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Understanding Agitation in Alzheimer's Disease

Dementia is a disabling brain disease characterized by cognitive decline and associated impairment in function. Alzheimer's disease (AD) is the most common cause of dementia. There are approximately 6.5 million adults 65 years of age and older in the United States who are living with AD, and this number is expected to rise as the population of older adults increases over the next decades.[1]

Individuals with dementia experience a profound loss of ability to process new information and stimuli. Although cognitive impairment is the primary symptom of AD, disabling behavioral and psychological symptoms of dementia (BPSD) are common and among the most distressing effects of dementia.[1,2] Up to 97% of people living with dementia experience BPSD.[2] BPSD can include agitation as well as other symptoms such as irritability, delusions, hallucinations, depression, anxiety, apathy, disinhibition, and sleep disturbances.[3,4] These symptoms have a profound impact on both those experiencing BPSD and the caregiver and, when unmanaged, can lead to high rates of institutionalization and recurrent hospitalizations.

The reported prevalence of agitation in AD (AAD) varies among populations and appears to increase as AD progresses. The prevalence has been reported to range from 30% to 80% of people living with dementia (depending on the population studied). Although agitation can occur along the entire spectrum of AD, it is reported at higher rates in those with more severe dementia.[5-7] Agitation may occur in a wide range of settings, including homes, long-term care facilities (LTCFs), hospitals, emergency departments, and others.

There are multiple complementary conceptual models that describe factors that underlie BPSD.[2] The competence-environmental press framework describes BPSD as a result of the interplay between declining cognitive capacity and external environmental factors. The progressively lowered stress threshold framework states that behavioral responses emerge when environmental demands exceed coping thresholds, which decline as dementia progresses.[2] The needs-driven dementia-compromised behavior model describes BPSD as attempts to communicate unmet needs. In this framework, BPSD are considered to be meaningful expressions.[2]

Tau pathology and neurodegeneration in the prefrontal cortex, a key contributor of executive control, and the amygdala, a key mediator of emotional drive, may increase the risk of AAD.[8-10] Research has demonstrated that AAD is associated with monoaminergic dysfunction in brain circuits mediating this balance between executive control and emotional drive.[11-14]

contents

2 Defining Agitation
3 Managing Agitation
9 Documenting Agitation
9 Caregiver Collaboration
12 Summary
12 Interdisciplinary Insight: Treatment Approaches Throughout the Course of AAD
14 Interdisciplinary Insight: Assessing and Managing Needs of Patients With AAD
16 Resources and Suggested Reading

Defining Agitation

Agitation has been an ambiguously defined term, complicated by individual, caregiver*, and provider interpretations of behaviors. Agitation can be described as increased, often undirected, motor activity, restlessness, aggressiveness, and emotional distress.[5] It may include nonaggressive behaviors such as pacing, repetitious movements, and general restlessness, or it may manifest as physically or verbally aggressive behaviors. Figure 1 displays words and themes that often emerge in conversations with caregivers when they describe their experiences managing agitation in persons with AD.[8]

A provisional consensus definition of agitation in cognitive disorders was published in 2015 by the International Psychogeriatric Association (IPA) Agitation Definition Work Group (ADWG).[7] These criteria have been broadly implemented in clinical trials, published literature, clinical populations, professional societies, and governmental guidelines, and are now generally accepted in the field. A revised definition that incorporated slight modifications based on experiences using the provisional definition was published in 2023 (Table 1).[7] This definition includes four criteria that must be met, along with types of behavior, including physical and verbal behaviors. Additionally, the criteria require that symptoms cause impairment and cannot be attributed to another condition.

Figure 1. Caregiver Perceptions of Agitation in Alzheimer's Disease



Source: Reference 15.

** The term "care partner" has recently been proposed to help improve the way people who provide care are viewed and to convey that those individuals are integral to the care of persons living with dementia who should have agency in their life as much as possible. However, the term "partner" may trigger other associations for many individuals. Therefore, the term "caregiver" will be used throughout this publication.*

Impact of AAD

AAD is associated with many negative outcomes. These include accelerated disease progression, physical and mental health deterioration, functional decline, higher risk of admission to LTCFs, and poor quality of life.[16-18] Notably, agitation is one of the most important factors that impacts whether an individual with dementia is placed in a LTCF. However, it can also complicate LTCF placement and additionally lead to repeated hospitalizations for behavior management. The increased risk of institutionalization among those who experience agitation may be attributed to the negative impact of agitated behaviors on caregivers, deterioration in quality of life, and safety risks for both the caregiver and those who experience agitation.[21]

Agitation in people living with dementia is predictive of more rapid progression to severe dementia and death.[17] Other impacts include increased risk of hospitalization and longer length of stay, mental health impairment, higher costs, and increased mortality.[7,16,17,19-22] Approximately one-third of costs of care for people living with dementia have been attributed to management of these symptoms.[20] In the United States, the annual total incremental costs of institutionalization associated with agitation in individuals with AD were estimated at $4.3 billion in 2018.[23]

BPSD including agitation have a negative impact on many people involved in the life of the person with dementia. Negative effects for caregivers include reduced quality of life, worse health, increased stress and depression, and reduced income from employment, as well as stigma and social isolation in the community. Caregivers managing people living with AAD have higher levels of distress and depression compared with caregivers for people with dementia alone or with other chronic diseases.[20] The impact of BPSD can extend to other friends and family members. For example, long-distance monitoring by adult children can require stressful activities such as coordinating care among health care providers and home health aides, responding to concerns, and telemonitoring well-being. To address these needs, education and support should be offered to all individuals involved in the care of the person living with dementia.

Table 1. International Psychogeriatric Association Consensus Clinical and Research Definition of Agitation in Cognitive Disorders

Criterion A.	The patient meets criteria for a cognitive impairment or dementia syndrome (e.g., Alzheimer's disease, frontotemporal dementia, dementia with Lewy bodies, vascular dementia, other dementias, a pre-dementia cognitive impairment syndrome such as mild cognitive impairment or other cognitive disorder).
Criterion B.	The patient exhibits at least one of the following behaviors that are associated with observed or inferred evidence of emotional distress (e.g., rapid changes in mood, irritability, outbursts). The behavior has been persistent or frequently recurrent for a minimum of 2 weeks or the behavior represents a dramatic change from the patient's usual behavior.* **(a)** Excessive motor activity (e.g., pacing, rocking, gesturing, pointing fingers, restlessness, performing repetitious mannerisms). **(b)** Verbal aggression (e.g., yelling, speaking in an excessively loud voice, using profanity, screaming, shouting). **(c)** Physical aggression (e.g., grabbing, shoving, pushing, resisting, hitting others, kicking objects or people, scratching, biting, throwing objects, hitting self, slamming doors, tearing things, and destroying property).
Criterion C.	Behaviors are severe and associated with excess distress or produce excess disability, which in the clinician's opinion is beyond that due to the cognitive impairment and including at least one of the following: **(a)** Significant impairment in interpersonal relationships. **(b)** Significant impairment in other aspects of social functioning. **(c)** Significant impairment in ability to perform or participate in daily living activities.
Criterion D.	While comorbid conditions may be present, the agitation is not attributable solely to another psychiatric disorder, medical condition, including delirium, suboptimal care conditions, or the physiological effects of a substance.

* In special circumstances, the ability to document the behaviors over 2 weeks may not be possible and other terms of persistence and severity may be needed to capture the syndrome beyond a single episode.

Source: Reference 7.

Importantly, BPSD may be triggered or exacerbated when a caregiver is feeling stressed, depressed, or experiencing other psychological or psychiatric difficulties.[20] Caregiver communication styles (e.g., anger, screaming, negative affect) and poor coping abilities or strategies can trigger or worsen agitation.[20] A lack of caregiver understanding of AD symptoms and recommended management strategies can contribute to increased agitation in the person with BPSD.

Managing Agitation

A person-centered approach to care is central to the management of AAD. In a person-centered care culture, agitation behaviors are viewed as clues to the presence of distress in a person who is no longer able to communicate an issue through other means.[24] The goal of care should be to consider: "What is this person expressing, what is causing this reaction, and how can we respond to reduce their distress?" rather than "How do we manage this behavior?"[24] Anticipating and avoiding circumstances that may trigger distress are preferred to managing agitation after it starts.

