least mentioning CINAHL and psycINFO searches as well, especially since the researchers doing nonpharmacological studies are far more likely to be from nursing and psychology fields than from medicine per se. Are journals in those fields that Medline and Embase don't capture?	We have updated our search and included bibliographic database searching in PsychINFO. We did not expand our search to include the CINAHL database. Our extensive experience has demonstrated that we rarely identify unique and eligible trials in the CINAHL database that have not already been identified with one of the other databases. Besides Medline and Embase, we also search the Cochrane Library and conduct extensive citation searching.
TEP #1	Methods	The analytic framework including intermediate, final and secondary outcomes in prescient for future study designs but suffers from the recency of the call for anti-psychotic medication reductions. In other words, few studies to date have considered this as an outcome as opposed to a moderating variable in the design.	We consider agitation/aggression to be the major outcomes that would add value to the field. Changes in antipsychotic medication is an intermediate outcome and this research in and of itself is not likely to change behaviors.
TEP #1	Methods	Delineation of the scales used in these studies is perhaps an accurate reflection of the literature but it is surprising that nursing home studies do not have simply counts of episodes of aggression/agitation culled from mandatory incident reports or the common behavioral log. Recognizing that there is bias in this approach, still this is the common naturalistic mechanism for tracking these target behaviors in the facilities where they occur.	The trials that we analyzed primarily used validated instruments to report behavioral outcomes.
TEP #2	Abstract	The last sentence of the conclusion in the abstract (p. 5) should be reworded. The issue is the level of evidence for non-pharm interventions, not whether or not we should continue to try to reduce antipsychotic medication use regardless of the level of evidence for alternatives. If something is harmful (e.g., AP use) and increases the risk of death and has other serious side effects (over-sedation, reduced quality of life), we should not continue to do it, even if evidence for alternatives is lacking. For example, if major surgery for a problem is found to be ineffective or increases the risk of death, we would not generally continue to do that surgery while waiting to find a better treatment. The conclusion can state that more research is needed to guide clinicians, but should not state that we will continue to use AP medications in frail elders while waiting for the results of new studies. The summary paragraph in the discussion section is much better - that should be used as the basis for the conclusions in the abstract	The revised discussion clearly indicates that future practice should concentrate on nonpharmacologic interventions.

Commentator & Affiliation	Section	Comment	Response
TEP #2	Methods	Why was the literature report limited to studies in English? A great deal of this work has been done in Scandanavia, the Netherlands and other countries. The authors note that a number of the studies they reviewed were conducted outside the U.S.Wouldn't it have been important to review studies in countries with particularly low rates of antipsychotic medication use in these populations, and those with higher rates of use of alternative interventions, even if they were published in non-English journals? This gets at basic cultural differences in the way dementia and aging are viewed and treated in other societies. It is quite possible that the reason non-pharm approaches are more effective in those countries is because of fundamental differences in attitudes and behavior of medical professionals and caregivers. The researchers should state why they excluded articles in non-English journals.	The language restrictions reflect the language abilities of the research team and evidence suggesting that English language journals reflect the vast majority of the science on medical topics with the exception of complementary and alternative medicine. However, our review includes many trials conducted outside of the United States published in English-language journals.
TEP #2	Methods	Would change "we meta-analyzed" to, "we conducted a meta-analysis".	We have revised the text as suggested.
TEP #3	Methods	The inclusion and exclusion criteria are appropriate and justifiable with one caveat. The authors seem to have included studies randomized at the level of the person and excluded studies randomized at the level of the provider or setting. If that is correct, it would be helpful to readers familiar with the research on nonpharmacologic interventions in dementia if the distinction were stated explicitly where the criteria are noted in both the executive summary and the full report.	That is not correct, our review included cluster randomized trials.
TEP #5	Methods	Table 2: I was unclear how the intermediate outcomes measure category was determined, and why there is only one measure included. Is this because this is the only measure considered in the literature reviewed? If so, that should be specified, as there are clearly many other measures of potential intermediate outcomes that could influence behaviors, or perhaps more importantly, the severity of behavior problems.	Our topic refinement and protocol development process identified outcomes most relevant to the topic. These were the ones included in the review. Research on final health outcomes is much more important to move the field forward.
TEP #5	Methods	Several of the measures included, and this not immediately apparent in Table 2, assess not only frequency but severity of behavior problems. One could argue that these are two very different domains, in part because agitation and aggression are likely not that frequent among certain populations of persons with dementia. How was this addressed in the review?	Our review was limited to how the outcomes were measured and reported in the eligible trials. We used the measures provided by the original research. We did not pool frequency measures with severity measures.

Commentator & Affiliation	Section	Comment	Response
TEP #5	Methods	p. 49: "3) consistency (similarity of effect direction and size);" Why is this a criterion for quality of evidence? Some interventions may have stronger effects on certain outcomes than others?	An intervention must be precise to be effective, meaning that both ends of the confidence interval around the mean difference between groups show a clinically meaningful improvement compared to the control group. Some interventions will have stronger effects than others (i.e. small, moderate, large effect size).
TEP #5	Methods	Risk of bias is used in various areas of the review up to this point, but is never defined in text. Simply pointing the reader to the appendix is not sufficient. As risk of bias seems to be the main metric used to determine strength of evidence, it should be explained more clearly earlier in the review.	We have enhanced our discussion of risk of bias assessment in the methods section.
TEP #5	Methods	Similar to risk of bias, "low strength of evidence" is used in text throughout the review up to this point, but it is unclear to the reader what that actually means.	We describe in the methods section how strength of evidence is assessed for each comparison-outcome. Each strength of evidence assessment (insufficient, low, moderate, high) provides an indication of how reliable the conclusions are. These are explicitly described in the methods section.
Soo Borson University of Washington	Methods	Satisfactory overall given the scope you articulate however would have liked to see characteristics of participants and instruments in RCTs be dealt with more fully. You discuss the relative lack of detail about participants extensively in the Discussion and you point out limitations of instruments to some extent indicating that you have thought a lot about this. Ill have further comments later.	Characteristics of enrollees and instruments are provided in the results section. Additional data are available in extraction forms that will be available publically after the report is posted. Unfortunately, some trials do not provide details beyond age and sex of participants.
Robert Gibson	Methods	I have worked in a SNF setting as a psychologist for 10 years. In considering the interventions used most have been successful with certain SNF residents. I think a major methodological flaw is the use of randomized controlled trials. While this is seen as the gold standard for research it presumes that any sample is relatively homogenous. In my experience SNF residents are not. This approach also typically applies a set model or approach to all subjects that are in the test sample and again with the inherent variability of SNF residents one size will not fit all. In my experience interventions for agitation and aggression in persons with dementia when they work are based on knowledge of the individual developed over time and constantly adapted to that same individual. As such standard approaches are only useful when they happen to align with the residents particular characteristics.	Selection bias in observational studies would not provide confidence in results. Many trials recognize that interventions need to be tailored to the situation and many of the trials we analyzed had interventions that were tailored.

