



Unmet Needs In Agitation Associated With Dementia Due To Alzheimer's Disease

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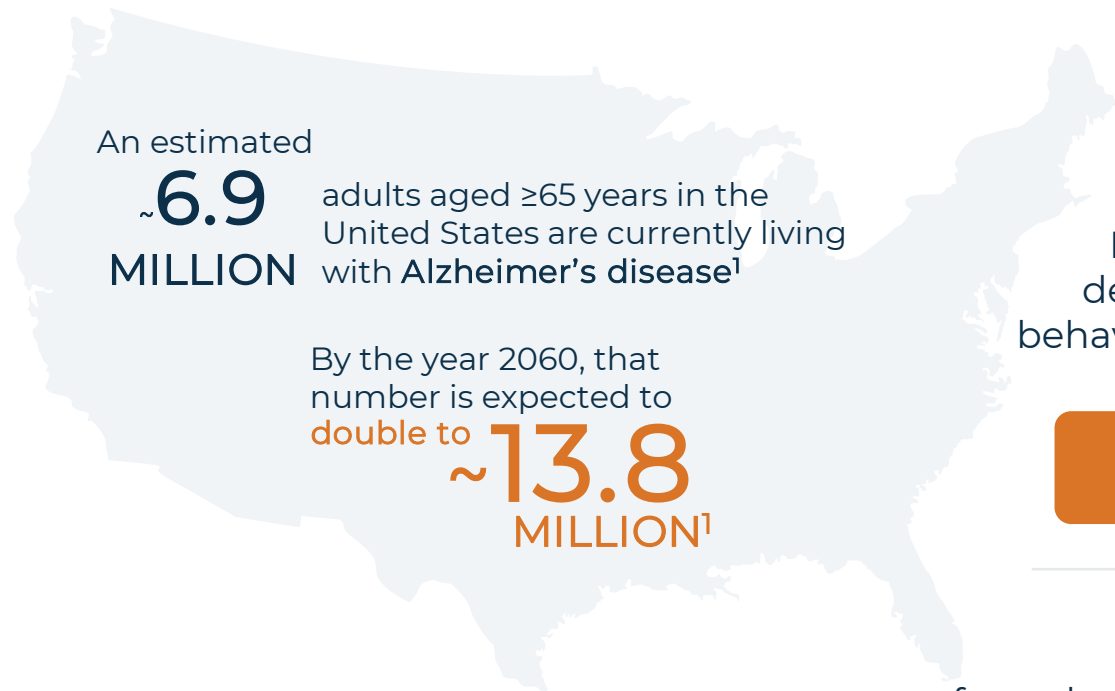
Objectives

Understand the scope and impact of agitation associated with dementia due to Alzheimer's disease: prevalence, brain changes, and patient burden

Learn to identify and discuss agitation symptoms in patients with Alzheimer's dementia using established criteria and assessment tools

Explore current treatment options and management strategies for agitation in patients with Alzheimer's dementia

Alzheimer's Dementia Is Highly Prevalent And Predicted To Increase Over Time¹



People with Alzheimer's dementia can experience behavioral and psychological conditions, with

agitation being one of the most common²



Agitation is present in

~1 out of 2

individuals with dementia due to Alzheimer's disease

Agitation is associated with increased chances of placement into long-term care (LTC)³

~65% of people with Alzheimer's or other forms of dementia lived  **in the community,** receiving more care from family members and other unpaid caregivers as their disease progressed¹



~75%

of people with Alzheimer's dementia at age 80 live in an

LTC facility

compared with 4% of the general population aged 80 years¹

References:

1. 2024 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2024;20(5):3708-3821.
2. Halpern R, et al. *Int J Geriatr Psychiatry.* 2019;34(3):420-431.
3. Fillit H, et al. *Int J Geriatr Psychiatry.* 2021;36(12):1959-1969.