Agitation in people living with dementia is predictive of more rapid progression to severe dementia and death.

The Describe, Investigate, Create, and Evaluate (DICE) approach provides a framework for person-centered care (Table 2).[20] This approach begins with an assessment that is designed to identify and share the person's life history to support the unique life of experiences and sense of personhood. The DICE approach allows for gathering information that can be used to creatively develop individualized care plans that proactively address care recipient needs and inform care interactions.[24]

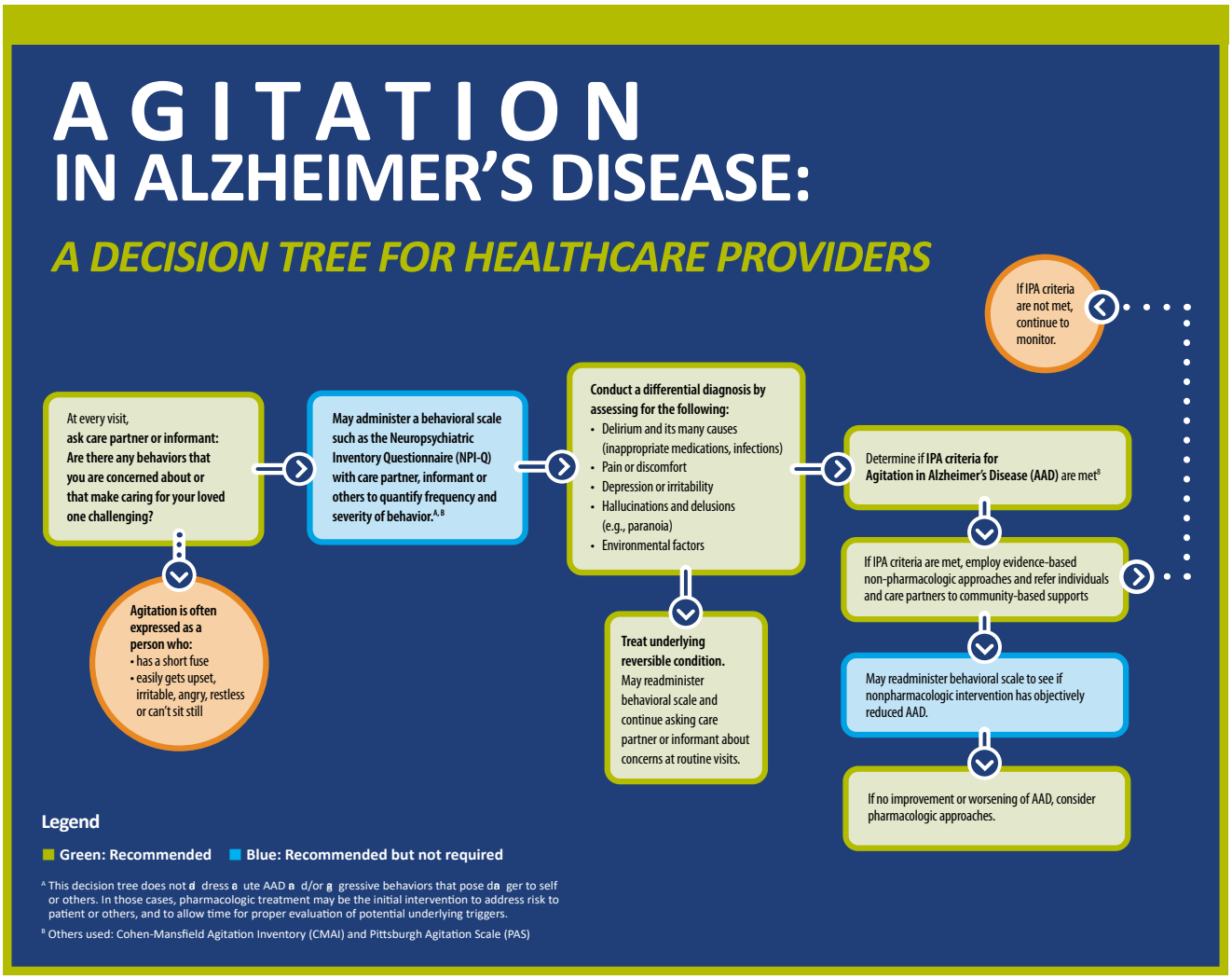
Grossberg and colleagues have developed a treatment algorithm for interventions to ameliorate and prevent agitation that supports the implementation of the IPA definition in practice—and is complementary to the DICE framework.[25] This decision tree for guiding the management of AAD outlines several steps that should be followed for assessing and managing AAD, starting with ongoing assessment for the emergence of symptoms, differential diagnosis, and nonpharmacologic and pharmacologic treatment approaches (Figure 2).[25]

Table 2. The DICE Approach to Behavioral Symptom Management

STEP 1: DESCRIBE
• Elicit a thorough description of the symptoms and the context in which they occur through discussion with the caregiver and the person with dementia (if possible). • The description should include consideration of possible antecedents or triggers of the behavior. • Seek to identify which aspects of the symptoms are most distressing or problematic to the person with dementia and the caregiver, as well as their treatment goals.
STEP 2: INVESTIGATE
• Identify possible underlying and modifiable causes, including possible undiagnosed medical conditions, such as psychiatric comorbidities, as well as assess the current medication profile. • Assess the caregiver relationship with the person with dementia, communication styles, expectations, overestimation and underestimation of the person's abilities, and the caregiver's own stress and depression that may inadvertently exacerbate behaviors. • Evaluate the environment for potential triggers, including whether the environment is overstimulating or understimulating, difficult for the person with dementia to navigate, or lacks predictable routines and pleasurable activities.
STEP 3: CREATE
• The multidisciplinary care team, caregiver, and person with dementia (if possible) collaborate to create and implement a treatment plan. • Any medical or environmental issues identified in the "investigate" step should be addressed (e.g., antibiotics for a urinary tract infection, fluids for dehydration, discontinuing medications that may have behavioral side effects, modifications of the environment, improving sleep hygiene). • Providers should brainstorm behavioral and environmental approaches with the caregiver, person with dementia (when possible), and other team members (e.g., visiting nurse, social worker, occupational therapist). • Medications may be implemented if behavioral and environmental approaches are not effective. • Medications may be attempted initially if: – Major depression with or without suicidal ideation (e.g., an antidepressant). – Psychosis causing harm or with great potential for harm (e.g., an antipsychotic). – Aggression causing risk to self or others (e.g., an antipsychotic or citalopram).
STEP 4: EVALUATE
• Assess whether recommended strategies were implemented, whether they were effective, and whether there were intolerable side effects or impacts. • Because behaviors change and fluctuate over the course of dementia, ongoing monitoring is essential, and removal of interventions (especially medications) should be considered periodically. • If psychotropic drugs were prescribed, consider a trial of dose reduction or discontinuation.

Source: Reference 20.

Figure 2. Agitation Decision Tree



IPA = International Psychogeriatric Association.

Source: Reference 25.

Assessment

Recognition and awareness of agitation early on during the course of care for individuals with dementia can help to improve management. Further, the quality of assessment and planning has a critical impact on the quality of care of persons living with dementia.[25] Therefore, ongoing assessment for agitation and other BPSD is beneficial.

A person-centered approach to assessing individuals with dementia should convey respect and seek to understand their experiences. Information about individual preferences, needs, values, routines, sources of joy, and personal meaning should be elicited as part of the assessment.[26] Identification of caregivers and their needs should also be incorporated. In LTCFs, the assessment should evaluate staff needs, resources, satisfaction, and person-centered communication skills.[26]

Several approaches can be used for assessing dementia and BPSD. For example, the Gerontological Society of America has developed the KAER Framework and Toolkit to **K**ickstart the brain health conversation, **A**ssess for cognitive impairment, **E**valuate for dementia, and **R**efer for community resources.[27] This framework calls on clinicians to raise the topic of brain health with patients, possibly during Annual Wellness Visits, and continue the conversation over subsequent visits. Clinicians should also listen for concerns from patients and their families about any changes in memory, cognition, or behavior; evaluate patients for dementia;

document the diagnosis when appropriate; and refer the patient for community resources. Likewise, if agitation is suspected, clinicians can ask prompting questions and/or use screening tools, evaluate the patient, provide a diagnosis when appropriate, and refer for additional resources. Caregiver well-being should also be assessed as part of a comprehensive evaluation for an individual with dementia.

