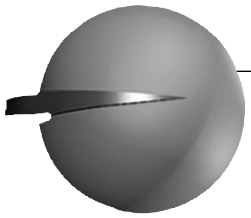

Evidence Review

Nonpharmacological Therapy for the Management of Neuropsychiatric Symptoms of Alzheimer's Disease: Linking Evidence to Practice

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Keywords
Alzheimer's disease, dementia, nonpharmacological interventions, agitation, behavioral and psychiatric symptoms of dementia, caregivers, training program

ABSTRACT

Background: Behavioral and psychiatric symptoms of dementia affect up to 90% of all patients at some point during their dementing illness. Today, many of these symptoms are treated with pharmacological therapy alone, incongruent with clinical recommendations. Barriers to the use of nonpharmacological interventions with dementia include a lack of education among caregivers on available options, shortage of time for implementation, lack of education on effects of nonpharmacological therapy, poor staff to resident ratios, and unmodifiable physical environments.

Aims: The purpose of this paper is to explore current literature regarding the implementation of nonpharmacological therapy as an adjunct treatment to manage agitation in dementia, to identify practice discrepancies seen commonly among formal and informal caregivers, and to make recommendations for implementing evidence into practice.

Methods: A systematic review of the literature published between 2009 and 2014 was conducted. Four databases were searched including CINAHL, Pubmed, the Cochrane Library, and PsycInfo.

Findings: The most prevalent and substantial conclusion among the 10 studies evaluated is that nonpharmacological therapy is safe and effective. Although not every study was able to show statistically significant outcomes when compared to controls, all studies demonstrated a positive trend toward decreasing agitation without any adverse side effects.

Linking Evidence to Action: A multicomponent caregiver education program focused on evidence-based nonpharmacological strategies for addressing agitation in persons with Alzheimer's disease has the potential to decrease agitation, improve patient outcomes, and increase caregiver satisfaction.

BACKGROUND AND SIGNIFICANCE

Advancing medical treatments and cutting-edge technologies are providing many individuals with a longer life expectancy. This growing percentage of the aging population places a substantial weight on countries throughout the globe as they struggle to provide community resources, sustain interpersonal relations, and maintain the caregiver and patient dyad. Additionally, countries are now faced with a healthcare economic crisis that includes a paradigm shift in loss of health and life associated with noncommunicable and chronic diseases, such as Alzheimer's disease, rather than those caused by infectious pathology (United States National Institute on Aging, 2007).

Problem Statement

According to the *World Alzheimer Report 2012 Overcoming the Stigma of Dementia*, 36 million people worldwide were living with Alzheimer's disease in 2010 (Batsch, Mittelman, & Alzheimer's Disease International [ADI], 2012). Estimates suggest that by the year 2050, these numbers will rise to an astounding 115 million, an increased morbidity of 24.6 million cases a year (Batsch, Mittelman, & ADI, 2012). With a population health focus, Alzheimer's disease management is a priority. In 2010, Alzheimer's disease was estimated to consume just over 600 billion dollars of the global budget; 1% of the world's gross domestic product (Batsch, Mittelman, & ADI, 2012). Experts in the field have stated that by the year 2030, the worldwide societal costs of dementia will rise by nearly 85%, necessitating that this epidemic be moved to the forefront of our healthcare and financial systems (Batsch, Mittelman, & ADI, 2012).

Hallmark symptoms of Alzheimer's disease include memory loss, poor judgment, expressive or receptive aphasia, severe difficulty with completion of activities of daily living, and neuropsychiatric symptoms (Alzheimer's Association [AA], 2013). Neuropsychiatric symptoms, also called behavioral and psychiatric symptoms of dementia (BPSD), affect up to

Worldviews on Evidence-Based Nursing, 2015; 12:2, 108–115.

90% of all patients at some point during their dementing illness. These behaviors cover a wide range of clinical presentations and include symptoms such as hallucinations, anxiety, agitation, irritability, depression, abnormal motor movements, apathy, and sleep changes (Cerejeira, Lagarto, & Mukaetova-Ladinska, 2012; Gledmacher & Kerwin, 2013). Agitation is one of the most difficult behaviors to manage and is currently the leading reason for institutionalization and pharmacological therapy among patients with Alzheimer's disease (Gauthier et al., 2010). Moreover, BPSD plays a momentous role in declining quality of life with rising dementia care dollars, placing a significant burden on caregivers and leaving many susceptible to a multitude of health-related issues of their own (Richardson, Lee, Berg-Weger, & Grossberg, 2013; Toot, Devine, Akporobaro, & Orrell, 2013).

