



Non-Pharmacological Approaches to Managing Dementia-Related Anxiety and Agitation

Manaswi Chigurupati

RPh, PharmD, MPH, Independent Researcher, USA

* Corresponding Author: **Manaswi Chigurupati**

Article Info

ISSN (online): 2582-7138

Volume: 04

Issue: 01

January-February 2023

Received: 26-01-2023

Accepted: 21-02-2023

Page No: 1041-1048

Abstract

Dementia affects millions of people worldwide, and behavioral and psychological symptoms (BPSD), including agitation and anxiety, significantly impair the quality of life of individuals with dementia. These symptoms often lead to caregiver burden, accelerated cognitive decline, and increased institutionalization. While pharmacological treatments, such as antipsychotics, are commonly prescribed, their efficacy is limited and associated with severe risks, including stroke and mortality. Consequently, there has been a growing emphasis on non-pharmacological interventions as safer and more effective alternatives. These include approaches such as music therapy, exercise programs, sensory stimulation, psychosocial interventions, and environmental adjustments. Recent studies highlight the effectiveness of person-centered care and structured caregiver training in alleviating BPSD, offering practical strategies for managing agitation and anxiety. Additionally, therapies such as reminiscence, relaxation techniques, and animal-assisted therapy have demonstrated positive outcomes in reducing these symptoms. Despite promising results, the widespread implementation of these non-pharmacological strategies remains inconsistent, and further research is needed to standardize interventions and assess their long-term efficacy. This review consolidates current evidence on non-pharmacological treatments for dementia-related anxiety and agitation, emphasizing their clinical applications, benefits, and areas where further investigation is needed to optimize care strategies.

DOI: <https://doi.org/10.54660/IJMRGE.2023.4.1.1041-1048>

Keywords: Dementia, agitation, anxiety, non-pharmacological interventions, caregiver training

Introduction

Dementia affects nearly 50 million people worldwide, and this number is rising with population aging ^[1]. Alongside cognitive decline, most individuals with dementia develop behavioral and psychological symptoms (BPSD) such as agitation and anxiety ^[1, 2]. Agitation is one of the most common neuropsychiatric symptoms, reported in up to 70% of people with dementia, while anxiety symptoms affect roughly 40% ^[3, 4]. In addition, agitation often results in caregiver burnout and breakdown in care ^[5]. Their presence correlates with accelerated functional decline, diminished quality of life, premature nursing home placement, and increased mortality ^[6]. Thus, there is an urgent need for safe and practical approaches to address dementia-related agitation and anxiety ^[7].

Managing agitation and anxiety related to dementia is quite challenging. While pharmacological options like antipsychotics or sedatives are commonly used, they typically provide only limited relief and carry significant safety risks, including stroke and an increased risk of death ^[8]. Alarming, about one-third of dementia patients are prescribed antipsychotic medications despite these hazards ^[9]. Importantly, no medication has received specific approval for treating agitation in dementia ^[1]. Given these difficulties, there has been a growing focus in clinical practice on non-pharmacological approaches as primary treatment options ^[1, 10].

UK National Institute for Health and Care Excellence (NICE) recommends identifying and addressing any underlying causes like untreated pain, discomfort, or environmental stressors before using tailored non-drug strategies to alleviate discomfort, only considering medication afterward ^[10].

Various non-pharmacological methods have been explored to alleviate agitation and anxiety in individuals with dementia. These methods include sensory stimulation therapies such as music therapy, aromatherapy, and massage; psychosocial interventions like reminiscence therapy, validation therapy, cognitive stimulation, and customized activities; structured exercise programs; and animal-assisted therapy ^[11, 12, 13]. A cluster-randomized trial in nursing homes demonstrated that training staff in person-centered care significantly reduced agitation compared to standard care ^[14]. Some approaches specifically target anxiety relief; techniques like guided relaxation and adapted cognitive-behavioral therapy have proven effective in lowering anxiety levels in dementia patients ^[15]. A summary of systematic reviews highlighted that music-based therapies and psychological interventions substantially decreased anxiety symptoms in dementia ^[16]. Data from systematic reviews and meta-analyses show that specific interventions can significantly reduce agitation and enhance patient comfort ^[17]. Recent network meta-analytic results indicate that therapies such as massage and personalized activity programs rank among the most effective for alleviating agitated behaviors ^[18]. However, the practical application of these non-pharmacological techniques remains limited, emphasizing the need for improved adoption of best practices in dementia care ^[19].

Given the increasing focus on comprehensive, person-centered dementia care, this review article seeks to consolidate the latest evidence regarding non-pharmacological approaches for managing anxiety and agitation related to dementia. It will outline the various interventions available, assess their effectiveness as supported by clinical guidelines, and address practical factors to aid clinicians and caregivers in addressing these problematic symptoms while highlighting areas where further research is needed.

Pathophysiology and underlying mechanisms of anxiety and agitation in dementia

Neuropsychiatric symptoms are exceedingly common in dementia, with anxiety and agitation among the most prevalent manifestations ^[20]. Over 80% of individuals with Alzheimer's disease (AD) or other dementia develop at least one behavioral or psychological symptom during illness ^[20]. Anxiety often co-occurs with agitation, and both symptoms contribute to patient distress, caregiver burden, and earlier institutionalization ^[21]. Notably, anxiety and agitation are not merely "reactive" behaviors; they reflect underlying neurobiological changes in the dementing brain. Post-mortem and in vivo imaging studies indicate that these neuropsychiatric symptoms are linked to core neuropathology of dementia. For example, higher burdens of tau protein deposition in frontal and temporal lobes correlate with more significant agitation and related behaviors in AD. In contrast, amyloid load shows weaker associations, suggesting that the emergence of anxiety and agitation is tied to the progression of the disease process itself, especially tau pathology in neural circuits subserving emotion and behavior ^[20].