Detection and assessment of agitation symptoms in individuals with AD are often based on caregiver reports.[28,29] Caregivers often first experience and manage agitation-associated behaviors and can play an important role in early detection of symptoms.[30,31]

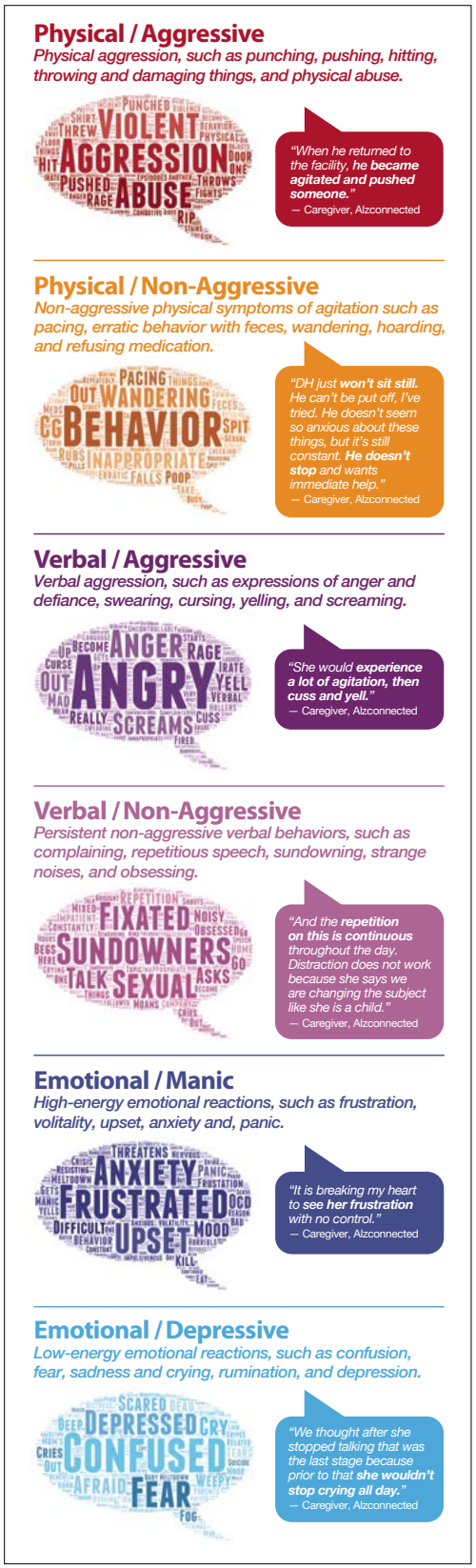
In a Momentum Discussion Podcast episode, the Gerontological Society of America provides insights into AAD from the perspective of a professional caregiver and a family member whose loved one lives with AAD. They share how the condition impacts the person with Alzheimer's disease and those around them and offer strategies to prevent and address troubling BPSD associated with AAD.

Tools for Assessing AAD

Several validated rating scales exist for assessing the prevalence and severity of agitation, however these are primarily used in research settings. A few of the more commonly used scales include the Neuropsychiatric Inventory–Questionnaire (NPI-Q), Cohen-Mansfield Agitation Inventory (CMAI), and Pittsburgh Agitation Scale (PAS). The CMAI is a frequency rating scale that is completed by caregivers to assess agitation behaviors quantitatively. The PAS measures dementia-related agitation severity.[5]

The CMAI identifies three distinct agitation syndromes: aggressive behavior, physically non-aggressive behavior, and verbally aggressive behavior. Word clouds that depict caregiver qualitative perceptions of each of these agitation syndromes are shown in Figure 3.[9] The NPI-Q provides a brief assessment of neuropsychiatric symptomatology in routine clinical practice settings.[32] Although these and other tools are available, barriers such as limited time and provider familiarity (as well as challenges obtaining accurate reports from caregivers) limit the implementation of these tools in clinical practice.

Figure 3. Caregiver Experiences of Agitation Grouped by Cohen-Mansfield Agitation Inventory Categories



Source: Reference 15.

Differential Diagnosis

Agitation can be precipitated by many underlying factors, including neurological, psychiatric, metabolic, medication-related, and other medical conditions such as delirium due to infections, pain, and other causes (Table 3).[5,33] Change in care settings as well as hospitalization may trigger agitation; psychological distress related to these changes can play a role. Agitation occurs in up to 15% of all people aged 65 years and older who are hospitalized for medical illness and is more common in intensive care units.[34-36] The loss of cognition and ability to process the situation in persons with dementia can exacerbate the situation.

External environmental factors may contribute to agitation: temperature, unpleasant noises/smells, soiled undergarments, or a sudden change in routine or caregiver arrangements. A resident/roommate altercation in a senior living setting may incite undesirable verbal or physical responses in persons with AD. Overstimulation (as well as boredom due to understimulation) may precipitate agitation, especially in assisted living and LTCFs. Persons with AD may also experience "sundowning," which is a period of agitation that occurs later in the day.

Internal factors can include clinical features specific to various types of dementia. AAD often arises from misidentifications, paranoia, or visual hallucinations of deceased family members. Verbal and physical agitation in Parkinson's psychosis may be a secondary reaction to the illusions, passage hallucinations, and vividly real visual and auditory hallucinations. Similarly, visual hallucinations in dementia with Lewy bodies can be so brilliantly detailed that the images terrify the individual, resulting in the person acting out the scenario verbally, emotionally, or physically. Depression often occurs secondary to vascular dementia; restlessness, anxiety, and sleep deprivation lower the usual stress threshold, thereby placing the individual at a greater risk for agitation.

To identify any underlying medical and psychiatric conditions that warrant intervention, as well as environmental conditions that can be ameliorated, a comprehensive assessment of persons who present with agitation is necessary. The evaluation should include a diagnostic workup with a complete medical, psychiatric, and detailed medication history, including potentially inappropriate Beers Criteria medications, over-the-counter products, and dietary supplements as well as use of alcohol, cannabis, or other illegal substances. History of adverse drug reactions, especially those associated with benzodiazepines or antipsychotics, should be noted. Input should be obtained from individuals living with dementia, caregivers, significant others, and family members. Friends or neighbors may be queried if there are no available or involved family members. Missing historical information in the absence of knowledgeable family members should be sought through admission/discharge summaries or obtaining records from previous primary care providers.

Underdiagnosis of AAD may result from incorrect or incomplete reporting by caregivers.[37] Caregivers may not always recognize or may not readily talk about agitation-associated behaviors with health care providers. Challenges associated with providing care may bias the caregiver's recognition and reporting of symptoms.[28,30,31] Caregivers commonly score symptoms of agitation differently than clinicians, tend to use a different vocabulary to describe agitation, and attribute it to causes that differ from those identified by the clinician.[7,28]

Table 3. Conditions That May Contribute to Agitation in Persons Living With Dementia

Category	Conditions
Neurological	Pain Sleep disturbance Sensory impairment Stroke Central nervous system tumors Intracranial hemorrhage Meningitis Encephalitis
Psychiatric	Bipolar disorder Schizophrenia Delusions or hallucinations Depression
Metabolic	Electrolyte abnormalities Hyper- or hypoglycemia Hyper- or hypothyroidism
Toxicological	Anticholinergic agents Serotonergic agonists Benzodiazepines Steroids Neuroleptics Alcohol abuse Alcohol withdrawal Carbon monoxide toxicity
Infections	Systemic infections Fever-related delirium Sepsis Urinary tract infections
Other acute medical conditions	Urinary retention Constipation Change in pharmacologic treatment
Other	Environmental triggers (e.g., too hot, too cold) Interpersonal triggers

Source: References 5, 33.

Behavioral Approaches

Person-centered nonpharmacologic interventions are integral to the prevention and management of AAD. Available data suggest that improvements in person-centered communication can result in decreased antipsychotic prescribing.[24]

Behavioral support approaches with individualized efforts to support a person's changing ability to communicate may be particularly helpful for preventing agitation and should be implemented in all interactions with a person living with dementia.