Rationale

There are no definitive measures to cure Alzheimer's disease, thus precedence is shifting to the prevention of Alzheimer's disease and proper management of those persons affected. Current clinical guidelines endorsed by the National Institute for Health and Care Excellence recommend that, after diagnosis, management of patients with Alzheimer's disease focus on promoting independence and maintaining function (National Collaborating Centre for Mental Health, 2007). For this reason, several governmental bodies across the world have developed national policies that encourage dementia research, provide support to patients and their families, and address the financial impact Alzheimer's disease has on their nation.

In countries like France, Australia, and England, strategies focus on increasing community awareness of Alzheimer's disease, whereas Scotland has declared access to diagnostic testing and disease management as a national priority (Batsch, Mittelman, & ADI, 2012). In the United States, the National Alzheimer's Project Act, statute Public-Law 111–375, stands as the first nationally developed plan to address Alzheimer's disease. This act provides a blueprint for disease management and enhances current strategies for removing the burdens associated with Alzheimer's disease symptoms (United States Department of Health & Human Services, 2014). Out of this law, the first Alzheimer's disease proposal was generated, The Healthy Brain Initiative, which has been instrumental in the development of clinical practice guidelines for disease management (AA, 2013; Centers for Disease Control & Prevention [CDC], 2013). In 2010, the Healthy People 2020 (2013) project released its next 10-year agenda for improving the health of the U.S. nation, which for the first time, included the health objectives of lowering the cost and morbidity associated with Alzheimer's disease and increasing the quality of life of those afflicted.

Purpose

At this time, to control BPSD, antidepressants, antianxiety, and antipsychotic medications are used since they have been shown to produce a mild but significant short-term affect (Ballard & Corbett, 2013). However, in 2012, the American Geriatric Society suggested avoiding antipsychotic use in the elderly population due to the increased mortality from cerebrovascular events. Other side effects of antipsychotic therapy include falls, extra pyramidal symptoms, metabolic effects, infections, and further cognitive decline (Steinberg & Lyketsos, 2012). In fact, patients taking an antipsychotic medication in the community are 3.2 times more likely to be hospitalized than their counterparts, related to complications from therapy (Rochon et al., 2008).

Nonpharmacological therapy includes strategies such as removing stressors and providing a safe environment, to patient participation in activity-based interventions comprised of music, exercise, massage, and art (Sadowsky & Galvin, 2012). Benefits of nonpharmacological therapy implementation include fewer adverse side effects, increased patient and caregiver satisfaction, and reduced healthcare costs (Hulme, Wright, Crocker, Oluboyede, & House, 2010). Cited in several studies, nonpharmacological therapy has the ability to decrease the frequency and severity of neuropsychiatric behaviors in patients with Alzheimer's disease when implemented early and consistently and tailored to the individual patient's preferences (Brodaty & Arasaratnam, 2012; Deudon et al., 2009; Kolanowski & Hill, 2013; Ueda, Suzukamo, Sato, & Izumi, 2013). Therefore, if improving quality of life and decreasing the costs associated with care are international objectives, as such, there is an identified need for improved management of these neuropsychiatric symptoms. Hence, the purpose of this paper is to explore current literature addressing the use of nonpharmacological therapy as adjunctive therapy for the management of agitation in dementia, to discuss the barriers associated with employing this treatment in current patient care, and to conclude with an evidenced-based intervention for translating evidence into practice. To facilitate this thorough literature review, a clinically relevant PICO (i.e., patient population, intervention, comparative intervention, outcome) question was developed, "In older adults diagnosed with Alzheimer's type dementia (P), how does the implementation of nonpharmacological therapy in combination to pharmacological therapy (I), compared to pharmacological therapy alone (C), affect agitation (O)?"