Neuropathologically, degeneration of key cortical and

subcortical regions impairs the brain's ability to regulate mood and behavior. Dementia-related damage in the prefrontal cortex and anterior cingulate regions responsible for executive control and emotional inhibition likely contributes to disinhibition and agitation ^[22]. Likewise, the locus coeruleus and other brainstem nuclei undergo early neurodegeneration in AD, disrupting neurotransmitter systems that modulate anxiety. Indeed, neurotransmitter alterations have been documented in agitated patients, for example, loss of cholinergic neurons and dopaminergic dysfunction can precipitate agitation, as can imbalances in serotonergic and noradrenergic pathways ^[22]. Low serotonin levels are hypothesized to reduce anxiety thresholds, while cholinergic deficits and frontal lobe dysfunction impede the patient's capacity to interpret and cope with environmental stimuli ^[23]. This neurochemical disruption creates a state of heightened arousal and reduced impulse control, laying a biological foundation for anxiety and agitated behaviors. Beyond molecular pathology, clinicians recognize that psychosocial and environmental factors critically modulate these symptoms. The "Stress Threshold" model posits that dementia lowers an individual's ability to tolerate stressors, so relatively minor challenges can trigger anxiety or agitation once a certain threshold is exceeded. Common triggers include acute medical insults (pain, infection, medication side effects) and unmet needs (hunger, toileting, discomfort), which the person with dementia cannot articulate ^[24, 25, 26]. Sensory impairments (e.g. poor vision or hearing) and changes in lighting or noise levels (such as at sundown) may also precipitate agitation by causing misperceptions or confusion ^[24, 25, 26]. Thus, agitation often reflects an interplay between neurobiological vulnerability and environmental stressors. An individual with dementia and underlying frontal lobe damage may become agitated when in pain or faced with a chaotic setting, due to inability to communicate discomfort or filter excess stimuli ^[27, 28].

Pharmacological vs. Non-Pharmacological Approaches

A growing body of research, including randomized controlled trials and meta-analyses, supports the efficacy of non-pharmacological interventions in reducing agitation and anxiety in dementia. Overall, these approaches can lead to meaningful improvements in behavioral symptoms, though the magnitude of benefit varies by intervention type and individual.

Pharmacological treatments, such as antipsychotic medications, sedative-anxiolytics, and antidepressants have historically been used to manage agitation and anxiety in dementia. Antipsychotics (e.g. risperidone, haloperidol) can provide modest short-term reduction in severe aggression or psychotic-related agitation ^[27]. However, their overall efficacy for agitation is limited (typically producing only small-to-moderate effect size improvements) and significantly, they do not improve patients' overall functioning or quality of life ^[28, 29, 30, 31]. Moreover, decades of research have revealed significant risks associated with pharmacotherapy in this population. Antipsychotics carry a black box warning for increased mortality in elderly dementia patients, as well as heightened risk of stroke, falls, metabolic side effects, and extrapyramidal symptoms ^[28, 29]. One meta-analysis of 15 trials estimated 1.6-fold increase in mortality risk with antipsychotic use in dementia, and the U. S. FDA has cautioned that both first- and second-generation antipsychotics are associated with a greater risk of death in

elderly patients with dementia^[27, 32]. Sedative anxiolytics like benzodiazepines are also problematic while they may transiently reduce anxiety or agitation, they frequently cause paradoxical disinhibition in dementia (worsening agitation), along with excessive sedation, falls, and further cognitive impairment^[33, 34]. For example, benzodiazepine use in older adults with dementia can trigger behavioral disinhibition and confusion instead of calming^[34]. Anticholinergic medications and even some antidepressants can exacerbate agitation or confusion as side effects^[35, 36]. Given these safety concerns and the only modest benefits of drugs, expert consensus is that medication should not be the first-line approach for most patients. Indeed, there are currently no FDA-approved pharmacotherapies for dementia-related agitation despite its prevalence, highlighting the challenges in finding safe and effective drugs for these behaviors.

In contrast, non-pharmacological interventions address the behavioral symptoms through environmental, psychosocial, and behavioral modifications, targeting root causes rather than just sedating the patient^[37]. Clinical guidelines and consensus statements uniformly recommend that non-drug strategies be attempted before resorting to medications in the management of agitation or anxiety in dementia^[38, 39]. For instance, the UK's NICE guidelines and the American Psychiatric Association practice guideline emphasize that psychosocial interventions, such as personalized activities, caregiver training, and environmental adjustments, should be the first-line treatment for agitation/aggression in dementia, with drugs reserved for severe cases or those unresponsive to non-pharmacological measures^[10, 39]. Non-pharmacological approaches also align with the principle of person-centered care, seeking to understand and meet the unmet need the behavior is communicating (e., a pacing patient might be under stimulated or need to use the toilet, an anxious patient might be frightened by not recognizing their environment). By contrast, pharmacological treatment "short-circuits" this assessment and often merely sedates the patient, failing to address the underlying cause of distress^[27, 40]. Furthermore, any benefits from drugs tend to be temporary; behaviors usually return when the medication is stopped. Non-drug interventions can yield more durable improvements by altering the caregiving environment or teaching new strategies^[41, 42]. As Kales *et al.* note, there is no "one-size-fits-all" solution to behavioral symptoms, so treatments must be tailored to the individual and their context; an approach inherently suited to non-pharmacological, personalized strategies^[37].