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Commentator & Affiliation	Section	Comment	Response
Sonya Barsness, Sonya Barsness Consulting LLC	Methods	while it is clear that this study only included RCT it should be included that there has been research in this area that is not RCT that is worth noting as important to our understanding of how to care for people with dementia.	Observational studies are unlikely to provide sufficient evidence given their risk of bias, particularly selection bias.
Peer Reviewer #3	Results	Here are the results of the review, which are very clear: "Our findings are consistent with many prior reviews, but more pessimistic than others, which showed benefit for certain interventions." Of course they overlooked studies, based on their initial criteria and set of assumptions.	We did not overlook studies. In the first phase of our analysis we rejected studies based on title and abstract (i.e., studies that were clearly not related to our research question). When conducting the full text review we excluded some studies that did not meet our inclusion criteria. We also excluded from analyses studies that were rated as having a high risk of bias. To reiterate, we reviewed all studies and then decided to omit those that did not meet our inclusion and quality criteria. This is different than simply overlooking or not identifying studies.
TEP #1	Results	What is lacking, given that is was discussed clearly in the key questions is any description of harms. Perhaps this merely reflects the state of the literature, where most studies don't report harms including medication trials but especially behavioral trials. If that latter is true this is an important point to more strongly emphasize in the discussion and future research sections.	It is true that few trials reported specific harms.
TEP #5	Results	Of the patient- and caregiver-level interventions delivered in the community, how many were delivered jointly to the caregiver and care recipient?	These are broken out into separate groups in the results section (patient level and caregiver level).
TEP #5	Results	Is it usual in an AHRQ review to present a narrative summary of each study in text in the Results section? This seems antithetical to the notion of synthesizing results across studies.	We summarized individual trials to provide detailed information on the interventions since they were heterogeneous.
TEP #5	Results	-p. 56: "...having an immediate effect by measuring the outcome just after the intervention and again within 30 minutes after the intervention. ⁶⁰ This evidence is insufficient to draw conclusions regarding the efficacy of music to immediately decrease agitation/aggression among individuals with dementia." Why? Agitation and aggression are not likely long-lasting symptoms, but instead ones that occur periodically and perhaps abruptly. If that is the case, than an intervention of this type that is short and focused may be one that is most likely to actually work in this context.	The strength of evidence assessment with all components is summarized in the appendices. Results from only one trial rarely are sufficient to achieve low strength evidence.
TEP #5	Results	p. 61: "Studies had methodological limitations and estimates were imprecise." Again, based on the text descriptions, it is difficult to ascertain what these were. This occurs later in the review as well.	Imprecision refers to the numerical data found in the tables.

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Commentator & Affiliation	Section	Comment	Response
TEP #5	Results	p. 61: should be "the Montessori model"	Thank you. We have revised the text as suggested.
TEP #5	Results	p. 63: is the description of the Rodriguez-Mansilla study identical to above? If so, why is it repeated here?	This study compared massage, ear acupuncture, and a control group. We report results from the massage versus control group on page 22. On page 24 (which the reviewer refers to as page 63) we report results from the acupuncture versus control group.
TEP #5	Results	Table 5: as with the earlier text sections, it is stated for many of the studies that strength of evidence is "low," but how the review team came to such conclusions is unclear.	How strength of evidence is assessed at the body of evidence level, not at the individual trial level. This process is described in the Methods section and the detailed assessment by strength of evidence component is provided in the appendices.
TEP #5	Results	Table 6 could replace much of the repetitive description of each study in text, unless again that is an AHRQ EPC review convention.	Thank you. We tried to express different information in the text and tables. Some overlap cannot be avoided.
TEP #5	Results	p. 87: Was PCC clearly defined in terms of an intervention approach in these studies? How similar were the interventions?	All three studies explicitly used the term person-centered care and trained staff in person-centered care methods. Although studies are not replications of each other they all implemented a version of person-centered care that we believe were similar enough to group for a pooled analysis.
TEP #5	Results	As noted earlier, much of this review seems to pivot on risk of bias assessment (e.g., p. 125).	We agree. Assessing risk of bias is a critical component of systematic review and key to a high quality systematic review.
Anonymous Public Reviewer #1	Results	Page: 29 paragraph 1 This study seems to be one of the few that looked at the effects of differences in concomitant medications between the control and intervention groups. Is it possible to draw any conclusions about the role of non-pharmacologic or pharmacologic interventions in reducing restraint use based on the facts that "restraints were used less on residents in the intervention group than those in usual care (p <0.024). However, during this same period of time fewer psychotropic drugs were used in residents in usual care than those in the intervention group (0.002)"? If so, this would be worth additional discussion.	Given few studies evaluated psychotropic drug use and even fewer evaluated restraint use it is not possible to extrapolate any additional conclusions.
Anonymous Public Reviewer #1	Results	Page: 82 under the Eligible Trial paragraph The phrase "(such as)" seems to be an apparent editing notation that was not addressed prior to draft dissemination.	Thank you. We have revised the text accordingly.
Peer Reviewer #1	Discussion	The implications are clearly stated. I could not identify studies not included. The future research section was excellent and a highlight of this report. It was well-done.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	Discussion	Discussion starts on page 101, not page 104 as listed in the Contents?	The discussion starts on page 104 and the Table of Contents has been updated accordingly.
Peer Reviewer #2	Discussion	Examples of language that this reviewer is able to understand but finds challenging to read and to interpret are as follows: on page 104 of the Discussion, lines 44-45, "While we did identify a large number of trials that tested interventions for improving behavioral symptoms in dementia; fewer specifically measured agitation/aggression."	Many trials studied interventions targeting behavioral symptoms in general, not specifically agitation/aggression. They measured outcomes with instruments measuring behavioral symptoms more generally, such as the NPI.
Peer Reviewer #2	Discussion	Examples of language that this reviewer is able to understand but finds challenging to read and to interpret are as follows: page 104, second sentence of Discussion, lines 5-6, "It will require strong evidence that nondrug treatments can effectively reduce agitation/aggression and improve patient quality of life."	We intended to suggest that providers would be more likely to recommend nonpharmacologic interventions if evidence supported their efficacy.
Peer Reviewer #3	Discussion	"Despite great interest in nonpharmacologic interventions to manage agitation/aggression in dementia, as well as changes in practice toward reducing the use of antipsychotics, the current evidence base does not indicate specific effective approaches. Interventions should be proven effective before being implemented."	While several individual studies produced significant results, as a body of literature results are inconclusive. We have provided additional details in the methods section regarding the strength of evidence assessment and how conclusions regarding the body of literature are made.
Peer Reviewer #3	Discussion	It is amazing that the entire literature base cannot produce any specific effective approach. One would assume that by chance alone, at least one study would pass the test.	There are no tests that trials need to pass. The body of evidence is what provides insufficient evidence. While certainly there are a few trials that show an effect, there are many more that show no effect. A strong body of evidence is multiple well-done trials that demonstrate a similar effect.
Peer Reviewer #3	Discussion	Has any one of the authors been able to create a successful nonpharmacologic intervention for persons with dementia showing agitation or aggression? The conclusion must be "no," at least by their definition, else that intervention would be highlighted and we would have a path out of the wilderness.	Systematic review authors are independent from the field and do not conduct research on the topic.
Peer Reviewer #3	Discussion	One can only conclude from this review that not only is it extremely difficult to intervene successfully with aggression or agitation in persons with dementia using a nonpharmacologic intervention, but that it is well nigh impossible to prove it.	Unfortunately, the literature on this topic is limited. This is expressed in our discussion and conclusions.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Discussion	Furthermore, they recommend that no such intervention be tried unless it has been shown effective -- by their standards, which apparently they themselves cannot meet. And so, once again, we are told that there really is nothing we can do, and that the attempt to replace pharmacologic treatment for agitation and aggression in persons with dementia should wait until we have evidence of the effectiveness of such treatments, which is impossible to demonstrate at this time and well nigh impossible to achieve. Meanwhile, an extensive literature demonstrating effective nonpharmacologic treatment (in peer reviewed journals) should be ignored. This is how learned helplessness as the standard training message for dementia care is continually reinforced.	We did not intend to suggest that interventions not be tried without sufficient evidence. We aim to summarize the evidence and leave it to the field to make recommendations about how to move forward. Evidence of effectiveness would be an improvement to the current state of the literature on this topic. Practitioners may consider replacing interventions with proven harms with those with little chance for harms if they know of promising interventions. Insufficient evidence should not be confused with evidence of ineffectiveness.
TEP #2	Discussion	The authors break down interventions individually, and include some that have 2-3 components, (e.g., training and caregiver support) but do not discuss truly comprehensive, multi-component interventions. Perhaps there were none. A comprehensive approach would include the environmental aspects that the authors mention, staff training and ongoing support, leadership and management of staff (ongoing), engagement of the prescribers, family, etc. Essentially, culture change and transformation of the approach to individuals with dementia. Again, there may not have been randomized trials of these approaches. As with fall prevention, studying individual interventions may not reveal which combinations are effective. So with dementia, for example, combining staff training with individualized dementia care mapping and music therapy might have a stronger effect than any one of those interventions alone; but this effect might only be seen with other operational or management changes in a nursing home or AL. The potential benefit of a comprehensive approach could be mentioned for future studies, and also as a potential reason for the failure to see an effect in current research designs.	We did not identify trials with comprehensive interventions described by the reviewer.
TEP #2	Discussion	In terms of the effect of staff training, the implementation issues such as high turnover in nursing homes should be mentioned. The authors note the many methodological issues with these types of studies; however specific implementation issues are likely to be very important and could be highlighted more, particularly in Table H (research gaps). The authors should address intervention fidelity in the studies, a common reason for failure to see results, particularly in a challenging environment such as nursing home, AL or home care.	Treatment fidelity is assessed in risk of bias assessment and is mentioned as a limitation.