SEARCH STRATEGY

To complete this literature review, the following databases were searched: CINAHL, Pubmed, the Cochrane Library, and PsycInfo. Initial search strategy included the keywords: dementia, Alzheimer's (disease), nonpharmacological (interventions), agitation, behavior(s), and psychological symptoms. The population was defined as dementia or Alzheimer's disease and the outcome of interest included agitation or behavior or psychological symptoms. To yield a more manageable initial search, the limitations of humans and adults (18 years of age and older) were applied to the keywords. This modified search generated 14,588 references in CINAHL; 139,927 references in Pubmed; and 41,277 references in PsycInfo. No limitations

were applied to the initial search in the Cochrane library as these limitations remain unavailable. Next, the keywords nonpharmacological, dementia or Alzheimer's disease, and agitation or behavior or psychological symptoms were searched in all four databases. Limitations were set requiring research articles only and studies published between the years 2009 and 2014 to facilitate a clinically up-to-date search. This specific search produced 13 references in CINAHL, 33 references in Pubmed, 19 references in PsycInfo, and 9 references in the Cochrane Library.

An extensive search of previously yielded articles provided several more medical subject headings (MESH) for the keyword nonpharmacological. These terms, which included: music, music therapy, touch, massage, exercise, aromatherapy, and multisensory, were independently searched in all four databases. From there, a more precise search was conducted using MESH terms and the Boolean connector "and" with the keywords for population and outcome. Explicit inclusion criteria were used including being published between the years 2009 and 2014, and research articles only.

To complete this exhaustive search, a hand ancestry was executed on current references. All of the references in the identified articles were reviewed, but results led to studies published beyond the 5-year inclusion criteria and thus are not included in this literature review. A search of gray literature was conducted for background and significance and included position papers, practice guidelines, and quality improvement projects but again were excluded based on a low level of evidence. Of those studies meeting inclusion criteria, several were discarded related to obvious flaws in methodology (including the absence of standardized measuring tools and standardization of treatment), ethical considerations not being upheld, poor documentation, and incomplete statistical analysis.

CRITICAL APPRAISAL

After applying Melnyk and Fineout-Overholt's (2011) rapid critical appraisal strategy, 10 studies were included in this literature review; all studies are presented in a synthesis table for analysis of data (Table 1). Overall, the strength of the studies was high, including one systematic review (SR) and three meta-analyses (MTA) for Level I evidence, five randomized control trials (RCT) for Level II evidence, and one nonrandomized control trial for Level III evidence. Large sample sizes were used in the controlled trials with a high volume of studies evaluated in the SR and MTAs. All articles required a medical diagnosis of dementia and included strict definitions for what was to be considered nonpharmacological therapy.

Reliability and validity of evidence is assumed through the use of standardized measuring tools for outcome evaluation and the production of statistically significant data. Although none of the studies listed specificities or sensitivities for their measuring instruments, six of the studies documented a standardized measuring tool well known to the field of research titled, The Cohen-Mansfield Agitation Inventory (CMAI; Cohen-Mansfield, Thein, Marx, Dakheel-Ali, & Freedman, 2012) while the other studies chose from an array of alternative high-quality measuring tools including the Pittsburg Agitation Scale and the Neuropsychiatric Inventory. All studies implemented interventions on patients with significant cognitive impairment, thus actual results may underestimate the true benefits of nonpharmacological therapy on mild cognitive impairment. Of the four studies that provided narrow confidence intervals in their statistical findings, three were able to validate significance. Three of the 10 studies listed significant effect sizes; however, all were of weak power.

A moderate degree of homogeneity was identified among the studies in regard to population demographics. The majority of study participants was between the ages of 70 and 90 years and most were women (Table 1). Although this would appear as a limitation, it is important to note the epidemiology of Alzheimer's disease—most people affected are over the age of 65 and more women than men are diagnosed. Transferability is negatively impacted due to the failure of the SR and MTAs to provide specifics on population characteristics. However, the fact that six of the studies were performed internationally with limited exclusion criteria drastically increases the generalizability of study findings.

EVIDENTIARY SYNTHESIS

There was a mild degree of heterogeneity regarding study interventions and outcome evaluation, although all studies examined nonpharmacological therapy and some aspect of BPSD (Table 1). The most common interventions assessed were exercise programs, aromatherapy, massage, music therapy, and caregiver education and skills training. To promote transferability of results, the studies evaluated patients in both inpatient units and outpatient settings and included both formal and informal caregivers.