There are many possible strategies that should be individualized to the person living with dementia, the caregiver, and the environment to minimize agitation. General behavioral strategies that have been identified to help prevent and manage agitation include:[20]

- Provide education for the caregiver.
- Enhance effective communication (verbal and nonverbal) between the caregiver and the person living with dementia.
- Apply function-focused care to help maintain physical function and prevent frustration with not being able to perform various activities.[38]
- Create meaningful activities for the person living with dementia.
- Simplify tasks and establish structured routines.
- Simplify and enhance the living environment to ensure safety.

Involving persons with dementia in activities, especially those that include live socialization, may help to address agitation that arises from boredom.[5]

Finally, after instances of agitation, it is helpful for caregivers (and possibly the care team) to review the event. The review should include seeking to detect the triggers of the event and identifying which interventions were (or were not) helpful. This information can be used to implement preventive strategies and better manage future events.

Involving persons with dementia in activities, especially those that include live socialization, may help to address agitation that arises from boredom.

Nonpharmacologic Modalities

Numerous nonpharmacologic treatment modalities have been investigated for managing agitation in adults with cognitive impairment. For example, one systematic review of nonpharmacological modalities for AAD found that listening to music is associated with patients' behavioral improvement and reduction of aggressiveness and agitation. Benefits are greatest when the music selections are individualized to elicit positive memories and when music is combined with interactive activity (e.g., clapping, singing, dancing).[39] Therapeutic touch has been found to produce significant reductions in some behaviors associated with agitation.[39] On the other hand, this review found that bright light therapy did not have clinically significant benefits and may actually worsen symptoms, and aromatherapy was not superior to placebo.[39]

Another systematic review focused on nonpharmacologic strategies for BPSD found that aromatherapy (lavender or lemon balm) improved NPI-Q and PAS scores. Simultaneous use of aromatherapy and acupressure reduced agitation significantly. Combining activities (e.g., music, art, exercise) decreased NPI scores, including agitation.[40]

Pharmacologic Approaches

In May 2023, brexpiprazole became the first medication to be approved by the U.S. Food and Drug Administration (FDA) for the treatment of agitation associated with dementia due to Alzheimer's disease.[41] This was the first FDA approval for the treatment of agitation due to any form of dementia.[41] Prior to this approval, medications used off-label were the only pharmacologic options for AAD; they were used in approximately 60% of residents in LTCFs and 40% of persons living with dementia in the community.[42-43] Classes of medications that have been used off-label to treat AAD include benzodiazepines, antihistamines, antidepressants, antiepileptics, and antipsychotics.[44] These agents are limited by only moderate efficacy and most have serious safety and tolerability concerns that are often increased in elderly populations.[45]

Historically, antipsychotics have been used as first-line pharmacologic treatment for AAD, even though such use was off-label.[45] Atypical antipsychotics, including olanzapine, quetiapine, and risperidone, have been used off-label to treat agitation in persons living with AD, with some clinical benefits noted. However, antipsychotics are associated with an increased risk of several adverse events and increased mortality.[5]

Currently, all antipsychotic medications, including brexpiprazole, carry an FDA boxed warning in the label for the increased risk of death in elderly patients with dementia-related psychosis.[46] This boxed warning was based on an FDA meta-analysis of 17 placebo-controlled studies in elderly patients (aged 65 years or older) with dementia-related psychosis, mostly treated with atypical antipsychotics.[47] In placebo-controlled trials, elderly patients showed an increased rate of death of about 4.5% in the drug-treated group compared to a rate of about 2.6% in the placebo group

(1.6- to 1.7-fold increased risk of death compared to placebo). Most deaths were caused by either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) events. The boxed warning for brexpiprazole was modified with the approval for treatment of agitation associated with dementia due to AD to clarify that brexpiprazole is not approved for the treatment of patients with dementia-related psychosis without agitation associated with dementia due to AD.[46]

Caregiver discussion regarding black box antipsychotic risks and benefits is essential for informed consent and should be documented.

Clinical trials of selective serotonin reuptake inhibitors, including citalopram, escitalopram, and sertraline, have found similar efficacy to atypical antipsychotics for reducing agitation in persons with AD and are associated with a reduced risk of adverse events.[5] Benzodiazepines are also used off-label for managing AAD. Safety concerns associated with the use of benzodiazepines in older adults include increased risk of cognitive impairment, falls, and fractures.[48] Benzodiazepines may have a paradoxical effect on AAD, resulting in behavioral disinhibition and a worsening of agitation.[5]

Documenting Agitation

Documentation of agitation by clinicians is needed to track and evaluate the effectiveness of interventions, monitor any progression of the agitation, and support the development of an ongoing plan of care for persons with AAD. In addition to documenting BPSD, clinicians should document positive outcomes of interventions (e.g., smiles more, engages in activities) to help capture data about quality of life. Documentation is also essential to support communication among providers and continuous follow-up care.

If agitation is reported during a patient visit, the presence of agitation should be recorded in the visit notes and problem list. Clinicians also need to include this information in the electronic health record to coordinate the care of individuals living with dementia who frequently transition across settings. Primary care teams should consider instituting routine documentation of behavioral symptoms associated with dementia (such as agitation) in the list of diagnoses and include relevant check boxes in the electronic health record.[42]



Caregiver Collaboration

Treatment of the care recipient and family members as equal partners is a foundational concept for person-centered care.[24] Providers should approach caregivers as crucial team members who will be carrying out and evaluating the effects of the recommended interventions. Supports may be needed for caregivers to sustain positive and healthy interactions with the person with dementia and avoid mistreatment, which could be precipitated by caregiver frustration with BPSD.[49]

Providers should aim to model problem-solving approaches and involve caregivers, as well as the person living with dementia to the extent possible, in decision-making and brainstorming strategies to manage agitation. Examples that caregivers have reported using to manage BPSD in AAD include: (1) modifying interactions within the care dyad (e.g., simplifying communication); (2) modifying the care environment (e.g., using written prompts); (3) tapping into activity engagement; (4) using humor; (5) engaging in self-care; and (6) availing oneself of social support.[50]

Strategies that caregivers can use to help prevent and respond to agitation are listed in Table 4.[50-53]

Table 4. Strategies for Care Providers to Prevent and Respond to Agitation

PREVENTING AGITATION
• **Deliver preference-based person-centered care.** Use concepts embedded in the Institute for Healthcare Improvement age-friendly initiative (address 4Ms: monitor and address what matters, medications, mentation, and mobility).
• **Create a calm environment.** Remove stressors. This may involve moving the person to a safer or quieter place or offering a security object, rest, or privacy. Try soothing rituals and limiting caffeine use.
• **Avoid environmental triggers.** Noise, glare, and background distraction (e.g., having the television on) can act as triggers. Reduce noise, clutter, or the number of people in the room. Keep well-loved objects and photographs around to help the person feel more secure.
• **Monitor personal comfort.** Check for pain, hunger, thirst, constipation, full bladder, fatigue, infections, and skin irritation. Make sure the room is at a comfortable temperature. Be sensitive to fears, misperceived threats, and frustration with expressing what is wanted.
• **Simplify tasks and routines.** Try to keep a regular schedule, such as bathing, dressing, and eating at the same time each day.
• **Provide an opportunity for exercise.** Go for a walk. Garden together. Put on music and dance.
• **Support self-management.** Allow the person to keep as much control over his or her life as possible.
RESPONDING TO AGITATION
• **Listen to the frustration.** Find out what may be causing the agitation and try to understand.
• **Provide reassurance.** Speak calmly. Use phrases such as: "You're safe here"; "I'm sorry that you are upset"; and "I will stay until you feel better." Let the person know you are there and demonstrate empathy if the person is angry, fearful, or frustrated.
• **Redirect the person.** Try to distract the person with a favorite snack, object, or activity.
• **Involve the person in activities.** Try using art, music, or other activities to help engage the person and divert attention away from the anxiety.
• **Modify the environment.** Decrease noise and distractions or relocate.
• **Find outlets for the person's energy.** The person may be looking for something to do. Take a walk or go for a car ride.
• **Check yourself.** Do not raise your voice; show alarm or offense; or corner, crowd, restrain, criticize, ignore, or argue with the person. Take care not to make sudden movements out of the person's view.