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Commentator & Affiliation	Section	Comment	Response
TEP #2	Discussion	The authors make a very important point about the lack of studies that focus on environmental changes. This is an important recommendation for Table H and a major finding of this study that is often overlooked.	We've added this suggestion to the future research needs table.
TEP #2	Discussion	One recommendation not listed (or at least I did not see it) that follows from the data is that more technical assistance could be provided by AHRQ or other entities to researchers/institutions UP FRONT, in designing future research studies in these populations/settings. Rather than simply let trends continue, with multiple methodological problems in these studies, why not require more robust designs in order to obtain funding, and make resources available to assist teams that wish to conduct these types of studies? For example, civil money penalties (CMPs) are being used in several states to fund studies on this topic. AHRQ and CMS could work collaboratively to ensure that projects funded through CMPs will truly add to the literature in meaningful ways. The recommendation to provide some sort of enhanced technical assistance in the design phase of future studies would be an important outcome of this report.	While this is an important issue, it does not stem from our investigation of the research questions (we have no data on why the field suffers from methodological limitations). We enhanced our description of future research needs to address the role of funders and their responsibility to fund trials without methodological limitations that result in insufficient evidence.
TEP #3	Discussion	The authors note that their findings are pessimistic. This reviewer thinks that the findings are accurate (unfortunately), given the inclusion and exclusion criteria, definitions, and other parameters for the analysis. Two wording changes that could clarify the findings for some readers and perhaps reduce the pessimistic tone are listed below. 1. One purely semantic change pertains to the use of the term 'similar.' Beginning in the abstract and continuing through the report, the term 'were similar' is sometimes followed by 'to usual care' and sometimes followed by nothing. This reviewer thinks it would be good to always follow 'similar' by 'to' For example, in the abstract (p. v, lines 31-32), it would be good to add after 'similar' 'towhat.' Were they similar to usual care or to each other?	We have revised the text accordingly.
TEP #3	Discussion	2. Another change pertains to the phrase "may not be clinically meaningful." On p. 144, the authors note that, "Without an understanding of what constitutes a clinically meaningful change, interpretation of statistically significant differences ... was challenging." Yet in many places throughout the report, when a statistically significant result is noted, the phrase 'may not be clinically significant' appears next. This reviewer thinks that phrase should be deleted. It is gratuitously negative, suggesting that even good results may not be good.	At statistical difference in an instrument scale has little meaning if we do not understand what size difference is actually noticeable to patients. A statistical difference can be seen with very small differences in instrument scores if the sample size is large enough. Therefore, interpretation should always be with an understanding of the size of the difference that is actually noticeable and corresponds to actually doing better.

Commentator & Affiliation	Section	Comment	Response
TEP #3	Discussion	In addition, if the authors are aware of other changes in wording that do not reduce the accuracy of the text but ensure attention to positive findings, those changes would help researchers and clinicians identify interventions that are promising and should be further evaluated.	There were few positive findings. Those we did find were highlighted in the key points.
TEP #5	Discussion	p. 32: "In summary, the evidence for nonpharmacologic treatment of agitation/aggression in individuals with dementia is weak and obfuscated by an inconsistent and confusing terminology" *and* measurement approaches. I would argue that this is what complicates any attempt to synthesize the literature empirically; one could also make the case that the diversity in measures may make it less than wise.	We agree, this is the reason that we synthesized the evidence by setting and how the intervention was delivered and then qualitatively and not quantitatively in the vast majority of cases.
TEP #5	Discussion	p. 41: "Nonpharmacologic interventions aim to 1) prevent agitation/aggression behaviors, 2) respond to episodes of agitation/aggression to reduce their severity and duration, and/or 3) reduce caregiver distress." Please provide a reference, as non-pharmacological interventions (NPIs) often aim to do much more than that.	These were the intervention goals that we assessed in our systematic review. Our statement does not specify that these are the only objectives.
TEP #5	Discussion	p. 42: In addition to algorithms, clinical approaches are used to identify causes and contexts of behaviors; see the work of Judy Zarit, for exmple	Thank you for the information. These outcomes were beyond the scope of our review.
TEP #5	Discussion	p. 97: "methodological problem" should read "problems."	Thank you. We have revised the text accordingly.
TEP #5	Discussion	"Research on the nonpharmacologic management of aggression in dementia is still a cottage industry." what exactly does this mean? If funders are not providing the support for the larger-scale, standardized trials recommended in this report, the investigators are not the ones at fault.	We mean that the state of the science in this field is developing and not yet established. We have revised the text to clarify.
TEP #5	Discussion	One could also argue one limitation is the review's focus on agitation/aggression alone; it is a fairly restrictive and infrequently occurring behavior in the larger constellation of behavioral disruptions in people with dementia.	Our topic refinement process identified agitation/aggression as priority behaviors. Due to the complexity of nonpharmacologic interventions and the broad variety of instruments used to measure outcomes, scope expansion would have been detrimental to this project. Other behaviors are also important and future evidence synthesis could address these if there is research gap.

Commentator & Affiliation	Section	Comment	Response
Anonymous Public Reviewer #1	Discussion	<p>Page 104 paragraph 1</p> <p>Overall, there are a number of areas of the discussion that seem to extend beyond the intent of the review and into opinion and/or guidelines for practice.</p> <p>For example, the initial paragraph notes that antipsychotics rob individuals of experiencing life. However, for those individuals in whom antipsychotic medication is helpful, denying them treatment may increase their level of distress and similarly rob them of experiencing life. Agitation/aggression can also present harms to others. The balance of these considerations does not seem to be fully represented in the text as written.</p>	Revised discussion explains the balance that should be achieved in patients that need antipsychotic medication.
Anonymous Public Reviewer #1	Discussion	<p>Page 104 paragraph 1</p> <p>In terms of the need to taper antipsychotics, it may be preferable to state that attempts should be made to taper them. If there were a dramatic worsening of dangerous aggressive behavior with antipsychotic tapering or recurrent agitation that is extremely distressing to the patient, then continuing the taper to the point of discontinuation would not be warranted. Alternatively, this information may be better deleted as it is not related to the evidence from this review.</p> <p>Non-pharmacological options could also be used first before initiating antipsychotics and not just as a substitute treatment in the context of medication tapering.</p>	Revised text to avoid use of term, 'tapering'.
Anonymous Public Reviewer #1	Discussion	<p>Page 104 paragraph 2</p> <p>In terms of the observation that "Each investigator seems anxious to add something new," this definitely has an impact on collecting a body of evidence that has a consistent methodology. Unfortunately, this problem is not unique to this topic -- publishability and grant funding are typically aided by framing a intervention as "innovative". This also extends into the realm of policy and is probably outside the scope of this review.</p>	Sufficient evidence will only be achieved by repeating results of well-conducted, adequately-powered trials with similar interventions and comparisons. Systematic review methods better suited for complex interventions are currently being examined.
Anonymous Public Reviewer #1	Discussion	<p>Page 104 paragraph 2</p> <p>In terms of the observation that "interventions were not effective in reducing agitation/aggression", many of the interventions seemed relatively brief in duration making it hard to imagine how they could influence agitation on a long-term basis, especially in individuals with little or no recall. Future research may need to incorporate different frequencies and durations of interventions to look for "dose-response" effects on outcomes.</p>	Investigating dose-response relationships requires several trials studying similar comparisons (interventions and controls). The field is immature to do such analyses at this point.