Based in a community setting, a systematic review composed of five studies varying in quality and methodology, supported exercise treatment as a nonpharmacological therapy for agitation in dementia, noting that therapy reduced the prevalence of BPSD (Hulme et al., 2010). This article provides support for ease of implementation with informal caregivers living with dementia patients in their homes. Unfortunately, no specifics regarding the patient's exercise therapy protocol were provided. Examining exercise programs in an inpatient unit, an RCT conducted by Aman and Thomas (2009) described a protocol consisting of 40 minutes of therapy 3 days a week with 15-minute walking sessions, 15-minute weight-lifting sessions, 5-minute sit and stand exercises, and 5 minutes of beach ball throwing. Outcome measures indicated exercise therapy significantly decreased agitation in patients that were agitated at baseline ($p < .001$) and those not agitated at baseline ($p = .034$), thus providing great generalizability of study results (Aman & Thomas, 2009).

Aromatherapy and massage therapy did not produce statistically significant results; however, a positive trend in decreasing agitation symptoms was consistently noted. Studies representing these results include both an RCT examining

Worldviews on Evidence-Based Nursing, 2015; 12:2, 108–115.

Table 1. Synthesis Table

	Author									
	Aman	**Brodaty**	**Cohen-Mansfield**	**Deudon**	**Fu**	**Hulme**	**Lin**	**Ueda**	**Vasionyte**	**Vink**
Study characteristics										
Year	2009	2012	2012	2009	2013	2010	2011	2013	2013	2012
Design:										
Systematic review						X				
Systematic review + meta-analysis		X						X	X	
Randomized controlled trial			X	X	X		X			X
Nonrandomized controlled trial	X									
Setting:										
Community-dwelling		X				X		X	X	
Inpatient	X		X	X	X		X	X	X	X
Population demographics										
Sample:										
Number of sites	2		6	16	3		3			4
n			231	306	67		104	651	478	77
N		23				33		20	19	
Duration of intervention	3 wk	6 wk- 24 months	2 wks	8 wks	6 wks		6 wks			4 months
Patient characteristics:		N.P.				N.P.		N.P.	N.P.	
Age (mean)	IG= 78.8		85.7	IG= 86.5	84		IG= 82.15			IG= 82.42
	CG= 81.1			CG= 86			CG= 81.46			CG= 81.76
Female gender (%)	IG= 77.5		74.4	IG= 77	59		IG= 53.06			IG= 67
	CG= 70			CG= 78.7			CG= 52.94			CG= 74
Caucasian race (%)			76.8							
Cognitive status:										
GDS (%)										Stage 3: IG= 0% CG= 3% Stage 4: IG= 2% CG= 12% Stage 5: IG=35% CG= 18%

(*Continued*)

Table 1. Continued

	Author									
	Aman	**Brodaty**	**Cohen-Mansfield**	**Deudon**	**Fu**	**Hulme**	**Lin**	**Ueda**	**Vasionyte**	**Vink**
										Stage 6: IG= 30% CG= 50% Stage 7: IG= 19% CG= 9%
MMSE (mean):			8.12	IG= 9.2	All		IG= 12.8			
				CG= 12.1	<24/30		CG= 13.8			
SLUMS (mean):	IG= 1.4									
	CG= 1.7									
Independent variables										
Cg iInterventions:										
Education		X	X	X						
Skills training		X	X	X						
Environmental Redesign		X	X							
Protocol Implementation			X	X						
NPI:										
Aromatherapy					X	X				
Cognitive stimulation Therapy						X				
Light therapy						X				
Massage					X	X				
Music therapy							X	X	X	X
Exercise program	X					X				
Measurable outcomes										
Agitation	X		X	X	X		X			X
BPSD		X				X		X	X	
Cg reaction to BPSD		X								
Anxiety								X		
Physiologic parameters									X	

Note. BPSD, behavioral psychological symptoms of dementia; CG, control group; Cg, caregiver; GDS, global deterioration scale; IG, intervention group; MMSE, mini-mental status examination; N, sample size (studies); n, sample size (people), N.P., not provided by article; SLUMS, St. Louis University Mental Status Examination; Wks, weeks.

Worldviews on Evidence-Based Nursing, 2015; 12:2, 108–115.

the effects of aromatherapy alone (lavender spray to a patient's chest twice a day for 6 weeks) compared to both aromatherapy with massage (lavender spray twice a day for 6 weeks with a 2.5-minute hand massage) and a systematic review investigating both aromatherapy and massage therapy independently (Fu, Moyle, & Cooke, 2013; Hulme et al., 2010). Strengths of these interventions include ease of implementation, ability to be applied in both inpatient and outpatient settings, and treatments that can be provided by both formal and informal caregivers.