Another key rationale for prioritizing non-pharmacological approaches is safety and ethical imperative^[43]. Given that pharmacologic options have notable adverse events and only moderate efficacy, it is safer to implement environmental or behavioral interventions that carry minimal risk first. In dementia care, the dictum "start low and go slow" applies not just to dosing medications, but also to the general strategy of escalating interventions: start with the least invasive, least risky option, which is usually a non-drug approach, and only move to medications if necessary (e.g. severe agitation posing immediate risk)^[44].

Types of non-pharmacological interventions

Non-pharmacological interventions for dementia-related anxiety and agitation encompass a broad range of person-centered, psychosocial, and environmental strategies. A comprehensive 2017 overview found that music therapy and

behavioral management were among the most effective strategies for alleviating behavioral and psychological symptoms of dementia (BPSD), yielding measurable reductions in agitation and related symptoms^[45].

Non-pharmacological interventions can be categorized into several overlapping domains: (1) person-centered care and caregiver-centered interventions, (2) activity-based and cognitive/emotional therapies, (3) sensory stimulation and relaxation therapies, and (4) environmental modifications. Notably, most effective interventions are multicomponent and tailored to the individual's history, preferences, and needs (6).

Person-Centered Care (PCC) and caregiver interventions

A foundational approach in managing agitation is to adopt a person-centered care philosophy, in which care strategies are customized to the person's life history, routines, and preferences^[46, 47]. PCC involves seeing the situation from the perspective of the person with dementia and partnering with them (and their family) to meet their needs in a dignified way^[46, 47, 48]. For example, knowing an individual's customary daily routines or past occupation can inform activities that soothe them or reduce triggers. One formalized method is the "DICE" approach (Describe, Investigate, Create, Evaluate), which guides caregivers to identify triggers of behaviors and implement creative solutions rather than immediately resorting to medication^[37]. Training professional and family caregivers in these techniques is itself a key intervention as caregiver education and support programs have effectively reduced behavioral symptoms^[49]. Non-pharmacologic approaches with the most substantial evidence base involve family caregiver interventions, enabling caregivers to understand better and manage behaviors. Teaching caregivers to recognize signs of anxiety or agitation early and to use de-escalation strategies (such as redirection or providing reassurance) can prevent full-blown episodes^[50]. Structured caregiver training programs (e.g., REACH, STAR-D) and psychotherapy for caregivers to reduce their stress have been shown to reduce patient agitation indirectly by improving the caregiving environment^[50]. In nursing homes, training staff in person-centered care principles and tailoring daily activities has led to reductions in agitation frequency and decreased use of antipsychotics^[50]. For example, a staff training intervention in UK care homes (the WHELD program) implemented personalized activities and social interaction for residents. It achieved measurable declines in agitation levels compared to usual care^[51].

Activity-based therapies and cognitive/social stimulation

Many individuals with dementia become anxious or agitated due to boredom, loneliness, or lack of meaningful engagement. Consequently, providing appropriate activities and social stimulation can significantly ameliorate these symptoms^[21]. Structured activities matched to the person's functional level, such as simple household tasks, puzzles, art projects, or reminiscence conversations, would help channel energy and attention, reducing restless or agitated behaviors^[52, 53, 54]. Notably, research shows that combined or multi-modal activities, as engaging the person in a mix of physical, social, and cognitive stimulation, are more effective than a single type of activity alone^[53, 54]. In one study, participating in a tailored activities program that included tasks like folding laundry, listening to favorite music, and light exercise led to reduced physical agitation – with live social interaction being

the most impactful component [6, 55].

Exercise is a vital non-pharmacological intervention that enhances health, alleviates anxiety, and improves mood. Supervised walking groups and chair aerobics can help channel energy and reduce aggression [56]. A randomized trial showed that a daily exercise program significantly lowered anxiety levels, nearly matching music therapy in effectiveness. Although the effects of exercise on agitation are mixed, it benefits depressive symptoms and sleep regulation, indirectly helping with agitation [57].

Reminiscence therapy engages individuals in recalling memories, often using photos or familiar objects to connect them with comforting past experiences, which can reduce anxiety and encourage social interaction [58, 59]. While results vary, some studies suggest that reminiscence sessions improve mood and decrease agitation in care home residents [60].

Sensory stimulation and relaxation therapies

Various sensory-based interventions have shown promise in soothing agitated or anxious individuals by providing calming sensory input [61, 62, 63]. Music therapy is among the most extensively studied in this category. Listening to music, especially music that is familiar and meaningful to the individual or engaging in music-making activities can significantly reduce agitation and anxiety in dementia [64]. Meta-analyses of randomized trials indicate that music therapy has a moderately significant effect in diminishing disruptive behaviors and a moderate effect in lowering anxiety levels in people with dementia [64]. Group music therapy in nursing homes has also significantly reduced overall agitation scores, likely by improving mood and providing social connection [62].

Aside from music, aromatherapy (fragrant plant oils) and massage/touch therapy are commonly used relaxation techniques [3, 65, 66]. Lavender oil, for instance, has mild sedative properties and some studies have reported that diffusing lavender aroma or gentle hand massage with lavender oil correlates with lower agitation levels [67]. However, the evidence on aromatherapy is mixed. A Cochrane review concluded that there is no convincing consistent benefit of aromatherapy for dementia behaviors overall, though individual trials have shown short-term calming effects [3, 65, 67, 68].