Commentator & Affiliation	Section	Comment	Response
Anonymous Public Reviewer #1	Discussion	Page 105 paragraph 3 In terms of the comment that underpowered studies should not be conducted, there is no way to assure this. Unless constraints are placed on registering and/or publishing such trials, they will continue to be conducted, providing misleading information and minimal helpful information. Again, this may be more of a policy consideration.	Agree. This is a challenge to many fields.
Anonymous Public Reviewer #1	Discussion	Page 105 paragraph 3 The phrasing that "Individuals with dementia change living status and die" may benefit from rewording. Presumably "change living status" here means moving to a different facility and becoming lost to followup.	We have revised the text to clarify our meaning.
Anonymous Public Reviewer #1	Discussion	Page 106 paragraph 1 The statement that "the level of agitation/aggression that practitioners feel compelled to medicate is unclear" may be more confusing than helpful. It implies that there is a level of agitation/aggression where medication might be compelled. This is likely to be true but will also vary a great deal with the level of the risk to the patient and others as well as factors related to the setting of care.	Removed confusing statement.
Anonymous Public Reviewer #1	Discussion	Page 106 paragraph 2 Since this review is aimed at non-pharmacological strategies, the question on justification for psychotropic use seems beyond the current scope/evidence. It also seems to move from systematic evidence review into practice guidelines. In particular, the text that reads "What, then, constitutes a behavior that requires treatment? Or more specifically, when is behavior problematic enough to justify the use of psychoactive medications?" seems more appropriate for a commentary than for an evidence based systematic review.	This was added to the discussion to place the results in the context of pressing issues.
Anonymous Public Reviewer #1	Discussion	The sentence that "A serene unit with a minimum of uninterpretable behavior or conversation may not be a desirable goal worthy of medicating patients to achieve" may benefit from re-wording. One could make the case that if a single, extremely agitated patient is frightening the other patients on the unit, disrupting their sleep, and leading many of them to become distressed, then interventions may be needed to reduce distress for the identified patient and for others, while simultaneously fostering a calmer environment. Also, the meaning of "uninterpretable behavior" is unclear.	Removed paragraph to avoid confusion.

Commentator & Affiliation	Section	Comment	Response
Anonymous Public Reviewer #1	Discussion	Page 106 paragraph 3 The style here again reads more like a commentary rather than a discussion of evidence limitations. (i.e., "In the case of agitation, one might question the impetus for treatment. Who is upset by this behavior?")	Removed paragraph to avoid confusion.
Anonymous Public Reviewer #1	Discussion	In the sentence "These two goals imply...", it would be better worded "These two goals may imply..." since diversion and distraction are mentioned in both categories of intervention.	Revised text as suggested.
Anonymous Public Reviewer #1	Discussion	Page 107 paragraph 2 The paragraph that begins "Changing the behavior of caregiving staff ..." is similar to the text earlier in the document and the same considerations apply here. This is also another section that includes some good points but also incorporates comments and opinions that may be over-generalizations (e.g., about nursing home staff attitudes and training). The meaning of "the more complex and judgmental the intervention" is unclear. Similarly, the phrase, "the staff in such settings is harder to define" is unclear as written.	We have revised the text accordingly.
Anonymous Public Reviewer #1	Discussion	Page 107 paragraph 4 The sentence that begins "Neither setting is included as a dummy variable" is confusing as written.	We have revised the text to clarify our meaning of the term "dummy variable."
Anonymous Public Reviewer #1	Discussion	Page 108 paragraph 2 and under Future research needs The meaning of "a clearer map" is not obvious, as noted previously.	We have revised the text to clarify our meaning.
Anonymous Public Reviewer #1	Discussion	Page 108 under Future Research Needs For both benefits and harms of treatments, there is a significant need for true effectiveness studies (rather than efficacy studies with multiple exclusion criteria). When clinical trials exclude individuals (or caregivers) who can not complete needed assessments due to the urgency of the situation or when clinical trials exclude subjects due to other common clinical characteristics, it becomes hard to use existing evidence to weigh the benefits and harms of interventions.	We did not find applicability in eligible trials to be limited so this suggestion does not arise from our review.

Commentator & Affiliation	Section	Comment	Response
Anonymous Public Reviewer #1	Discussion	Page 108 under Future Research Needs In the context of medications and agitation/aggression/psychosis in dementia, an unanswered question is the way in which a pre-existing serious mental illness affects treatment risks/benefits. In developing practice guidelines for the treatment of individuals with dementia, it would be helpful to know how response rates to nonpharmacological therapies differ between individuals with serious mental illness (who would ordinarily have been treated chronically with antipsychotics) as compared to individuals with other psychiatric diagnoses (e.g, nonpsychotic depression, anxiety) vs. dementia without psychiatric co-morbidity. Clinical trials are not typically designed to address the situation in which a patient has a new onset of agitation and a decision must be made about whether to start a non-pharmacological or pharmacological treatment based on factors such as efficacy, urgency and symptom severity.	Evidence was limited to assess the general population. Few studies conducted subgroup analysis.
Anonymous Public Reviewer #1	Discussion	In addition, several sentences in this section are a bit hard to follow: ----Also needed are more consistent measures and clearer rationales for how the measures address treatment goals as well as appropriate timelines.	Revised text "Trials should be designed to adequately address treatment goals within appropriate timelines."
Anonymous Public Reviewer #1	Discussion	----A more systematic approach to future research, where variations are tested sequentially and under more defined conditions, could move the field forward. An order of procedure that would be generally 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	Revised text "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."
Anonymous Public Reviewer #1	Discussion	Page: 110 and 111 See comments included with the similar table earlier in the document.	Revised future research needs table.
Anonymous Public Reviewer #1	Discussion	Page 112 The statement "Research on nonpharmacologic treatment of agitation/aggression seems to have developed in a rather hodgepodge fashion." may benefit from re-phrasing.	Revised text "Research on nonpharmacologic treatment of agitation/aggression seems to have developed in a piecemeal fashion without overarching coordination.'
Anonymous Public Reviewer #1	Discussion	The phrase "drug treatment from problem behaviors", needs to be reworded (e.g. "medication for treatment of problem behaviors").	Reworded as suggested.

Commentator & Affiliation	Section	Comment	Response
<p>Soo Borson University of Washington</p>	<p>Discussion</p>	<p>This is where some restructuring would enhance the impact of this important work. Would you consider creating more structure in this section so that your conclusions analysis of limitations will be more readily grasped by readers with less specialized expertise Key issues reflecting limitations in existing work would include not necessarily in this order</p> <ol style="list-style-type: none"> 1. Lack of clarity about key clinical features of agitation/aggression in target population and characteristics of the study sample. Important omissions from existing research include lack of data on predementia agitation/aggressive behavior i.e. predisposition toward such behavior in the premorbid period clinical experience suggests that this matters. Identification of thresholds of treatability and criteria for success as defined by investigators. You touch on this but it needs more it needs to be front and center as do criteria for success of an intervention how much better is better enough and how that figure was arrived at what percentage of people got better enough etc. 2. Lack of clarity about participants stage of dementia type etc 3. Focus to date has been on the what of specific interventions with investigators seeking to prove that their good idea or method works based on a particular theoretical framework. Nearly all studies have been developed by investigators without engaging a collaborative design process with end users care systems staff family caregivers. Might we get further if we did that 4. Say more about the physical and human environment as therapeutic agents for future trials. 5. Address exclusion of the worst cases from RCTs in other words individuals with the most problematic agitation/aggression are likely to be excluded because of the urgency to change the behavior. I am aware of one otherwise well done comparison study showing no difference in outcomes with either of 2 medications 1 behavioral intervention and 1 placebo group that excluded this most difficult group from enrollment for exactly this reason. 6. Propose alternative study designs other than RCTs that have potential to move the field forward and alternative methods of developing goals and testable interventions that could generate much larger numbers of participants prespecify criteria for success as adjudicated by users not just researchers focus on defining minimum clinically significant difference for the key instruments as well as criteria for success 	<p>We have restructured the discussion as much as possible, but we need to maintain consistency with the AHRQ report template.</p>