Three of the SRs and MTAs examined the effects of music therapy on BPSD, all providing positive results that music decreases agitation, but without statistical significance. Hulme et al. (2010) concludes that both music and music therapy reduces agitation, preferably when aligned with individual music choices, when played during high stimulation moments, and when complemented by group therapy interventions (singing and playing musical instruments). Ueda et al. (2013) reviewed 20 previously conducted studies and indicated that singing along with lyrics, listening to music, rhythmic exercises combined with music, and patient improvisation all reduce BPSD when implemented early and consistently. Vasionyte and Madison (2013) examined the difference between individual and group therapy along with the effects of live music versus recorded music and was able to conclude that all musical therapy interventions had a positive effect on decreasing BPSD or agitation, thus opening the possibility for a range of implementation strategies. In a RCT conducted in four different sites with a total of 77 participants, the effects of music therapy performed by a trained musical therapist was evaluated (Vink et al., 2012). The protocol included 40 minutes of therapy twice a week, alternating sessions of passive listening and active participation (e.g., singing, dancing, playing instruments), which lowered agitation from baseline to 4 hours after intervention ($p = .09$). The lack of statistically significant findings in this study is attributed to the control group participants being exposed to other therapeutic activities (Vink et al., 2012). To inspect the long-term effects of music therapy, Lin et al. (2011) performed an RCT using a similar standing protocol as above that stretched over 6 weeks, composed of a twice a week intervention. Again patients were exposed to rhythmic activities, therapeutic signing, passive music listening, and other musical activities. The intervention group experienced significantly lower agitation scores ($p < .001$) than the control group and maintained these lower agitation scores at 1 month follow-up (Lin et al., 2011).

Caregiver education also attested to be a valuable nonpharmacological therapy. Brodaty and Arasaratnam (2012) conducted a MTA reviewing the effects of a community-based caregiver education program on BPSD. Interventions consisted of a skills training session where caregivers learned communication strategies and therapies to enhance patient quality of life, and educational training that taught individuals about BPSD symptoms and nonpharmacological therapies available for implementation. Results demonstrated a decrease in both patient agitation scores ($p < .01$) and in negative caregiver attitudes ($p = .006$). Furthermore, three studies included in the review demonstrated a decrease in caregiver depression and an increase in general caregiver wellbeing after the educational program (Brodaty & Arasaratnam, 2012). Deudon et al. (2009) conducted a similar inquiry using an RCT; here, a 90-minute staff education session covering the topics of dementia, BPSD, and nonpharmacological interventions was provided to 231 formal caregivers among eight nursing homes in the experimental group. Goals of the session included increasing caregiver knowledge of BPSD and providing caregivers with examples of nonpharmacological therapies available for implementation. Patients residing in these facilities demonstrated significantly lower agitation scores after the initial education session ($p < .01$); 12 weeks after the intervention, these patients continued to exhibit lower agitation levels than their counterparts ($p < .01$; Deudon et al., 2009). Both of these studies lend appreciation to the idea that caregivers, including formal and informal, possess the ability to influence the occurrence and severity of BPSD. It is supported that group teaching sessions may decrease agitation in dementia patients and increase the implementation frequency of various nonpharmacological therapies (Deudon et al., 2009).

LIMITATIONS

The lack of coherence among the implementation strategies included in this review can be explained by the initial search strategy, all nonpharmacological therapies were investigated to facilitate a deeper understanding of the breadth of evidence available. As the results were narrowed, only articles containing therapies capable of being employed in a short time frame and those with the most feasible evidence for implementation in the described settings were retained. Another noted limitation is the absence of emerging terms such as patient-centered dementia care as a nonpharmacological therapy. Imploring an aspect for future research, this model of holistic care delivery has been supported internationally for its use in dementia care. Other aspects of future research include the measurement of long-term outcomes such as patient quality of life, caregiver satisfaction, and caregiver burden along with the recommended frequency, duration, and setting of educational sessions.