Environmental Modifications

Adjusting the patient's environment is another strategy to reduce triggers of agitation. Optimizing lighting is one approach: trials of bright light therapy have yielded mixed results. Some found improved sleep but no change in agitation [69], while one reported slightly lower agitation scores with morning light exposure [70]. Overall, reviews suggest bright light has a minimal clinical impact on agitation, though it might modestly reduce caregiver-reported agitation [71]. Beyond lighting, creating a soothing, familiar atmosphere and providing safe space for movement can help manage agitation. Outdoor garden access in nursing homes is linked to better mood and less agitation; staff in dementia units with unrestricted garden use report fewer agitated behaviors than those in more confined facilities [72]. While rigorous trials of other environmental tweaks are limited, tailored light exposure and outdoor environments are considered useful complements to reduce agitation in Alzheimer's patients.

Guideline recommendations and clinical implementation

Clinical practice guidelines across the world endorse non-pharmacological interventions as first-line treatments for managing agitation and other behavioral disturbances in dementia. The National Institute for Health and Care Excellence (NICE) guideline on dementia care recommends that patients with agitation or aggression receive an individualized assessment to identify possible triggers and that nonpharmacologic measures be tried before any medication is considered [10]. The American Psychiatric Association's 2016 practice guideline similarly advises that non-drug interventions be utilized as first-line, reserving antipsychotic medications only for cases of severe agitation or psychosis that pose safety risks [39]. This reflects a broad consensus that while medications have a limited role, psychosocial and environmental interventions should be the foundation of treatment.

The Scottish Intercollegiate Guidelines Network (SIGN) and the Alzheimer's Association dementia care practice recommendations highlight interventions like music therapy, reminiscence therapy, multi-sensory stimulation, exercise, and structured caregiver interventions as beneficial practices in dementia care [73]. The International Psychogeriatric Association (IPA) issued a consensus statement noting that person-centered care, tailored activities, and environmental adjustments constitute best practices for agitation, and that antipsychotics should only be used after these options are exhausted [6]. The European Society of Neurology guidelines for dementia discouraged routine use of antipsychotics and benzodiazepines and recommended non-drug approaches, citing their safety and the importance of preserving dignity and quality of life [74]. Regulatory bodies have also taken steps aligning with these recommendations. In the United States, the Centers for Medicare & Medicaid Services (CMS) implemented initiatives in nursing homes to monitor and reduce inappropriate antipsychotic prescribing, encouraging facilities to use non-pharmacologic behavioral management programs instead [75]. The overall message from guidelines and policy is consistent: focus on individualized, non-drug strategies to prevent and address agitation for as long as possible, and involve multidisciplinary teams (physicians, nurses, occupational therapists, music therapists, social workers) in delivering these interventions.

Guidelines also encourage monitoring and individualized adjustment as part of implementation. Following the initiation of a non-pharmacologic care plan, caregivers should monitor the frequency and severity of agitation using tools like the Agitation Inventory or anxiety scales and then refine interventions accordingly. If an intervention is not helping after a fair trial, alternate approaches should be tried. This process of assessment and tailoring is in fact the essence of non-pharmacological management – it is dynamic and responsive to the person's needs and situation [37].

Future Directions and Gaps in Research

While non-pharmacological interventions have become a mainstay of managing dementia-related anxiety and agitation, there remain important gaps in research and opportunities for future improvements. One notable gap is the relative paucity of high-quality, large-scale trials for many interventions. The existing literature, though promising, often consists of small studies with methodological limitations such as heterogeneity in outcome measures, unblinded designs, or variability in how interventions are

delivered^[17, 76]. This makes it challenging to compare results across studies or to determine which components of a complex intervention are most effective. Future research should focus on more rigorous and standardized evaluation of non-pharmacological therapies. Additionally, studies should report not only statistical significance but clinical significance. There is also a need for longer follow-up periods in trials, as studies examine outcomes only over a few weeks, but whether interventions have lasting effects or need periodic reinforcement is unclear.

Another research gap lies in under-studied symptoms like anxiety. Agitation and aggression have been the primary focus of many BPSD trials, whereas anxiety in dementia has received comparatively less attention, perhaps due to the challenge of measuring anxiety in cognitively impaired individuals. Anxiety often goes under-recognized (sometimes overshadowed by more overt agitation), and one study noted only ~10% of dementia patients with anxiety symptoms receive targeted treatment^[57].

Conclusions

In conclusion, non-pharmacological approaches to managing dementia-related anxiety and agitation are vital for improving the well-being of individuals with dementia. These strategies not only offer effective symptom relief but also minimize the significant risks associated with pharmacological treatments, such as antipsychotics. Interventions like music therapy, exercise, and caregiver training are integral components of a person-centered care approach, which considers individual needs and preferences. While numerous studies have shown the benefits of these therapies, challenges remain in their widespread adoption in clinical practice. More rigorous, large-scale trials are needed to further validate the effectiveness of these interventions and determine the most impactful combinations. Additionally, a focus on reducing caregiver stress and improving training in these non-drug approaches is essential to enhance the overall quality of dementia care. By prioritizing non-pharmacological treatments, clinicians can provide safer, more personalized care that addresses the underlying causes of agitation and anxiety, ultimately improving the lives of those affected by dementia.