Source: References 50-53.

Shared Decision-Making

Shared decision-making is defined by the Agency for Healthcare Research and Quality (AHRQ) as "a model of patient-centered care that enables and encourages people to play a role in the medical decisions that affect their health."[54]

This model of care recognizes the desire of patients to be more involved in their care in partnership with their care teams. Shared decision-making can increase patient satisfaction and lead to better health outcomes. In shared decision-making, patients and their caregivers are educated regarding the condition and treatment options as well as the risks and benefits of various treatment options.[54] Care providers should aim to fully educate caregivers as well as patients (to the extent possible) about anticipated disease progression and management strategies so that they can be informed partners in guiding care.

AHRQ's SHARE approach can be used to implement shared decision-making:[54]
Seek the person's perspective.
Help the person explore and compare treatment options.
Assess the person's values and preferences.
Reach a decision with the person.
Evaluate the person's decision.

Of note, a person's capacity to participate in shared decision-making is expected to decline as dementia progresses but should be supported to the extent possible. For example, in later stages of dementia, individuals may be capable of providing yes/no answers to simple questions about their care.

Care Planning and Goal Setting

There is a need for providers to facilitate conversations around BPSD as an integral component of advance care planning. Conversations should address four key points: the progressive nature of dementia, the commonality of BPSD, pharmacological treatment for BPSD, and the difficulty in balancing agitation and sedation to optimize well-being and safety. Discussions should begin as early as possible in the progression of AD to help facilitate meaningful care decisions.[55]

Caregivers as well as the person living with dementia (to the extent possible) should receive education about the anticipated disease trajectory and best practices of behavior management throughout the course of the disease. Education should include information about unmet needs that are common for persons living with dementia as well as how to identify changes in cognition or mood that can help prevent escalation of agitation.[24]

Discussions regarding the management of agitation (as well as other behavioral symptoms associated with dementia) should be initiated early in the disease process to develop guidance for decision-making as disease progresses. Clinicians should collaborate with caregivers to have ongoing discussions about how to manage behaviors and should assess for caregiver burnout at each encounter.

Owing to the progressive nature of dementia, the ability to make informed decisions declines over time. Advance directives are legal documents that identify one's medical preferences should one become unable to make decisions or become incapacitated. These documents also name another person (e.g., durable power of attorney) to make or implement those decisions in situations when the person living with dementia is unable to participate in a shared decision-making process. Laws governing advance directives and power of attorney vary among states; people with dementia and their caregivers may benefit from legal advice to determine which documents are most appropriate. Importantly, advance care planning should go well beyond the creation of an advance directive for end-of-life care to encompass a wide range of issues that may arise throughout the progression of dementia care.

Communication Strategies

Although well-informed individuals are best prepared to make educated decisions about their care, providers should be cautious about providing too much information immediately after an initial diagnosis of dementia. Individuals with dementia and their loved ones may find it overwhelming and depressing to learn about everything that can happen along the trajectory all at once, particularly when it does not align with the current experience of the disease process. Starting with introductory education that there may be changes in the way the person with dementia thinks and behaves can be helpful. For example, educating caregivers that the person with dementia may stop responding to logic and that their responses to various situations may shift can help those caregivers to prepare for the future, while detailed information about a range of potential challenges and management strategies can be shared with caregivers at a later time as those situations emerge. However, it is strongly advisable to have candid conversations relatively early in the disease process so that persons with dementia can engage with decision-making to the greatest extent possible.[55]

The Nursing Home Toolkit (see Resources) has been developed to help staff in all types of senior living communities manage the needs of residents with BPSD. Resources are built around a person-centered philosophy and can be implemented to help support effective communication with and about persons living with dementia.[56] Many of these resources are useful for educating staff to support residents with dementia.

Finally, emerging technologies may help support caregiver management of BPSD. For example, WeCareAdvisor is a web-based tool designed to assist family caregivers with assessing, managing, and tracking BPSD; this tool has been found to significantly decrease caregiver distress, but it did not significantly impact other outcomes.[57]

Summary

Agitation is a common symptom of AD that often causes substantial distress for persons with AD and their caregivers and in many instances results in negative outcomes. Agitation was poorly defined for many years; the recently published IPA definition and accompanying assessment and management decision tree can help provide greater clarity for the identification, assessment, and management of agitation in persons with AD.

Optimization of nonpharmacologic strategies based on person-centered approaches to managing agitation is the backbone of treatment approaches and modalities without medications for AD. Brexpiprazole, which was recently approved by the FDA for the treatment of agitation associated with AD, is a long-awaited pharmacologic option, but risks and benefits must be disclosed in accordance with the shared–decision-making framework. Because off-label medications for agitation have only modest clinical benefits and a high side-effect burden (e.g., negative impact on cognitive function, higher cerebrovascular side effects, longer hospitalizations, risk of mortality), they should be used with caution. Involving persons living with dementia (to the extent possible) and caregivers in guiding care is an essential component of person-centered care and can help with overall behavioral management of AAD.

Interdisciplinary Insight: Treatment Approaches Throughout the Course of AAD

Susan Scanland, MSN, CRNP, GNP-BC, CDP, founder of Dementia Connection, has 40 years of clinical practice in Alzheimer's and other dementias. A gerontological nurse practitioner, Scanland subspecialized as a long-term care dementia consultant to primary care providers (PCP) for 20 years. Her area of expertise is optimizing pharmacologic and nonpharmacologic management of dementia behaviors. She shared her insights and described her experiences managing a person living with AAD throughout the care continuum.

Emergence of AD and Agitation

Jane, an 82-year-old woman, is a retired certified public accountant (CPA). She is cared for by her daughter, Carol, who lives locally with her husband and two teenaged sons and holds a full-time job. Carol assists Jane with instrumental activities of daily living (e.g., shopping, paying bills, laundry) and has hired an aide for meal preparation and cleaning.

Carol notices that Jane is starting to struggle with money and her sleep patterns are becoming erratic. Jane begins phoning Carol numerous times per night, resulting in sleep deprivation and irritability for Carol. To help with sleep, Carol gave diphenhydramine HCl to her mother. Two nights later, Jane wandered out of her home in her nightgown, ringing the neighbor's doorbell and looking for her (deceased) husband. Carol was notified and called Jane's PCP the next morning. The PCP ordered a delirium workup (negative). Diphenhydramine HCl was immediately stopped, and the PCP made a referral for Jane to get a memory evaluation. The aide was hired to stay overnight. The PCP also referred Carol to an Alzheimer's Association caregiver support group.

After a 9-month delay due to a shortage of memory specialists, Jane was diagnosed with AD. Her Mini-Mental State Examination score was 16, indicating moderate cognitive impairment. Jane was referred to a geriatric psychiatrist/gerontological nurse practitioner team who initiated combination memantine/donepezil extended-release capsules 7 mg/10 mg daily, which was titrated over 4 weeks to the maximum dosage of 28 mg/10 mg daily. The team also encouraged cognitive exercises and outdoor walks with Carol.

Carol noticed overall functional improvement for a year, and Jane seemed to "hold her own" cognitively. Then, Jane began to exhibit anxiety, restlessness, and hostility. Jane accused her overnight aides of stealing her clothes and jewelry. Jane tried to lock the aides out of her house upon arrival. Because Jane's behaviors were presenting serious safety concerns, Carol could no longer balance her mother's acute situations with her own work and family demands, and she found a residential placement for Jane in a memory care center.

Managing AAD With Person-Centered Care

Following admission to the memory care center, Jane was restless—frequently pacing and exit-seeking. She walked to the locked doorway and would continuously bang and shake the exit door handles, yelling: "Open these doors! Taxes are due for my clients!" She physically resisted staff who attempted to redirect her. Jane screamed when other residents crossed her path.

Jane's care team developed a plan to modify her behavior and held unit conferences to help the care team refine communication strategies. They located an old desk from storage and created a "CPA workstation" with calculators, ledgers, and inactive checkbooks for Jane to use. Jane was delighted to be "back to work." This customized activity program kept her busy most of the day. Jane also loved when the unit's pet therapy Pomeranian snuggled by her feet. During sundowning hours, the nursing assistant would massage Jane's shoulders or hands with lemon balm.