PRACTICE DISCREPANCY

A discrepancy between evidence-based practice guidelines and the treatment of behavioral and psychological symptoms of dementia exists in the current healthcare system. In 2006, the American Board of Family Medicine initiated a standardized set of clinical practice guidelines for the management of behavioral problems in dementia. This document explicitly states that drug therapy should only be used as adjunct therapy when nonpharmacological therapy fails to fully control a patient's symptoms (Sadowsky & Glavin, 2012). Again in 2007, the National Institute for Health and Care Excellence published guidelines emphasizing nonpharmacological therapy for both noncognitive symptoms and challenging behavior unless the patient presents in severe distress or appears to be a danger to themselves (National Collaborating Centre for Mental Health, 2007). This suggestion strongly supports

that the management of patients with Alzheimer's disease focus on promoting independence, maintaining function, and endorsing quality of life (National Institute of Health, 2007).

Although nonpharmacological therapy appears to be first-line treatment for the management of agitation in dementia, current clinical practice remains subpar. Many arguments have been made for this practice discrepancy with common barriers cited as a lack of education among caregivers regarding availability and efficacy of nonpharmacological therapy, time restraints that hinder nonpharmacological therapy implementation, poor staff to resident ratios, and unmodifiable physical environments (Janzen, Zecevic, Kloseck, & Orange, 2013). Furthermore, both formal and informal caregivers struggle to understand agitation as a symptom and many do not possess the skills to accurately assess agitation or to intervene early and consistently. This obstacle is closely related to the fact that formal and informal caregivers alike are receiving minimal training and preparation in regards to dementia care. Not only does this lack of education lend to poor patient outcomes, but it promotes vulnerability in regard to poor job satisfaction and early burnout. As a solution, the World Health Organization is strongly endorsing that all long-term care facilities and outpatient programs participate in a structured training platform to provide these caregivers with increased knowledge, stronger support systems, and a wider range of clinical skills (Batsch, Mittelman, & ADI, 2012).

DISCUSSION AND IMPLICATIONS FOR PRACTICE

Fortuitously, even on the verge of an economic and healthcare epidemic, evidence has provided a solution with the implementation of nonpharmacological therapy in the management of neuropsychiatric symptoms. Nonpharmacological therapy is safe and effective. Although not every study was able to show statistically significant outcomes, all studies demonstrated a positive trend toward decreasing BPSD without adverse side effects. Overall, nonpharmacological interventions are feasible in both an inpatient and outpatient setting and may be implemented by formal and informal caregivers.

Research has demonstrated that a reduction in neuropsychiatric symptoms decreases patient injuries, hospitalization rates, and caregiver burden. Thus, a practice change facilitating nonpharmacological therapy presents a potential cost benefit for the current healthcare system and serves as a tertiary prevention strategy. A recommendation to improve the dissemination of this evidence is a multicomponent education program, supported by evidence as being an effective nonpharmacological therapy for reducing agitation. Serving as merely a foundation for the systematic changes needed in care delivery, this program will require coupling with ongoing and supportive environmental changes and process modifications that too serve to address the noted barriers of implementation and tailor to all aspects of nonpharmacological therapy.

As an evidence-based practice program, the education provided would address the lack of knowledge regarding agitation as a symptom of dementia by attending to the pathophysiology of the disease and highlighting clinical skills to assess agitation symptoms. In addition, the program would provide caregivers with education on the various nonpharmacological therapies available (e.g., music, aromatherapy, massage, and exercise) and provide interactive coaching on ways to implement them in daily patient care, thus increasing the frequency of nonpharmacological therapy implementation and decreasing the occurrence and severity of neuropsychiatric symptoms. Goals of such a training program embrace increased knowledge of nonpharmacological therapy, the acquisition of positive attitudes regarding multicomponent therapy, and a stronger perceived self-efficacy with respect to the implementation of nonpharmacological therapy. **WVN**

LINKING EVIDENCE TO ACTION

- Caregivers play a pivotal role in the evaluation and management of BPSD.
- Research has demonstrated that a reduction in neuropsychiatric symptoms decreases patient injuries, hospitalization rates, and caregiver burden.
- Nonpharmacological therapy, including music, exercise, aromatherapy, and massage, is safe and effective.
- Group education programs and interactive coaching tailored to the unique needs of the caregiver is effective at decreasing BPSD.
- A multicomponent education program that addresses noted barriers to nonpharmacological therapy implementation and tailors to all aspects of nonpharmacological therapy should be considered as an evidence-based practice change.
- Short-term outcomes of such a program include increased caregiver knowledge, improved caregiver perceived self-efficacy, and positive attitudes regarding nonpharmacological therapy.

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