References

1. Ijaopo EO. Dementia-related agitation: a review of non-pharmacological interventions and analysis of risks and benefits of pharmacotherapy. *Translational Psychiatry*. 2017 Oct 31;7(10):e1250. Available from: <https://www.nature.com/articles/tp2017199>
2. Steinberg M, Shao H, Zandi P, Lyketsos CG, Welsh-Bohmer KA, Norton MC, *et al*. Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry*. 2008 Feb 1;23(2):170–7. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1002/gps.1858>
3. Yang MH, Lin LC, Wu SC, Chiu JH, Wang PN, Lin JG. Comparison of the efficacy of aroma-acupressure and aromatherapy for the treatment of dementia-associated agitation. *BMC Complementary Medicine and Therapies*. 2015 Mar 29;15(1):1–8. Available from: <https://bmccomplementmedtherapies.biomedcentral.com/articles/10.1186/s12906-015-0612-9>
4. Mendez MF. The relationship between anxiety and Alzheimer's disease. *Journal of Alzheimer's Disease Reports*. 2021;5(1):171. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8075566/>
5. Gitlin LN, Kales HC, Lyketsos CG. Nonpharmacologic management of behavioral symptoms in dementia. *Journal of the American Medical Association*. 2012 Nov 21;308(19):2020–9. Available from: <https://jamanetwork.com/journals/jama/fullarticle/1392543>
6. Carrarini C, Russo M, Dono F, Barbone F, Rispoli MG, Ferri L, *et al*. Agitation and dementia: prevention and treatment strategies in acute and chronic conditions. *Frontiers in Neurology*. 2021 Apr 16;12:644317. Available from: <https://www.frontiersin.org>
7. Cerejeira J, Lagarto L, Mukaetova-Ladinska EB. Behavioral and psychological symptoms of dementia. *Frontiers in Neurology*. 2012;3:73. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3345875/>
8. Porsteinsson AP, Drye LT, Pollock BG, Devanand DP, Frangakis C, Ismail Z, *et al*. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. *Journal of the American Medical Association*. 2014 Feb 19;311(7):682–91. Available from: <https://jamanetwork.com/journals/jama/fullarticle/1829989>
9. Kirkham J, Sherman C, Velkers C, Maxwell C, Gill S, Rochon P, *et al*. Antipsychotic use in dementia: is there a problem and are there solutions? *Canadian Journal of Psychiatry*. 2016 Mar 1;62(3):170. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5317021/>
10. National Institute for Health and Care Excellence (NICE). Management of aggression, agitation and behavioural disturbances in dementia: valproate preparations. Available from: <https://www.nice.org.uk/advice/esuom41>
11. Ayalon L, Gum AM, Feliciano L, Areán PA. Effectiveness of nonpharmacological interventions for the management of neuropsychiatric symptoms in patients with dementia: a systematic review. *Archives of Internal Medicine*. 2006 Nov 13;166(20):2182–8. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/411279>
12. Kales HC, Gitlin LN, Lyketsos CG. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. *Journal of the American Geriatrics Society*. 2014 Apr 1;62(4):762–9. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/jgs.12730>
13. Passmore MJ, Gardner DM, Polak Y, Rabheru K. Alternatives to atypical antipsychotics for the management of dementia-related agitation. *Drugs & Aging*. 2008 May;25(5):381–98. Available from: <https://link.springer.com/article/10.2165/00002512-200825050-00003>
14. Chenoweth L, King MT, Jeon YH, Brodaty H, Stein-Parbury J, Norman R, *et al*. Caring for Aged Dementia Care Resident Study (CADRES) of person-centred care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. *The Lancet Neurology*. 2009 Apr;8(4):317–25. Available from:

- <https://pubmed.ncbi.nlm.nih.gov/19282246/>
15. National Institute for Health and Care Excellence (NICE). Quality statement 6: Managing distress | Dementia | Quality standards. Available from: <https://www.nice.org.uk/guidance/qs184/chapter/quality-statement-6-managing-distress>
 16. Kishita N, Backhouse T, Mioshi E. Nonpharmacological interventions to improve depression, anxiety, and quality of life (QoL) in people with dementia: an overview of systematic reviews. *Journal of Geriatric Psychiatry and Neurology*. 2020 Jan 1;33(1):28–41. Available from: <https://pubmed.ncbi.nlm.nih.gov/31203712/>
 17. Abraha I, Rimland JM, Trotta FM, Dell'Aquila G, Cruz-Jentoft A, Petrovic M, *et al.* Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia: the SENATOR-OnTop series. *BMJ Open*. 2017 Mar 1;7(3):e012759. Available from: <https://pubmed.ncbi.nlm.nih.gov/28302633/>
 18. Leng M, Zhao Y, Wang Z. Comparative efficacy of non-pharmacological interventions on agitation in people with dementia: a systematic review and Bayesian network meta-analysis. *International Journal of Nursing Studies*. 2020 Feb 1;102:103512. Available from: <https://pubmed.ncbi.nlm.nih.gov/31862527/>
 19. Jakobson E, Avari J, Kalayam B. Non-pharmacologic interventions for treatment of agitation in dementia in nursing home residents. *The American Journal of Geriatric Psychiatry*. 2015 Mar 1;23(3):S139–40. Available from: <https://www.ajgponline.org/action/showFullText?pii=S106474811400517X>
 20. Tissot C, Theriault J, Pascoal TA, Chamoun M, Lussier FZ, Savard M, *et al.* Association between regional tau pathology and neuropsychiatric symptoms in aging and dementia due to Alzheimer's disease. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. 2021 Jan 1;7(1):e12154. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1002/trc2.12154>
 21. Carrarini C, Russo M, Dono F, Barbone F, Rispoli MG, Ferri L, *et al.* *Frontiers in Neurology*. 2021 Apr 16;12:644317. Agitation and Dementia: Prevention and Treatment Strategies in Acute and Chronic Conditions. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8085397/>
 22. Gottlieb M, Long B, Koyfman A. *Journal of Emergency Medicine*. 2018 Apr 1;54(4):447–57. Approach to the Agitated Emergency Department Patient. Available from: <https://www.jem-journal.com/action/showFullText?pii=S0736467917312155>
 23. Chaudhary S, Zhornitsky S, Chao HH, van Dyck CH, Li CSR. *American Journal of Alzheimer's Disease and Other Dementias*. 2022 Mar 22;37:15333175221082834. Emotion Processing Dysfunction in Alzheimer's Disease: An Overview of Behavioral Findings, Systems Neural Correlates, and Underlying Neural Biology. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9212074/>
 24. Bachman D, Rabins P. *Annual Review of Medicine*. 2006 Feb 18;57:499–511. "Sundowning" and other temporally associated agitation states in dementia patients. Available from: <https://www.annualreviews.org/content/journals/10.1146/annurev.med.57.071604.141451>
 25. Goldberg TE, Chen C, Wang Y, Jung E, Swanson A, Ing C, *et al.* *JAMA Neurology*. 2020 Nov 1;77(11):1373–81. Association of Delirium With Long-term Cognitive Decline: A Meta-analysis. Available from: <https://jamanetwork.com/journals/jamaneurology/fullarticle/2768000>
 26. Bellelli G, Morandi A, Di Santo SG, Mazzone A, Cherubini A, Mossello E, *et al.* *BMC Medicine*. 2016 Jul 18;14(1):1–12. "Delirium Day": A nationwide point prevalence study of delirium in older hospitalized patients using an easy standardized diagnostic tool. Available from: <https://bmcmmedicine.biomedcentral.com/articles/10.1186/s12916-016-0649-8>
 27. Ralph SJ, Espinet AJ. *Journal of Alzheimer's Disease Reports*. 2018;2(1):1. Increased All-Cause Mortality by Antipsychotic Drugs: Updated Review and Meta-Analysis in Dementia and General Mental Health Care. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6159703/>
 28. Sheehan R, Hassiotis A, Walters K, Osborn D, Strydom A, Horsfall L. *BMJ*. 2015 Sep 1;351:h4326. Mental illness, challenging behaviour, and psychotropic drug prescribing in people with intellectual disability: UK population based cohort study. Available from: <https://www.bmj.com/content/351/bmj.h4326>
 29. Wang PS, Schneeweiss S, Avorn J, Fischer MA, Mogun H, Solomon DH, *et al.* *New England Journal of Medicine*. 2005 Dec 1;353(22):2335–41. Risk of Death in Elderly Users of Conventional vs. Atypical Antipsychotic Medications. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa052827>
 30. Jeste DV, Blazer D, Casey D, Meeks T, Salzman C, Schneider L, *et al.* *Neuropsychopharmacology*. 2007 Jul 18;33(5):957–70. ACNP White Paper: Update on Use of Antipsychotic Drugs in Elderly Persons with Dementia. Available from: <https://www.nature.com/articles/1301492>
 31. Schneider LS, Tariot PN, Dagerman KS, Davis SM, Hsiao JK, Ismail MS, *et al.* *New England Journal of Medicine*. 2006 Oct 12;355(15):1525–38. Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer's Disease. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa061240>
 32. Kuehn BM. *JAMA*. 2005 May 25;293(20):2462. FDA Warns Antipsychotic Drugs May Be Risky for Elderly. Available from: <https://jamanetwork.com/journals/jama/fullarticle/200951>
 33. Mancuso CE, Tanzi MG, Gabay M. *Pharmacotherapy*. 2004 Sep 4;24(9):1177–85. Paradoxical reactions to benzodiazepines: literature review and treatment options. Available from: <https://pubmed.ncbi.nlm.nih.gov/15460178/>
 34. Tampi RR, Tampi DJ. *American Journal of Alzheimer's Disease and Other Dementias*. 2014 Nov 20;29(7):565–74. Efficacy and Tolerability of Benzodiazepines for the Treatment of Behavioral and Psychological Symptoms of Dementia. Available from: <https://journals.sagepub.com/doi/10.1177/1533317514524813>
 35. Ables AZ, Nagubilli R. *American Family Physician*.