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Commentator & Affiliation	Section	Comment	Response
Kelly Carney Phoebe Ministries	Discussion	As a licensed psychologist working within a long term care organization I have been eagerly awaiting this report. The conclusions are disappointing but I wonder if perhaps the context in which the studies are conducted might account for the paucity of evidence in support of nonpharmacologic interventions. The challenges of conducting RCT in an active long term care setting serving frail elders are substantial. In most settings staff are not familiar with research and are overburdened by clinical care duties making enlistment of staff in a clinical trial very difficult. In addition the heavy regulatory burden and limited financial resources of these settings render controlled research trials even more challenging. In light of the many barriers present and in acknowledgement of the fact that the research in these settings ought to reflect the reality of the context I would argue that the standard of applying RCT criteria to the studies may be unrealistic and unnecessary. Is there another framework from which the literature can be evaluated that might allow for greater insight than is provided by this evaluation of the literature.	Observational studies in these populations have substantial selection bias that impairs the internal validity of that evidence. This is especially a problem with behavioral interventions and subjective outcomes. Systematic review methods better suited for complex interventions are currently being examined.
Kelly Carney Phoebe Ministries	Discussion	In addition the final statement in the discussion section states Interventions should be proven effective before being implemented. In a setting where challenging behavioral expressions due to dementia are common and the use of unnecessary pharmacological interventions are discouraged there is little choice but to use nonpharmacological interventions to respond to agitation. Personal experience and observational data suggest that these interventions can be very effective in many circumstances. It is not realistic or reasonable to advise against their use while we wait for RCT to prove their effectiveness.	Revised discussion does not make this statement.
Peer Reviewer #2	Conclusion	The Conclusions on ES-25 are clear in a certain context, although the absence of anything at all about other (implicit: pharmacological) approaches is a bit unsettling. Is the reader to conclude that "usual care" and pharmacological approaches should be used until more evidence is obtained regarding non-pharmacologic interventions?	Pharmacologic approaches were beyond the scope of this review.
Peer Reviewer #3	Conclusion	The report is well structured and organized, and its main points are clearly presented. The conclusions, however, should most definitely NOT be used to inform policy or practice decisions	Thank you for your opinion; decisionmakers are free to use our results as they see best.

Commentator & Affiliation	Section	Comment	Response
TEP #2	Abstract	The last sentence of the conclusion in the abstract (p. 5) should be reworded. The issue is the level of evidence for non-pharm interventions, not whether or not we should continue to try to reduce antipsychotic medication use regardless of the level of evidence for alternatives. If something is harmful (e.g., AP use) and increases the risk of death and has other serious side effects (over-sedation, reduced quality of life), we should not continue to do it, even if evidence for alternatives is lacking. For example, if major surgery for a problem is found to be ineffective or increases the risk of death, we would not generally continue to do that surgery while waiting to find a better treatment. The conclusion can state that more research is needed to guide clinicians, but should not state that we will continue to use AP medications in frail elders while waiting for the results of new studies. The summary paragraph in the discussion section is much better - that should be used as the basis for the conclusions in the abstract	Reworded statement “Future research is needed to guide providers and informal caregivers towards effective interventions for agitation/aggression in dementia.”
Peer Reviewer #1	Figures	Figures and tables are adequate, although I think references should be included in all tables that list individual studies.	References are provided in tables with research results.
TEP #2	Results	Did not see STAR-VA studies here (Bradley Karlin and others) - some may have come out after the 2014 cut off or were determined to be ineligible. Do not believe that they would change the results, but just noting that.	These were not eligible for the review.
TEP #2	Results	Did not see any articles by Dolores Gallagher-Thompson, on culturally proficient dementia care, and care of non-english speaking populations.	We have included on study authored by Gallagher-Thompson; others were not eligible. Her studies typically address depression, not agitation/aggression.

Commentator & Affiliation	Section	Comment	Response
TEP #3	Results	<p>This reviewer is attaching a table showing a few studies that MIGHT been missed (emphasis on the 'MIGHT'). The authors are probably aware of these studies, but this reviewer did not see them in the excluded studies appendix. The authors can probably scan the list quickly and determine whether any should be added to the analysis, added to the excluded studies appendix, or otherwise noted.</p> <p>Bourgeois, M.S., Schulz, R, Burgio, L.D., and Beach, S. (2002) "Skills training for spouses of patients with Alzheimer's disease: Outcomes of an intervention study." <i>Journal of Clinical Geropsychology</i> 8(1):53-73.</p> <p>Burgio, L., Stevens, A., Guy, D., Roth, D.L., and Haley, W.E. (2003) "Impact of two psychosocial interventions on white and African American family caregivers of individuals with dementia." <i>Gerontologist</i> 43(4):568-579</p> <p>Coon, D.W., Thompson, L., Steffen, A., Sorocco, K., and Gallagher-Thompson, D. (2003) "Anger and depression management: psychoeducational skill training interventions for women caregivers of a relative with dementia." <i>Gerontologist</i> 43(5):678-689.</p>	<p>We have conducted a full text review of each selected study and included those deemed eligible after our screening process.</p>

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Commentator & Affiliation	Section	Comment	Response
TEP #3	References	<p>Gallagher-Thompson, D., Coon, D., Solano, N., Ambler, C., Rabinowitz, Y., and Thompson, L. (2003) "Change in indices of distress among Latino and Anglo female caregivers of elderly relatives with dementia: Site-specific results from the REACH National Collaborative Study." <i>Gerontologist</i> 43(4):580–591.</p> <p>Gallagher-Thompson, D., Gray, H.L., Tang, P.C.Y., Pu, C.Y., Leung, L.Y.L., Wang, P-C., Tse, C., Hsu, S., Kwo, E., Tong, H-Q., Long, J., and Thompson, L.W. (2007) "Impact of in-home behavioral management versus telephone support to reduce depressive symptoms and perceived stress in Chinese caregivers: Results of a pilot study." <i>American Journal of Geriatric Psychiatry</i> 15(5):425-434</p> <p>Gant, J.R., Steffen, A.M., and Lauderdale, S.A. (2009) "Comparative outcomes of two distance-based interventions for male caregivers of family members with dementia." <i>American Journal of Alzheimer's Disease and Other Dementias</i> 22(2):120-128.</p> <p>Gonyea, J., O'Connor, M., and Boyle, P. (2006) "Project CARE: A randomized controlled trial of a behavioral intervention group for Alzheimer's disease caregivers." <i>Gerontologist</i> 46(6):827–832.</p>	We have conducted a full text review of each selected study and included those deemed eligible after our screening process.
TEP #3	References	<p>Mahoney, D.F., Tarlow, B.J., and Jones, R.N. (2003) "Effects of an automated telephone support system on caregiver burden and anxiety: Findings from the REACH TLC intervention study." <i>Gerontologist</i> 43(4):556-567</p>	We have conducted a full text review of each selected study and included those deemed eligible after our screening process.