Initiation of Pharmacotherapy for AAD

Six months later, Jane began pacing and having verbal outbursts and altercations with other residents. She physically resisted the nursing assistants who tried to bathe or dress her, and she became less interested in the CPA workstation and recreational activities. Escitalopram 10 mg was initiated, which enabled Jane to return to her "accounting office" and prevented agitation.

After about a year, Jane became restless and agitated again and began screaming at other residents. In one incident, she punched another resident.

Jane's daughter, Carol, was notified and consulted with the nurse practitioner and physician assistant. In their conversation (which occurred prior to FDA approval of brexpiprazole for the indication of agitation associated with dementia due to AD), they explained that antipsychotics are not FDA-approved for dementia and are generally only used as a last resort. They detailed the boxed warning and the risk of mortality due to stroke, cardiac events, or pneumonia. Carol felt the benefit of preventing her mother from hurting other residents while also allowing her to more fully engage in activities she found enjoyable was worth the risk of using an antipsychotic. She agreed to Jane's treatment with risperidone and signed a consent form for antipsychotic use for dementia. Risperidone 0.5 mg daily prevented physical aggression toward other residents for 3 to 4 months; then the dosage was increased to 1.0 mg daily when Jane twisted an aide's wrist, resulting in a severe sprain.

The staff noticed that Jane was more somnolent during the day and stiff during activities of daily living care. The dining room care attendants observed that Jane was experiencing mild dysphagia but did not have any choking episodes. Her diet was changed to minced and moist foods. Attempts were made to decrease risperidone to 0.5 mg daily, but Jane's physical and verbal aggression returned, so she was maintained on 1.0 mg daily.

Two months later, Jane developed dyspnea, hypoxia, tachycardia, and fever. She was admitted to the hospital and died the next day from aspiration pneumonia.

Interdisciplinary Insight: Assessing and Managing Needs of Patients With AAD

Laura Medders, LCSW, is a clinical social worker and administrative director at a nurse-led primary care clinic for people living with dementia. She communicates with patients and caregivers to assess needs, coordinate care, and plan for future needs. She regularly makes treatment recommendations within the integrated, interdisciplinary care teams that align with patient goals of care and aims to fully involve caregivers in treatment plans.

Patient-Centered Approaches to Agitation

Medders observes that many of her patients experience some sort of agitation. It becomes very distressing for both the person with dementia and the caregiver. Agitation frequently emerges as the patients lose their ability to understand the world and become confused and frustrated. Because their ability to reason is reduced, logic-based strategies to address confusion are generally unhelpful and can conversely increase frustration, especially if caregivers are unable to identify effective management strategies and become frustrated themselves. This situation may occur as the disease progresses and strategies that worked initially lose their effectiveness. Instead, "It is important for caregivers to understand that the person cannot self-regulate or control their behaviors in the same way as before, and aim to join the person in their reality," observes Medders.

Efforts to redirect persons living with dementia and engage them in other activities may also be helpful. For example, if the person insists on going to work, verbal assurance that the person retired from work is often not helpful and can lead to repetitive arguments that result in agitation (and often frustrate the caregiver). Instead, redirection by involving the person in other activities (e.g., eating breakfast first, accompanying the caregiver to run errands) can help shift the focus and de-escalate situations.

It is also advantageous to assess the environment for triggers that prompt the person living with dementia to insist on activities. For example, keys sitting on the kitchen counter could trigger a desire to go somewhere. Regularly assessing the environment and how the person with dementia reacts can help to identify appropriate management strategies.

Managing agitation in LTCFs may be more complex, particularly when the impact on other residents is considered, and creative solutions are often needed, explains Medders. "We had one resident who was a retired flight attendant, who would regularly go into other residents' rooms to check on them, and this behavior became very disruptive. In this case, the staff gave her a cart to push around and offer drinks to other residents in the community, and this approach effectively managed the situation." However, identifying such solutions can be complicated, particularly when facilities have high staff turnover and have to rely on agency staff to fill gaps.

Tailoring Responses to Cognitive Capacity

How agitation is expressed and how it can be managed also depend on the cognitive capacity of individuals with AAD. Sometimes caregivers share that it would be much easier if the people they care for comprehended that they have dementia, Medders reports. In these situations, helping caregivers understand that the disease has impacted the person's insight and that the person is unable to change the agitated behavior can help the caregivers shift how they approach the person. Furthermore, individuals who are earlier in the disease process often do have insight and are distressed by their cognitive symptoms; thus, it may be kinder not to try to convince them that they have a disease. Instead, caregivers can be coached to seek to understand the person's experience on an emotional level rather than on a rational level.

"Therapeutic lying" is a strategy that some people in the aging industry employ or recommend, in which caregivers and providers tell falsehoods to people living with dementia. "In some cases, lying may alleviate the immediate conflict but it can backfire significantly if the person realizes the caregiver is lying," cautions Medders.

For example, Cathy's family convinced her to move closer to them and placed her in an assisted living community by telling Cathy that she was only staying for the winter. Since Cathy thought she was a snowbird, this strategy was effective at first during the winter months. However, when springtime came around, Cathy wanted to return home and became fixated on

trying to leave the facility. She constantly tried to pack her things and leave, had called a moving company, and refused to engage in activities. This situation was difficult because Cathy remembered her previous home and wanted to return. Consequently, the family's lie created persistent frustration because Cathy had unrealistic expectations based on what her children told her.

The social worker tried to identify strategies to help Cathy better connect with the new community and worked with the family to provide coaching on how to manage their mother's understandable frustration. This approach aims to delay the desire to move home while waiting for the disease to progress. However, since the disease course is unpredictable, this is not an ideal strategy.

"Because of situations like this, I don't recommend the practice of therapeutic lying," shares Medders. "I've seen too many situations like this one where caregivers underestimated patients' cognitive capacity and the lie results in significant distress."

Finally, if individuals living with dementia no longer recognize their spouse, it can present unique challenges. Under this circumstance, the person may not understand why the spouse is in the house, view the spouse as a threat, become hostile, and escalate behaviors. "Arguing 'I am your husband,' will not be effective." Instead, the caregiver leaving the person with dementia safely alone may often reset the situation and the person may forget about it a few minutes later. "We tell caregivers to leave the room when something like this happens and to change their clothes or do something else to adjust their appearance and then come back a few minutes later to see if the situation resolves itself," recommends Medders.

Medders shared that she has had patients call the police to report an intruder when they do not recognize their spouse. Failure to recognize people can become a significant safety risk, especially if there are firearms in the home. Additionally, in LTCFs, if a resident does not recognize staff or understand why they are providing personal care, the resident may view them as a threat and become hostile or violent. This can further exacerbate issues with staff turnover.

When to Explore Pharmacotherapy

Individual reactions to behavioral approaches vary. In some cases, persons living with dementia can be easily redirected, but in others their agitation persists. In those situations, particularly if there is a safety risk or high level of distress, the team will discuss using medications with the family, shares Medders.

Additionally, medications can help reduce the need for inpatient psychiatric hospitalizations. "Inpatient psych stays can be very disruptive and traumatic for patients, particularly if they are prescribed medications with significant side effects in elderly and frail patients. We often see [these medications] precipitate a need for a higher level of care, so we really try to avoid them," reports Medders.

For example, Sam was an LTCF resident who spent a few weeks in an inpatient psychiatric hospital. During that time, he became very deconditioned. Although he previously could independently ambulate, he was unable to walk and was "a different person" when he returned to the LTCF following his hospitalization. The lack of routine, individual support, and activity; the change in the environment; and the additional medications had a significant toll on his body, and he died a few months after the hospitalization, reports Medders.

Multidisciplinary Care Teams

Multidisciplinary care teams can effectively leverage different perspectives to identify solutions for patients. "When one provider on the team feels stuck, there is usually someone on the team who can have an impact on the situation," says Medders. In some cases, this involves a geriatric psychiatrist who optimizes medication management. In others, it includes a social worker who can provide coaching and support to caregivers or brainstorm behavioral solutions or entails an occupational therapist who can recommend environmental modifications that reduce frustration.