Agitation Presents A Broad Spectrum Of Symptoms

- Agitation associated with dementia due to Alzheimer's disease is a **common and treatable condition** with a broad range of symptoms. It requires distinct treatment options from those used for cognitive impairment¹⁻³
- Despite its prevalence, **agitation is often under-recognized** by caregivers and underdiagnosed by HCPs⁴⁻⁶

Symptoms of agitation manifest as both non-aggressive and aggressive behaviors, such as^{7,8}

EXCESSIVE MOTOR ACTIVITY:

Pacing, restlessness, repetitiveness, and gesturing



VERBAL AGGRESSION:
Screaming, using profanity, and asking repetitive questions

PHYSICAL AGGRESSION:
Hitting, kicking, punching, biting, and throwing things

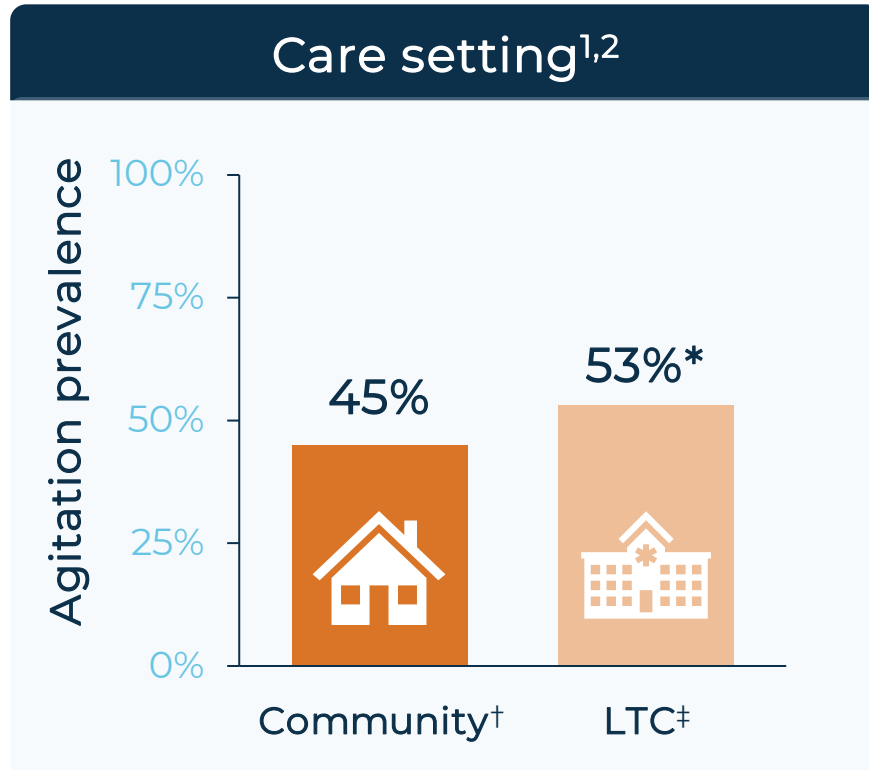
HCP, health care provider.

References:

1. Cummings J, et al. *Int Psychogeriatr*. 2015;27(1):7-17.
2. Cohen-Mansfield J. Instruction manual for the Cohen-Mansfield Agitation Inventory (CMAI). Research Institute of the Hebrew Home of Greater Washington; 1991.
3. Gilmore-Bykovskiy A, et al. *Gerontologist*. 2020;60(5):896-904.
4. Halpern R, et al. *Int J Geriatr Psychiatry*. 2019;34(3):420-431.
5. Lanctôt KJ, et al. *Alzheimers Dement (N Y)*. 2017;3(3):440-449.
6. Stella F, et al. *Int J Geriatr Psychiatry*. 2015;30(12):1230-1237.
7. Sano M, et al. *Int Psychogeriatr*. 2024;36(4):238-250.
8. Rabinowitz J, et al. *Am J Geriatr Psychiatry*. 2005;13(11):991-998.

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Agitation Is Prevalent Across Care Settings And Alzheimer's Severities^{1,2}



*Nursing home percentage reported includes those with Alzheimer's dementia and other dementias.