- 2010 May 1;81(9):1139–42. Prevention, Diagnosis, and Management of Serotonin Syndrome. Available from: <https://www.aafp.org/pubs/afp/issues/2010/0501/p1139.html>
36. Han JH, Wilber ST. Clinics in Geriatric Medicine. 2013 Feb 1;29(1):101–36. Altered Mental Status in Older Patients in the Emergency Department. Available from: <https://www.geriatric.theclinics.com/action/showFullText?pii=S0749069012000857>
 37. Kales HC, Gitlin LN, Lyketsos CG. BMJ. 2015 Mar 2;350:h369. Assessment and management of behavioral and psychological symptoms of dementia. Available from: <https://pubmed.ncbi.nlm.nih.gov/25731881/>
 38. Ooi CH, Yoon PS, How CH, Poon NY. Singapore Medical Journal. 2018 Oct 1;59(10):514–8. Managing challenging behaviours in dementia.
 39. Reus VI, Fochtmann LJ, Eyler AE, Hilty DM, Horvitz-Lennon M, Jibson MD, *et al.* American Journal of Psychiatry. 2016 May 1;173(5):543–6. The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia. Available from: <https://psychiatryonline.org/doi/10.1176/appi.ajp.2015.173501>
 40. Sultzer DL, Davis SM, Tariot PN, Dagerman KS, Lebowitz BD, Lyketsos CG, *et al.* American Journal of Psychiatry. 2008 Jul;165(7):844–54. Clinical symptom responses to atypical antipsychotic medications in Alzheimer's disease: Phase I outcomes from the CATIE-AD effectiveness trial. Available from: <https://psychiatryonline.org/doi/10.1176/appi.ajp.2008.07111779>
 41. Devanand DP, Mintzer J, Schultz SK, Andrews HF, Sultzer DL, de la Pena D, *et al.* Relapse risk after discontinuation of risperidone in Alzheimer's disease. New England Journal of Medicine. 2012 Oct 18;367(16):1497–507. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa1114058>
 42. Banerjee S. The use of antipsychotic medication for people with dementia: time for action. A report for the Minister of State for Care Services. Department of Health; 2009.
 43. Millán-Calenti JC, Lorenzo-López L, Alonso-Búa B, de Labra C, González-Abraldes I, Maseda A. Optimal nonpharmacological management of agitation in Alzheimer's disease: challenges and solutions. Clinical Interventions in Aging. 2016 Feb 22;11:175. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4769004/>
 44. Contemporary Geriatric Medicine. Contemporary Geriatric Medicine. 1988.
 45. Abraha I, Rimland JM, Trotta FM, Dell'Aquila G, Cruz-Jentoft A, Petrovic M, *et al.* Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series. BMJ Open. 2017 Mar 1;7(3). Available from: <https://pubmed.ncbi.nlm.nih.gov/28302633/>
 46. Keszycki RM, Fisher DW, Dong H. The hyperactivity-impulsivity-irritability-disinhibition-aggression-agitation domain in Alzheimer's disease: current management and future directions. Frontiers in Pharmacology. 2019 Sep 27;10:475005. Available from: <https://www.frontiersin.org/articles/10.3389/fphar.2019.00902/full>
 47. Brooker D. What is person-centred care in dementia? Reviews in Clinical Gerontology. 2003 Aug;13(3):215–22. Available from: <https://www.cambridge.org/core/journals/reviews-in-clinical-gerontology/article/abs/what-is-personcentred-care-in-dementia/05526FC63B5923B299DEB2D8A57BCDC8>
 48. Sloane PD, Hoeffler B, Mitchell CM, McKenzie DA, Barrick AL, Rader J, *et al.* Effect of person-centered showering and the towel bath on bathing-associated aggression, agitation, and discomfort in nursing home residents with dementia: a randomized, controlled trial. Journal of the American Geriatrics Society. 2004 Nov 1;52(11):1795–804. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1532-5415.2004.52501.x>
 49. Whitlatch CJ, Orsulic-Jeras S. Meeting the informational, educational, and psychosocial support needs of persons living with dementia and their family caregivers. The Gerontologist. 2018 Jan 18;58(suppl_1):S58–73. Available from: <https://dx.doi.org/10.1093/geront/gnx162>
 50. Ballard C, Corbett A, Orrell M, Williams G, Moniz-Cook E, Romeo R, *et al.* Impact of person-centred care training and person-centred activities on quality of life, agitation, and antipsychotic use in people with dementia living in nursing homes: a cluster-randomised controlled trial. PLOS Medicine. 2018 Feb 1;15(2):e1002500. Available from: <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002500>
 51. Ballard C, Orrell M, Moniz-Cook E, Woods R, Whitaker R, Corbett A, *et al.* Improving mental health and reducing antipsychotic use in people with dementia in care homes: the WHELD research programme including two RCTs. Programme Grants for Applied Research. 2020;8.
 52. Cohen-Mansfield J, Thein K, Marx MS, Dakheel-Ali M, Freedman L. Efficacy of nonpharmacologic interventions for agitation in advanced dementia: a randomized, placebo-controlled trial. Journal of Clinical Psychiatry. 2012;73(9):1255–61.
 53. Cohen-Mansfield J, Marx MS, Dakheel-Ali M, Regier NG, Thein K, Freedman L. Can agitated behavior of nursing home residents with dementia be prevented with the use of standardized stimuli? Journal of the American Geriatrics Society. 2010 Aug 1;58(8):1459–64. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1532-5415.2010.02951.x>
 54. Cohen-Mansfield J, Dakheel-Ali M, Marx MS, Thein K, Regier NG. Which unmet needs contribute to behavior problems in persons with advanced dementia? Psychiatry Research. 2015 Jul 30;228(1):59–64.
 55. O'Connor CM, Clemson L, Brodaty H, Jeon YH, Mioshi E, Gitlin LN. Use of the Tailored Activities Program to reduce neuropsychiatric behaviors in dementia: an Australian protocol for a randomized trial to evaluate its effectiveness. International Psychogeriatrics. 2014;26(5):857. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4091660/>
 56. de Souto Barreto P, Demougeot L, Pillard F, Lapeyre-