Resources and Suggested Reading

For Professionals

Desai A, Grossberg G. *Psychiatric Consultation in Long-Term Care: A Guide for Healthcare Professionals.* 2nd ed. Cambridge University Press; 2017. doi:10.1017/9781316687024

Fazio S, Pace D, Maslow K, Zimmerman S, Kallmyer B. Alzheimer's Association Dementia Care Practice Recommendations. *Gerontologist.* 2018;58(suppl 1):S1–S9. doi:10.1093/geront/gnx182

Fazio S, Zimmerman S, Doyle PJ, et al. What is really needed to provide effective, person-centered care for behavioral expressions of dementia? Guidance from the Alzheimer's Association Dementia Care Provider Roundtable. *J Am Med Dir Assoc.* 2020;21(11):1582–1586.e1. doi:10.1016/j.jamda.2020.05.017

National Center on Elder Abuse. Research Brief: Mistreatment of People With Dementia. 2023. https://ncea.acl.gov/

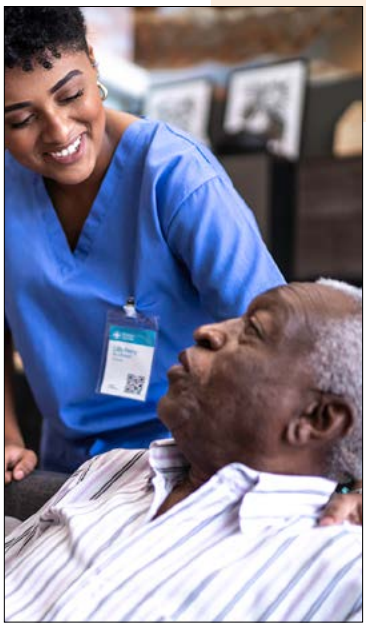
Nursing Home Toolkit
http://www.nursinghometoolkit.com

Preference Based Living
https://www.preferencebasedliving.com

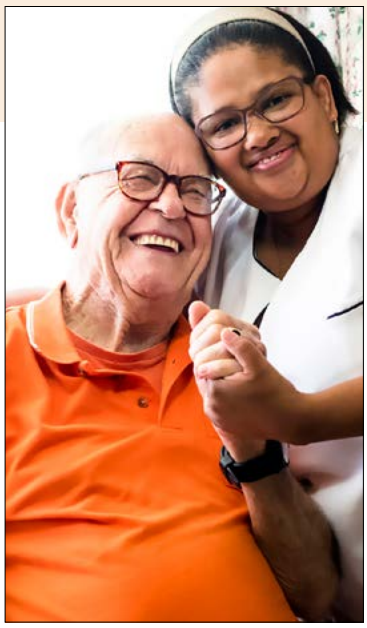
PsychU—Agitation Resources for Professionals
https://psychu.org/resource-library/agitation

Reach MD—AAD Treatment Guidelines: Addressing Challenges and Unmet Needs
https://reachmd.com/programs/medical-industry-feature/addressing-challenges-and-unmet-needs/13702/

Reach MD—An Introductory Look at Agitation in Alzheimer's Dementia
https://reachmd.com/programs/medical-industry-feature/an-introductory-look-at-agitation-in-alzheimers-dementia/13699/







For Caregivers

Alzheimer's Association—Anxiety and Agitation
https://www.alz.org/help-support/caregiving/stages-behaviors/anxiety-agitation

Caregiver Action Network
https://www.caregiveraction.org

National Alliance for Caregiving
https://www.caregiving.org

National Institute on Aging—Coping With Agitation and Aggression in Alzheimer's Disease
https://www.nia.nih.gov/health/coping-agitation-and-aggression-alzheimers-disease

WeCareAdvisor
https://wecareadvisorstudy.com





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References

1. Alzheimer's Association. 2022 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2022;18(4):700–789. doi:10.1002/alz.12638
2. Scales K, Zimmerman S, Miller SJ. Evidence-based nonpharmacological practices to address behavioral and psychological symptoms of dementia. *Gerontologist.* 2018;58(suppl 1):S88–S102. doi:10.1093/geront/gnx167
3. Lyketsos CG, Lopez O, Jones B, et al. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the Cardiovascular Health Study. *JAMA.* 2002;288(12):1475–1483. doi:10.1001/jama.288.12.1475
4. Reus VI, Fochtmann LJ, Eyler AE, et al. The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia. *Am J Psychiatry.* 2016;173(5):543–546. doi:10.1176/appi.ajp.2015.173501
5. Carrarini C, Russo M, Dono F, et al. Agitation and dementia: prevention and treatment strategies in acute and chronic conditions. *Front Neurol.* 2021;12:644317. doi:10.3389/fneur.2021.644317
6. Van der Mussele S, Le Bastard N, Saerens J, et al. Agitation-associated behavioral symptoms in mild cognitive impairment and Alzheimer's dementia. *Aging Ment Health.* 2015;19(3):247–257. doi:10.1080/13607863.2014.924900
7. Sano M, Cummings J, Auer S, et al. Agitation in cognitive disorders: progress in the International Psychogeriatric Association consensus clinical and research definition. *Int Psychogeriatr.* 2023;1–13. doi:10.1017/S1041610222001041
8. Rosenberg PB, Nowrangi MA, Lyketsos CG. Neuropsychiatric symptoms in Alzheimer's disease: what might be associated brain circuits? *Mol Aspects Med.* 2015;43–44:25–37. doi:10.1016/j.mam.2015.05.005
9. Banno K, Nakaaki S, Sato J, et al. Neural basis of three dimensions of agitated behaviors in patients with Alzheimer disease. *Neuropsychiatr Dis Treat.* 2014;10:339–348. doi:10.2147/NDT.S57522
10. Wright CI, Dickerson BC, Feczko E, et al. A functional magnetic resonance imaging study of amygdala responses to human faces in aging and mild Alzheimer's disease. *Biol Psychiatry.* 2007;62(12):1388–1395. doi:10.1016/j.biopsych.2006.11.013
11. Liu KY, Stringer AE, Reeves SJ, et al. The neurochemistry of agitation in Alzheimer's disease: a systematic review. *Ageing Res Rev.* 2018;43:99–107. doi:10.1016/j.arr.2018.03.003
12. Arnsten AF, Raskind MA, Taylor FB, et al. The effects of stress exposure on prefrontal cortex: translating basic research into successful treatments for post-traumatic stress disorder. *Neurobiol Stress.* 2015;1:89–99. doi:10.1016/j.ynstr.2014.10.002
13. Evers EA, Sambeth A, Ramaekers JG, et al. The effects of acute tryptophan depletion on brain activation during cognition and emotional processing in healthy volunteers. *Curr Pharm Des.* 2010;16(18):1998–2011. doi:10.2174/138161210791293060
14. Lindenmayer JP. The pathophysiology of agitation. *J Clin Psychiatry.* 2000;61(suppl 14):5–10.
15. Otsuka. Data on file. 2023.
16. Bransvik V, Granvik E, Minthon L, et al. Mortality in patients with behavioural and psychological symptoms of dementia: a registry-based study. *Aging Ment Health.* 2021;25(6):1101–1109. doi:10.1080/13607863.2020.1727848
17. Peters ME, Schwartz S, Han D, et al. Neuropsychiatric symptoms as predictors of progression to severe Alzheimer's dementia and death: the Cache County Dementia Progression Study. *Am J Geriatr Psychiatry.* 2015;172(5):460–465. doi:10.1176/appi.ajp.2014.14040480
18. Deardorff WJ, Grossberg GT. Behavioral and psychological symptoms in Alzheimer's dementia and vascular dementia. *Handb Clin Neurol.* 2019;165:5–32. doi:10.1016/B978-0-444-64012-3.00002-2
19. Toot S, Swinson T, Devine M, et al. Causes of nursing home placement for older people with dementia: a systematic review and meta-analysis. *Int Psychogeriatr.* 2017;29(2):195–208. doi:10.1017/S1041610216001654
20. Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. *BMJ.* 2015;350:h369. doi:10.1136/bmj.h369
21. Porter CN, Miller MC, Lane M, et al. The influence of caregivers and behavioral and psychological symptoms on nursing home placement of persons with Alzheimer's disease: a matched case-control study. *SAGE Open Med.* 2016;4:2050312116661877. doi:10.1177/2050312116661877
22. Knapp M, Chua KC, Broadbent M, et al. Predictors of care home and hospital admissions and their costs for older people with Alzheimer's disease: findings from a large London case register. *BMJ Open.* 2016;6(11):e013591. doi:10.1136/bmjopen-2016-013591
23. Cloutier M, Gauthier-Loiselle M, Gagnon-Sanschagrin P, et al. Institutionalization risk and costs associated with agitation in Alzheimer's disease. *Alzheimers Dement.* 2019;5:851–861. doi:10.1016/j.trci.2019.10.004
24. Fazio S, Zimmerman S, Doyle PJ, et al. What is really needed to provide effective, person-centered care for behavioral expressions of dementia? Guidance from the Alzheimer's Association Dementia Care Provider Roundtable. *J Am Med Dir Assoc.* 2020;21(11): 1582–1586.e1. doi:10.1016/j.jamda.2020.05.017
25. Grossberg GT, Sanford A, Scanland S, et al. Expert insights from the Gerontological Society of America Agitation in Alzheimer's Disease Workgroup. Poster presented at: Gerontological Society of America Annual Scientific Meeting; November 2–6, 2022; Indianapolis, IN.
26. Molony SL, Kolanowski A, Van Haitsma K, et al. Person-centered assessment and care planning. *Gerontologist.* 2018;58(suppl 1):S32–S47. doi:10.1093/geront/gnx173
27. Gerontological Society of America. *The GSA KAER Toolkit for Primary Care Teams.* 2020 edition. https://www.geron.org/brainhealth
28. Stella F, Forlenza OV, Laks J, et al. Caregiver report versus clinician impression: disagreements in rating neuropsychiatric symptoms in Alzheimer's disease patients. *Int J Geriatr Psychiatry.* 2015;30(12):1230–1237. doi:10.1002/gps.4278
29. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2023;19(4):1598–1695. doi:10.1002/alz.13016