Commentator & Affiliation	Section	Comment	Response
TEP #3	References	<p>Samus, Q.M., Johnston, D., Black, B.S., Hess, E., Lyman, C., Vavililkolanu, A., Pollutra, J., Leoutsakos, J-M., Gitlin, L.N., Rabins, P.V., and Lyketsos, C.G. (2014) "A multidimensional home-based care coordination intervention for elders with memory disorders: The Maximizing Independence at Home (MIND) pilot randomized study." <i>American Journal of Geriatric Psychiatry</i> 22(4):398-414</p> <p>Tanner, J., Black, B., Johnston, D., Hess, E., Leoutsakos, J., & Gitlin, L. et al. (2015). A Randomized controlled trial of a community-based dementia care coordination intervention: Effects of MIND at Home on caregiver outcomes. <i>The American Journal of Geriatric Psychiatry</i>, 23(4), 391-402.</p> <p>Tremont, G., Davis, J.D., Bishop, D.S., and Fortinsky, R.H. (2008) "Telephone-delivered psychosocial intervention reduces burden in dementia caregivers." <i>Dementia</i> 7(4):503-520</p> <p>Vickery, B.G., Mittman, B.S., Connor, K.I., Pearson, M.L., Della Penna, R.D., Ganiats, T.G., DeMonte, R.W., Chodosh, J., Cui, X., Vassar, S., Duan, N, and Lee, M. (2006) "The effect of a disease management intervention on quality and outcomes of dementia care." <i>Annals of Internal Medicine</i> 145:713-726.</p>	
TEP #4	References	<p>However, there was one study from 2012 that I did not see listed: Relapse Risk after Discontinuation of Risperidone in Alzheimer's Disease, D.P. Devanand, et al N Engl J Med 2012; 367:1497-1507 October 18, 2012 DOI: 10.1056/NEJMoa1114058</p> <p>It is possible that I missed this in review the bibliography and my apologies if I did.</p>	This study was excluded because there was no nonpharmacologic intervention. We didn't consider 'placebo' a nonpharmacologic intervention.
Soo Borson University of Washington	References	Missing the study I mentioned above Teri L et al that compared imipramine haloperidol a caregiver education module and placebo showing no differences in effects.	We included a Teri et al. 2000 study comparing these interventions. It is among those in the Caregiver Interventions section. Without the full citation, I cannot guarantee this is the same trial, but it seems so.
Peer Reviewer #1	General	The report is marginally clinically meaningful because no recommendations are made for non-pharmacologic interventions. Clinicians are left without any meaningful recommendations despite guideline recommendations for use of non-pharmacologic interventions.	AHRQ reports synthesize the evidence, but do not make recommendations.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	General	Future research section will be useful to inform RFPs. The null findings will not be useful in informing practice decisions.	Most of the evidence was insufficient to draw conclusions. Evidence for a few interventions showed that they were similar to no treatment. These results could inform practice decisions by showing how, when, and with whom a particular intervention did not work. Their knowledge of this evidence in combination with their understanding of their patient and input from the patient and family can inform their decisionmaking process.
Peer Reviewer #2	General	The manuscript is informative, the method appears to be well-considered and the product is scholarly. My overall rating of Good is with the assumption that the target audience is specific and expert in this area. There are times when the manuscript is not easily penetrable, or altogether clear. For example, while "usual care" is referred to in the structured abstract, considerations important to interpreting "usual care" are mentioned later, on page 30, and only in passing.	We elaborate on the control condition, usual care, used in many trials. This is definitely a methodological issue relevant to many topics.
Peer Reviewer #3	General	<p>The topic of the report is clinically meaningful, and the key questions are appropriate and explicitly stated. I simply disagree with the fundamental assumptions of the authors, their methods, and conclusions.</p> <p>I recommend the following article as a counter-argument to the assumptions of the authors:</p> <p>Jiska Cohen-Mansfield, Kathleen Buckwalter, Elizabeth Beattie, Karen Rose, Christine Neville, Ann Kolanowski (2014). Expanded Review Criteria: The Case of Nonpharmacological Interventions in Dementia. Journal of Alzheimer's Disease, Volume 41, Number 1, Pages 15-28.</p>	It is unclear what assumptions the reviewer is referring to. Selection bias inherent in observational studies and lack of adequate control conditions yields results that are very likely attributable to population, setting, or other characteristics, especially when outcomes are measured using subjective reports. Our review sought to identify trials most likely to provide reliable information.
TEP #1	General	This is a well conceptualized, articulated, and operationalized analysis of this area. The limits on defining the target population are inherent to the research in this area, not attributable to the efforts of analysis. The key questions are appropriate and explicitly stated. Though this report largely documents a lack of evidence to justify particular non-pharmacological approaches to managing dementia associated agitation and aggression it is nevertheless quite clinically meaningful. This is because it documents the weak state of research that exists in this area in spite of the desperate need for alternatives to anti-psychotic medications. The report is really a call to action to the research community and funders to direct resources to improving the methods, scope and size of research studies done in this area in order to improve the quality of care delivered to this vulnerable population.	Thank you for the well-articulated summation of the report.

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Commentator & Affiliation	Section	Comment	Response
TEP #1	General	Studies showing equal effectiveness may nevertheless be informative if nonpharmacologic interventions truly have fewer harms but harms needs to be operationalized as harm to others as well as harm to the patient. I am struck that few studies were designed as effectiveness trials that directly compare antipsychotic medications to nonpharmacological trials when this is what policy is calling for and when comparable effectiveness but lessened harms would important inform policy and practice. Thus I believe the most important outcome of the report should be for DHHS/CMS to be encouraged to support a large scale, well designed comparative effectiveness trial of anti-psychotics vs. behavioral best practice in this area.	This is not a future research need based upon our key questions. It is our understanding that the harms associated with antipsychotic treatment in individuals with dementia are well established and future research with these agents would be unethical.

Commentator & Affiliation	Section	Comment	Response
TEP #3	General	<p>As the authors' point out, the definition of the outcome measures (measures of agitation and aggression) is confusing for several reasons. Various behaviors of persons with dementia co-exist and overlap. More importantly for this report, the behaviors are usually not carefully distinguished by health care professionals, service providers or researchers. The authors chose to combine the two outcomes for the analysis and to refer to them as 'agitation/aggression.' The authors state that decisions clearly on the first page of the executive summary and the first page of the full report. They note on the 3rd page of the full report (p. 42) but not in the executive summary that "our understanding and measurement of agitation/aggression ... has changed over time and agitation/aggression are now more often considered distinct behaviors." Later, on pps ES 22-23 and 144-146, they discuss important differences between the two outcomes with respect to how they should be understood, when and how they should be treated, and when and how the results of treatment should be measured. This reviewer thinks that most people, including many researchers, clinicians, and policy makers, are not aware of these important differences, or if aware, do not incorporate them in their research plans or clinical care. The discussion about the differences is valuable for all these audiences. At the same time, the authors' decision to combine the outcomes for this analysis and their observations about the important differences between them could be seen as contradictory. This reviewer thinks that the reasons for the authors' decision to combine the outcomes should be noted briefly where the combination is first stated in the executive summary and full report. Perhaps it would also be good to add in both places that the reasons for (or the benefits and limitations of) combining the two outcomes are discussed later, citing the pages where the important differences between the two outcomes are discussed. The reasons and associated limitations would then have to be added in those places.</p> <p>This reviewer wonders if the decision to combine came early in the analysis and full awareness of the differences arose out of the review. If so, it might be helpful to readers to say that. In addition, it might be useful to say that in the future, clinicians, service providers, and researchers should report and measure the two outcomes separately.</p>	<p>The decision to combine the behaviors resulted from what was done in the original research. Systematic reviewers do not have individual patient-level data and are limited by what is provided in the individual trials.</p>

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TEP #5	General	-Citations should be provided for the measures	Citations relevant to commonly used instruments are provided in the table describing outcomes instruments.
TEP #5	General	Again, in several areas of the review whenever changes were identified that were significant, it is continually mentioned that such changes may "not be clinically meaningful." How can this conclusion be drawn when clinical cutpoints or similar information for these measures remains unknown? Moreover, given the disruptive nature of aggression and agitation, is it not possible that even a small change in reducing these problems could have considerable clinical impact?	It is important for a degree of clinical significance be established when outcomes are measured with scales that have a wide variety of score ranges. It is challenging to interpret changes in these scale scores without any guidance on the degree of change that is actually noticeable to persons with dementia or caregivers.
TEP #5	General	I would urge caution regarding whether change on these outcomes/measures are "clinically significant." It seems that throughout the review, the claim is made that these changes "may not be clinically significant," but as noted above I am not sure that is correct in this context.	It is important for a degree of clinical significance be established when outcomes are measured with scales that have a wide variety of score ranges. It is challenging to interpret changes in these scale scores without any guidance on the degree of change that is actually noticeable to persons with dementia or caregivers.
Ellon Caspi PhD	General	What is needed is holistic, comprehensive, whole person approaches consisting systematic and simultaneous implementation of all "culture change" components whether at home or in a LTC residence. There is a need to continue and shift from single-component interventions to multi-component interventions (which are much more successful).	Many of the interventions studied could be described as multi-component or comprehensive, whole person approaches.
Ellon Caspi PhD	General	Also, in most studies evaluating effects of psychosocial interventions in LTC residences, even when a reduction is shown in behavioral expressions (such as "aggressive" behaviors) immediately after the intervention, when you come back 3 months later the effects usually disintegrates because no mechanisms for sustaining the effects were put in place. There is an urgent need to ensure that every intervention will include these mechanisms for long-term sustainability of effects.	Agree, if we had found sufficient evidence that one intervention or another worked in decreasing agitation/aggression, we would have then assessed the data for the sustainability of that intervention. We did not find evidence of effectiveness, so therefore could not explore sustainability.
Ellon Caspi PhD	General	Emotion-Oriented Care. Validation Method (Feil, 2012) has been practiced for over 50 years with tremendous success in the U.S. and many other countries. This systematic and whole-person method substantially reduces various forms of behavioral expressions in persons with dementia (including "aggression") and improve the psychological well-being of this population. This is another example of why RCT are not always suitable to capture multi-level psychosocial approaches and interventions. Very difficult to capture the richness and therapeutic value of this method in RCTs.	Our reviewed included two randomized controlled trials that evaluated emotion-oriented care (total n = 297).