- Mestre M, Rolland Y. Exercise training for managing behavioral and psychological symptoms in people with dementia: a systematic review and meta-analysis. *Ageing Research Reviews*. 2015 Nov 1;24(Pt B):274–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/26369357/>
57. Dimitriou TD, Verykoui E, Papatriantafyllou J, Konsta A, Kazis D, Tsolaki M. Non-pharmacological interventions for the anxiety in patients with dementia. A cross-over randomised controlled trial. *Behavioural Brain Research*. 2020 Jul 15;390:112617.
 58. Cammisuli DM, Cipriani G, Giusti EM, Castelnovo G. Effects of reminiscence therapy on cognition, depression and quality of life in elderly people with Alzheimer's disease: a systematic review of randomized controlled trials. *Journal of Clinical Medicine*. 2022 Oct 1;11(19):5752. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9570531/>
 59. Huang LC, Yang YH. The long-term effects of immersive virtual reality reminiscence in people with dementia: longitudinal observational study. *JMIR Serious Games*. 2022 Jul 25;10(3):e36720. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/35877169>
 60. Woods B, O'Philbin L, Farrell EM, Spector AE, Orrell M. Reminiscence therapy for dementia. *Cochrane Database of Systematic Reviews*. 2018 Mar 1;2018(3). Available from: <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001120.pub3/full>
 61. Pedersen SKA, Andersen PN, Lugo RG, Andreassen M, Sütterlin S. Effects of music on agitation in dementia: a meta-analysis. *Frontiers in Psychology*. 2017 May 16;8(MAY):249528. Available from: www.frontiersin.org
 62. Pedersen SKA, Andersen PN, Lugo RG, Andreassen M, Sütterlin S. Effects of music on agitation in dementia: a meta-analysis. *Frontiers in Psychology*. 2017 May 16;8(MAY). Available from: <https://pubmed.ncbi.nlm.nih.gov/28559865/>
 63. Ridder HMO, Stige B, Qvale LG, Gold C. Individual music therapy for agitation in dementia: an exploratory randomized controlled trial. *Aging & Mental Health*. 2013 Aug 1;17(6):667. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4685573/>
 64. Chang YS, Chu H, Yang CY, Tsai JC, Chung MH, Liao YM, *et al*. The efficacy of music therapy for people with dementia: a meta-analysis of randomised controlled trials. *Journal of Clinical Nursing*. 2015 Dec 1;24(23–24):3425–40. Available from: <https://pubmed.ncbi.nlm.nih.gov/26299594/>
 65. Jimbo D, Kimura Y, Taniguchi M, Inoue M, Urakami K. Effect of aromatherapy on patients with Alzheimer's disease. *Psychogeriatrics*. 2009 Dec 1;9(4):173–9. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1479-8301.2009.00299.x>
 66. Graetz I, McKillop CN, Stepanski E, Vidal GA, Anderson JN, Schwartzberg LS. Use of a web-based app to improve breast cancer symptom management and adherence for aromatase inhibitors: a randomized controlled feasibility trial. *Journal of Cancer Survivorship*. 2018 Aug 1;12(4):431. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6054536/>
 67. Holmes C, Ballard C. Aromatherapy in dementia. *Advances in Psychiatric Treatment*. 2004 Jul;10(4):296–300. Available from: <https://www.cambridge.org/core/journals/advances-in-psychiatric-treatment/article/aromatherapy-in-dementia/8B21114D74C15A930436306D43D150AE>
 68. Yang MH, Lin LC, Wu SC, Chiu JH, Wang PN, Lin JG. Comparison of the efficacy of aroma-acupressure and aromatherapy for the treatment of dementia-associated agitation. *BMC Complementary and Alternative Medicine*. 2015 Mar 29;15(1):93. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4381454/>
 69. Burns A, Allen H, Tomenson B, Duignan D, Byrne J. Bright light therapy for agitation in dementia: a randomized controlled trial. *International Psychogeriatrics*. 2009 Aug;21(4):711–21. Available from: <https://pubmed.ncbi.nlm.nih.gov/19323872/>
 70. Dowling GA, Graf CL, Hubbard EM, Luxenberg JS. Light treatment for neuropsychiatric behaviors in Alzheimer's disease. *Western Journal of Nursing Research*. 2007 Dec;29(8):961–75. Available from: <https://pubmed.ncbi.nlm.nih.gov/17596638/>
 71. Millán-Calenti JC, Lorenzo-López L, Alonso-Búa B, de Labra C, González-Abraldes I, Maseda A. Optimal nonpharmacological management of agitation in Alzheimer's disease: challenges and solutions. *Clinical Interventions in Aging*. 2016 Feb 22;11:175. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4769004/>
 72. Liao ML, Ou SJ, Heng Hsieh C, Li Z, Ko CC. Effects of garden visits on people with dementia: a pilot study. *Dementia*. 2020 May 1;19(4):1009–28. Available from: <https://journals.sagepub.com/doi/10.1177/1471301218793319>
 73. Assessment, diagnosis, care and support for people with dementia and their carers: a national clinical guideline. Available from: [source link not provided – please verify and add if needed]
 74. Frederiksen KS, Cooper C, Frisoni GB, Frölich L, Georges J, Kramberger MG, *et al*. A European Academy of Neurology guideline on medical management issues in dementia. *European Journal of Neurology*. 2020 Oct 1;27(10):1805. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7540303/>
 75. Lucas JA, Bowblis JR. CMS strategies to reduce antipsychotic drug use in nursing home patients with dementia show some progress. *Health Affairs (Millwood)*. 2017 Jul 1;36(7):1299–308. Available from: <https://pubmed.ncbi.nlm.nih.gov/28679818/>
 76. Wang G, Albayrak A, Van Der Cammen TJM. A systematic review of non-pharmacological interventions for BPSD in nursing home residents with dementia: from a perspective of ergonomics. *International Psychogeriatrics*. 2019 Aug 1;31(8):1137–49. Available from: <https://pubmed.ncbi.nlm.nih.gov/30334500/>