30. Lindeza P, Rodrigues M, Costa J, et al. Impact of dementia on informal care: a systematic review of family caregivers' perceptions. *BMJ Support Palliat Care.* 2020;0:1–12. doi:10.1136/bmjspcare-2020-002242
31. Gallego-Alberto L, Losada A, Cabrera I, et al. "I feel guilty." Exploring guilt-related dynamics in family caregivers of people with dementia. *Clin Gerontol.* 2022;45(5):1294–1303. doi:10.1080/07317115.2020.1769244
32. Kaufer DI, Cummings JL, Ketchel P, et al. Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. *J Neuropsychiatry Clin Neurosci.* 2000;12(2):233–239. doi:10.1176/jnp.12.2.233
33. National Institute on Aging. Coping with agitation and aggression in Alzheimer's disease. Content reviewed May 17, 2017. https://www.nia.nih.gov/health/coping-agitation-and-aggression-alzheimers-disease
34. Mansutti I, Venturini M, Palese A, et al. Episodes of psychomotor agitation among medical patients: findings from a longitudinal multicentre study. *Aging Clin Exp Res.* 2022;32(6):1101–1110. doi:10.1007/s40520-019-01293-5
35. Almeida TM, Azevedo LC, Nosé PM, et al. Risk factors for agitation in critically ill patients. *Rev Bras Ter Intensiva.* 2016;28(4):413–419. doi:10.5935/0103-507X.20160074
36. Halpern R, Seare J, Tong J, et al. Using electronic health records to estimate the prevalence of agitation in Alzheimer disease/dementia. *Int J Geriatr Psychiatry.* 2019;34(3):420–431. doi:10.1002/gps.5030
37. Lyketsos CG. Neuropsychiatric symptoms in dementia: overview and measurement challenges. *J Prev Alzheimers Dis.* 2015;2(3):155–156. doi:10.14283/jpad.2015.60
38. Resnick B. Function Focused Care: Optimizing Function With Physical Activity in Assisted Living Residents [video]. Accessed May 24, 2023. https://functionfocusedcare.wordpress.com/
39. Millán-Calenti JC, Lorenzo-López L, Alonso-Búa B, et al. Optimal nonpharmacological management of agitation in Alzheimer's disease: challenges and solutions. *Clin Interv Aging.* 2016;11:175–184. doi:10.2147/CIA.S69484
40. de Oliveira AM, Radanovic M, de Mello PC, et al. Nonpharmacological interventions to reduce behavioral and psychological symptoms of dementia: a systematic review. *Biomed Res Int.* 2015;2015:218980. doi:10.1155/2015/218980
41. U.S. Food and Drug Administration. FDA approves first drug to treat agitation symptoms associated with dementia due to Alzheimer's disease [press release]. May 11, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treat-agitation-symptoms-associated-dementia-due-alzheimers-disease
42. Aigbogun MS, Cloutier M, Gauthier-Loiselle M, et al. Real-world treatment patterns and characteristics among patients with agitation and dementia in the United States: findings from a large, observational, retrospective chart review. *J Alzheimers Dis.* 2020;77(3):1181–1194. doi:10.3233/JAD-200127
43. Tractenberg RE, Weiner MF, Thal LJ. Estimating the prevalence of agitation in community-dwelling persons with Alzheimer's disease. *J Neuropsychiatry Clin Neurosci.* 2002;14(1):11–18. doi:10.1176/jnp.14.1.11
44. O'Gorman C, Khoury R, Anderson A, et al. A framework for developing pharmacotherapy for agitation in Alzheimer's disease: recommendations of the ISCTM working group. *J Prev Alzheimers Dis.* 2020;7(4):274–282. doi:10.14283/jpad.2020.37
45. U.S. Food and Drug Administration. FDA Briefing Document: Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Peripheral and Central Nervous System Drugs Advisory Committee. April 14, 2023. https://www.fda.gov/media/167066/download
46. Otsuka. Rexulti package insert. May 2023. https://otsuka-us.com/sites/g/files/qhldwo7141/files/media/static/Rexulti-PI.pdf
47. Jeste DV, Blazer D, Casey D, et al. ACNP white paper: update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology.* 2008;33(5):957–970. doi:10.1038/sj.npp.1301492
48. Defrancesco M, Marksteiner J, Fleischhacker WW, et al. Use of benzodiazepines in Alzheimer's disease: a systematic review of literature. *Int J Neuropsychopharmacol.* 2015;18(10):pyv055. doi:10.1093/ijnp/pyv055
49. National Center on Elder Abuse. Research Brief: Mistreatment of People With Dementia. 2023. https://ncea.acl.gov/
50. Polenick CA, Struble LM, Stanislawski B, et al. "I've learned to just go with the flow": family caregivers' strategies for managing behavioral and psychological symptoms of dementia. *Dementia.* 2020;19(3):590–605. doi:10.1177/1471301218780768
51. Alzheimer's Association. Anxiety and Agitation. Accessed March 30, 2020. https://www.alz.org/help-support/caregiving/stages-behaviors/anxiety-agitation
52. Preference Based Living website. Accessed May 25, 2023. https://www.preferencebasedliving.com
53. Institute for Healthcare Improvement. Age-friendly health systems. Accessed May 25, 2023. https://www.ihi.org/Engage/Initiatives/Age-Friendly-Health-Systems/Pages/default.aspx
54. Agency for Healthcare Research and Quality. Shared decisionmaking. Last reviewed April 2023. https://www.ahrq.gov/cahps/quality-improvement/improvement-guide/6-strategies-for-improving/communication/strategy6i-shared-decisionmaking.html
55. Richler LG, Shimizu M, Huang H, et al. Challenges of agitation in dementia: a plea for early discussion. *Harv Rev Psychiatry.* 2023;31(1):22–27. doi:10.1097/HRP.0000000000000352
56. The Commonwealth Fund. Nursing Home Toolkit. Accessed June 26, 2023. http://www.nursinghometoolkit.com
57. Kales HC, Gitlin LN, Stanislawski B, et al. Effect of the WeCareAdvisor on family caregiver outcomes in dementia: a pilot randomized controlled trial. *BMC Geriatr.* 2018;18(1):113. doi:10.1186/s12877-018-0801-8

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