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Commentator & Affiliation	Section	Comment	Response
Ellon Caspi PhD	General	<p>Several studies have shown wonderful outcomes when persons with dementia are engaged in meaningful activities. These include:</p> <p>Casey et al. (2014). Computer assisted direct observation of behavioral agitation, engagement, and affect in LTC residents. JAMDA.</p> <p>Schreiner et al. (2005). Positive affect among nursing home residents with Alzheimer’s dementia: The effect of recreational activity. Aging & Mental Health, 9(2), 129-134.</p> <p>Volicer et al. (2006). Effects of continuous activity programming on behavioral symptoms in dementia. JAMDA, 7, 426-431.</p> <p>Clark et al. (1998). Use of music to decrease aggressive behaviors in people with dementia. Journal of Gerontological Nursing</p> <p>Literature review Brotons et al. (1997). Music and dementias: A review of the literature. Journal of Music Therapy.</p> <p>Literature review Lou et al. (2001). The use of music to decrease agitated behavior of the demented elderly: The state of the science. Scand J Caring Sci</p> <p>Literature review showing reduction in restless behavior and improvement in sleep: Penrose et al. (2005). Can exercise affect cognitive functions in Alzheimer’s disease? A review of the literature. Activities, Adaptation, & Aging, 29(4), 15-40.</p>	
Ellon Caspi PhD	General	<p>If not done so, I also recommend looking into the research literature on intergenerational activities and pet therapy (“Animal-Assisted therapy”) with persons with dementia. Two of the most effective modalities for reduction of behaviors and improvement in psychological well-being.</p>	<p>Many of these interventions have been studied in observational studies. We did not identify trials that were conducted to confirm results from observational studies.</p>

Commentator & Affiliation	Section	Comment	Response
Ellon Caspi PhD	General	<p>Another very effective intervention is Care Farms for person with dementia. This intervention is implemented throughout the Netherlands and Sweden and only recently has started to be implemented in the U.S. (in Montana).</p> <p>Maarten Fischer who led this initiative in the Netherlands (got a 5 million Euro grant from the Dutch government to expand the program) who leads this initiative in Montana can tell you about the research studies that showed effectiveness of this innovative care model.</p> <p>Maarten can be reached at: mfischer@aplushc.com</p> <p>One study is:</p> <p>Schols et al. (2006). Day care for Demented elderly in a dairy farm setting: Positive first impressions. JAMDA.</p>	<p>Thank you for the reference. This study is a small observational study and was not eligible for our review. We did not identify any trials that may have been conducted to confirm results for this type of intervention.</p>
Lynn F. Bufka, PhD American Psychological Association	General	<p>The original proposal submitted by members of this organization for a comparative effectiveness review addressed a much broader range of questions than what this review eventually analyzed. The proposers were interested in nonpharmacological interventions that address a range of issues among individuals with dementia while this review focused on those interventions specifically reporting on changes in outcomes related to agitation and aggression. As the reviewers describe, the empirical evidence in this limited domain is under-whelming and has many limitations.</p>	<p>Agree. The original nomination undergoes a topic refinement process. We spoke with several Key Informants including representatives from APA. That process established agitation/aggression as the highest priority behaviors and we therefore revised the key questions to develop a project with a feasible scope focusing on the highest priority outcomes. Other behaviors may benefit from systematic review; however, evidence on interventions addressing other behaviors is likely also limited. The limitations are not with the number of trials and the amount of work necessary to conduct the systematic review, but on the quality of the evidence necessary to arrive at firm conclusions.</p>
Lynn F. Bufka, PhD American Psychological Association	General	<p>We very much appreciate the discussion of the limitations of the current research as well as the important points raised in the section on future research needs.</p> <p>We also believe a much wider range of behavioral issues and outcomes are important to address in this population and don't want this review to discourage future research.</p>	<p>We agree that many behaviors that commonly accompany dementia are important, our report focused on agitation/aggression, so we cannot comment on the state of the literature with regard to other behaviors.</p>

Commentator & Affiliation	Section	Comment	Response
Lynn F. Bufka, PhD American Psychological Association	General	It is important to note that even when interventions might not have changed the target of agitation or aggression, those that had a positive impact on caregivers are also important. Regrettably, again the authors noted that those trials examining such concerns were often limited in size or had methodological problems such that evidence was insufficient for comparisons. Highlighting that this is also an important outcome would be worthwhile.	While these secondary outcomes are important, it is not clear that these interventions are the best way to achieve those outcomes. If the interventions had worked as hypothesized and the interventions improved these secondary outcomes as well, that would be valuable information. A systematic review evaluating all caregiver interventions would best identify interventions most effective in improving caregiver outcomes.
Lynn F. Bufka, PhD American Psychological Association	General	Lastly, given the press to reduce medication management of behavioral problems within individuals with dementia, more attention to research that compares pharmacological and nonpharmacologic interventions, along with their associated benefits, harms and burdens, is of the utmost importance.	This is not a future research need based upon our key questions. It is our understanding that the harms associated with antipsychotic treatment in individuals with dementia are well established and future research with these agents would be unethical.
Lynn F. Bufka, PhD American Psychological Association	General	Reviewer comment on outcomes: It is important to note throughout the report that these analyses are specific to agitation and aggression. For instance, even in the Contents (vi) and corresponding report, changes in headings are needed. In the results section the term should be added to the headers on pages 80 and 83, "Patient-Level Interventions for Agitation/Aggression for Community-Dwelling Individuals with Dementia" and "Caregiver-Level Interventions for Agitation/Aggression for Community-Dwelling Individuals with Dementia," and in other places throughout the document to underscore the limited focus of this review.	Our intention was to look specifically at agitation/aggression outcomes, but many studies only measured behaviors using general behavior instruments. Those were also included. This is described in the report and given that agitation/aggression are in title of the report, we do not feel it is necessary to reiterate the specific behaviors in subheadings.
Lynn F. Bufka, PhD American Psychological Association	General	We wholeheartedly endorse the call for more research on nonpharmacological interventions and hope this report can spur additional research in this arena.	We agree.
Lynn F. Bufka, PhD American Psychological Association	General	We hope that readers of this report do not interpret the lack of evidence specific to this arena as a conclusion that non-pharmacological interventions are not effective for agitation and aggression nor generalize further to conclude that nonpharmacological are not effective for any problems. Rather, we hope that this report will spur further development and evaluation of behavioral and other nonpharmacological interventions to address the needs of individuals with dementia.	We agree, insufficient evidence is not evidence of ineffectiveness.

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Lynn F. Bufka, PhD American Psychological Association	General	Given the limited evidence, we suspect this review is unlikely to serve as a basis for a clinical practice guideline in this domain. However, we encourage the authors to consider the needs of future guideline developers and present information in a format that is most accessible to that audience (e.g. evidence profiles, etc.)	Summary tables including strength of evidence are provided in the report and executive summary.
Sonya Barsness, Sonya Barsness Consulting LLC	General	I offer these comments based on my over 20 years of experience in working with people with dementia, learning about the experience of dementia from people living with dementia, and ask that they be considered in providing a more balanced interpretation of current research as well as a call for further research to look more broadly than non-pharmacological interventions to the impact of person-centered paradigm of dementia care. As a co-developer of CMS' Hand in Hand Training Toolkit, we were very thoughtful in the creation of the Hand in Hand content so that it reflected a person-centered approach that seeks to see things from the perspective of the person with dementia and understand why she or he might be acting or reacting that way (what is the reason behind his/her "behavior"). In the interpretation and discussion of this analysis I respectfully ask that you consider including reference to this growing person-centered paradigm.	Our selection of outcomes reflects our emphasis on patient-centered outcomes.
Sonya Barsness, Sonya Barsness Consulting LLC	General	Overall, it should be noted that this report almost entirely reflects a purely medical model of dementia care that does not include the broader view of a person-centered paradigm. In order to fairly interpret the studies included in this review I believe it is important to acknowledge the foundational context of the medical paradigm underlying these studies, as well as an alternative person-centered paradigm that does not appear to be reflected in most studies on the use of non-pharmacological interventions. This person-centered paradigm is not merely a program or model, it is a philosophy and practice based on several values. A recent overview of person-centered dementia care can be found at http://www.ccal.org/wp-content/uploads/DementiaCareTheQualityChasm_020413.pdf .	Thank you for your input. Our report accesses the literature on interventions that aim to decrease agitation and aggression in patients with dementia. We found that many of the interventions had a patient-centered approach.
Valerie Perdue PhD, BCDMT	General	As a clinical psychologist and dancemovement therapist as well as the daughter of persons who have had dementia I strongly support the use of nonpharmacological interventions for the treatment of severe behavioral and thought disorders in this group of patients.	Thank You for your input.
G. Allen Power MD	General	Dear AHRQI did not hear about your article on Nonpharmacologic Approaches to Agitation and Aggression in Dementia during the comment window but I have a very important perspective that I feel you need to hear. I will attach two passages from my book Dementia Beyond Disease Enhancing WellBeing c. 2014 Health Professions Press Inc.	Thank You for your input.

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Commentator & Affiliation	Section	Comment	Response
<p>G. Allen Power MD</p>	<p>General</p>	<p>Why Nonpharmacological Interventions Do Not Work This provocative heading may seem out of line for the author of a book called <i>Dementia Beyond Drugs</i>. Rest assured I remain firmly rooted in the belief that most distress arises as expressions of unmet needs and that drugs are not the answer. The problem lies not in that underlying philosophy but in how it is applied. I will devote a bit more space in this book to this argument because it is extremely important and not as easily understood. To begin with I have two problems with the term nonpharmacological interventions nonpharmacological and interventions. The first term defines the approach by what it is not rather than what it is. It keeps medication use as our reference point in spite of our rejection of that approach. Even if it does not explicitly state that a drug approach is the gold standard it implies that it is at least a viable option an either/or choice for the care partner. This is not the language that will help us shift our paradigm.</p> <p>The second term brings to mind the act of holding an intervention. In that context an intervention is characterized by a group of caring people who lure a friend or relative to a meeting place under false pretenses then hold him captive while they confront him about a behavior of his that they feel is harmful and demand that he get back on the right track. What strikes me is how much our nonpharmacological interventions follow this same pattern. Generally they are devised and applied by a group of caring friends relatives or paid staff in response to a behavior that we have judged to be potentially harmful. There are often false pretenses involved whether through distraction diversion or even various degrees of deception those little white lies we often use to try to calm someone. Finally we tend to remain centered on the ultimate goal of bringing the person back in line with what WE feel is best for him either not considering what it is the person truly needs or discounting his stated needs as not being realistic.</p>	<p>Thank you for your insight. The term ‘nonpharmacologic’ is a term that encompasses the wide variety of interventions addressed in our review. It is also consistent with guideline recommendations to first use nonpharmacologic treatments to address challenging behaviors.</p> <p>The term ‘intervention’ is widely accepted in systematic review literature (i.e. PICOTS) and we have decided to continue using the term.</p>

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<p>G. Allen Power MD</p>	<p>General</p>	<p>There are many other reasons why nonpharmacological interventions fail to provide a solution to distress including the following1. They are reactive. They respond to a moment of crisis and whilethey may calm a situation they often do not seek to understandthe underlying causes and how they can be prevented in the future.For example if a person in distress responds to being movedto a quiet place and being given a hand massage then that approachwill be applied again and again ad infinitum withoutturning our attention to how to stop the distress from recurring inthe first place.2. They are treated like doses of pills. Fold washcloths once a day orPet a cat three times a day before meals do not explore the rootcause of the distress. As a result like doses of pills the effect ofsuch interventions will wear off and have to be readministered.Readers of my first book may recall that I previously addressedthis idea and did not quite get it right.3. They are not persondirected. A typical list of possible interventionsis often little more than a generic algorithm to apply in a trialanderror fashion based on what we feel might work. We may hiton something that seems to work once or twice and stop there.What we too often fail to do is to understand the person and lether unique perspective needs and abilities drive our approaches.As a result they are often devoid of meaning for the individual.4. They are superimposed upon the usual living environment and approachesto care. If the living environment and approach to care arean ongoing cause of the unmet need then we can never achievelasting success.5. They are not tied into domains of wellbeing. This is the main themeof the book and will be explored in detail in the pages that follow.</p>	<p>We found few trials that offered reactive treatments to particular behavioral episodes, most trials were unclear about their objectives, but appeared to have the purpose of preventing or decreasing the frequency of negative behaviors. Some interventions were based upon an unmet needs model.</p>

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Commentator & Affiliation	Section	Comment	Response
<p>G. Allen Power MD</p>	<p>General</p>	<p>In summary nonpharmacological interventions as they are mostcommonly applied are attempts to provide personcentered care from a biomedical mindset. As such it is only a halfhearted paradigm shift and so it falls short. The fatal flaw with either approach is a focus on the distress as the problem rather than as a symptom of a larger issue. I often equate it with treating pneumonia with cough syrup. People with pneumonia often have a very bothersome cough. If a doctor sees the cough as the primary problem then taking the cough away becomes the goal and cough syrup is prescribed. That may quiet the cough for a while but eventually the person will get worse because the pneumonia is still festering and has not been properly addressed. In a similar manner if we see the persons distress as the problem then our primary goal becomes the elimination of the distress. This explains why so often we become stuck in the pill paradigm. Of course just like the cough syrup a pill might quiet ones distress for a while often through some degree of sedation. We get in trouble when we conclude that we have successfully addressed the primary problem when all we really have done is covered it up by calming the symptom. And the person will eventually get worse either because we did not address the real cause or because the pill itself is causing additional harm.What Is Our Primary GoalAll of the above suggests that in spite of our efforts to reduce the useof potentially harmful medications we are still not going about it theright way. Our federal government is right to be concerned about theoveruse of such medications in people living with dementia but a directive to reduce medication use by X percent by a given date andthe pledges of longterm care organizations to do so puts the cart before the horse and sets us up for shorterterm gains that cannot be sustained over time. In this book I argue that although I am a strong supporter of reducing our reliance on psychotropic drugs this is not our primary goal. It is a highly desirable outcome but it is not the place to start. Furthermore I do not even believe that reducing distress should be our primary goal. Once again it is a very desirable longterm outcome but distress is the cough not the pneumonia. I believe that our primary goal is to enhance wellbeing. This isa concept I discussed briefly in Dementia Beyond Drugs but my subsequent work has convinced me that it is THE central issue in improving the lives of people with dementia and it provides the best vehicle for creating sustainable success. pp 36And this passage on the topic of research</p>	<p>Thank you for your insight. We agree that pharmaceutical interventions have been relied on heavily in the past.</p>

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		<p>During a speaking trip to Iowa in 2011 I heard the story of a gentleman who lived in an assisted living home in a rural part of the state. He was repeatedly attempting to exit the back door and each time was redirected by his care partners who did not feel he was safe walking outside alone. His attempts to go outside became more insistent with each redirection. Finally the administrator suggested that the staff not interfere the next time he opened the door but simply watch from the doorway to see what he might be trying to accomplish. When they did so the gentleman walked to the fence at the back of the yard which adjoined a cow pasture. He watched the cattle grazing for about 10 minutes and then turned around and came back inside. In soliciting more information about the gentleman they learned from his family that he had been a farmer who would go out every day to check on the cows. This pattern was being repeated at the home and once this longstanding practice was revealed he was able to do so daily with the knowledge that his identity was being preserved and his need fulfilled. This is a good example of why our attempts at nonpharmacological interventions and our research studies of these interventions often produce disappointing results. We may try aromatherapy music or laundry folding when maybe the person simply needs to check on the cows pp. 60611 hope you will accept this late submission as an important addition to your dialogue on how we need to rethink how we support people living with dementia and shift our paradigm about what nonpharmacological approaches really means.</p>	<p>Thank you for this example; we found no trials evaluating similar interventions.</p>