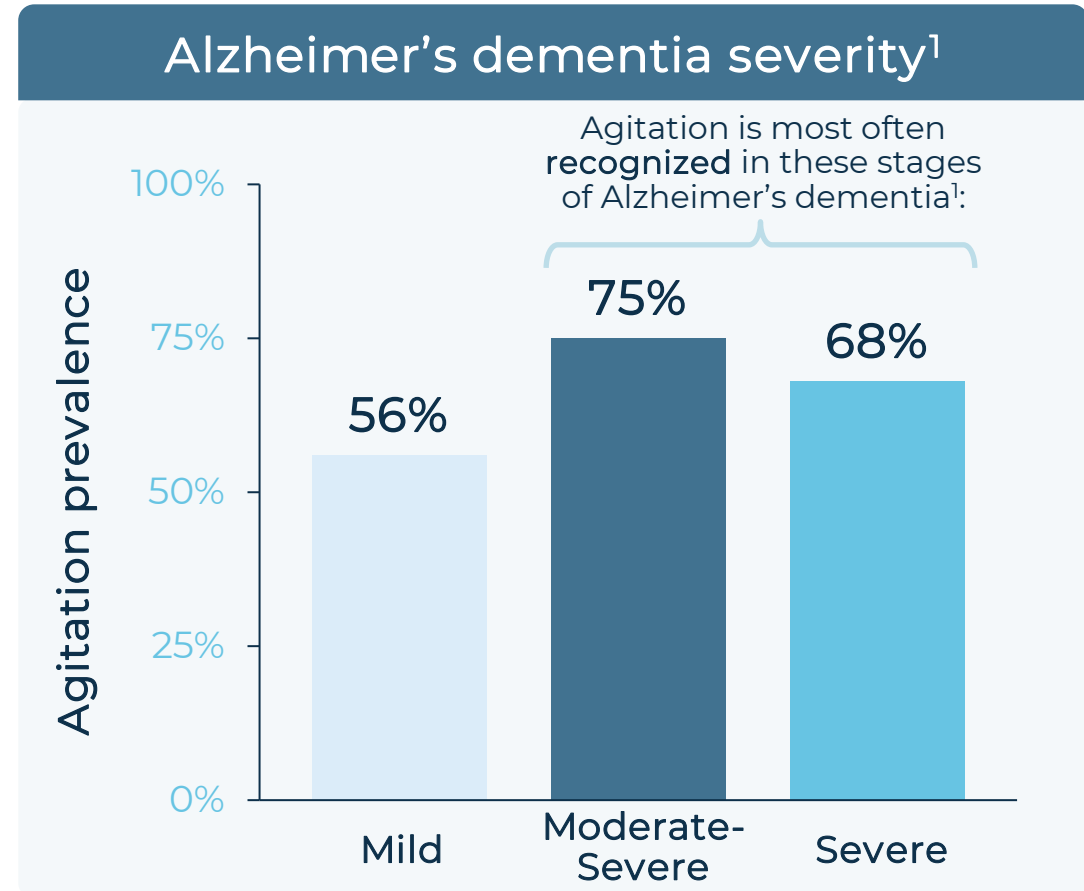
[†]Residential homes.

[‡]Nursing homes/skilled nursing facilities.

LTC, long-term care.

References:

1. Halpern R, et al. *Int J Geriatr Psychiatry*. 2019;34(3):420-431.
2. Fillit H, et al. *Int J Geriatr Psychiatry*. 2021;36(12):1959-1969.



IPA Criteria Offer A Foundation For Recognition Of Agitation In Cognitive Disorders¹

The IPA definition of agitation in cognitive disorders includes 4 criteria:

1. The patient meets the criteria for cognitive impairment or dementia syndrome
2. The patient exhibits ≥ 1 agitation behavior(s) with emotional duress that is persistent or frequently recurrent for ≥ 2 weeks or the behavior represents a dramatic change from the patient's usual behavior*
3. The behaviors are severe and associated with excess distress or produce disability beyond that due to cognitive impairment
4. The behaviors cannot be attributed to another psychiatric disorder, medical condition (including delirium), suboptimal care conditions, or the physiological effects of a substance

Agitation behaviors include:



Excessive motor activity behaviors:

- Pacing
- Rocking
- Gesturing
- Pointing fingers
- Restlessness
- Performing repetitious mannerisms



Verbal aggression behaviors:

- Yelling
- Speaking in an excessively loud voice
- Using profanity
- Screaming
- Shouting



Physical aggression behaviors:

- Grabbing
- Shoving
- Pushing
- Resisting
- Hitting others
- Kicking objects or people
- Scratching
- Biting
- Throwing objects
- Hitting self
- Slamming doors
- Tearing things
- Destroying property

*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.

IPA, International Psychogeriatric Association.

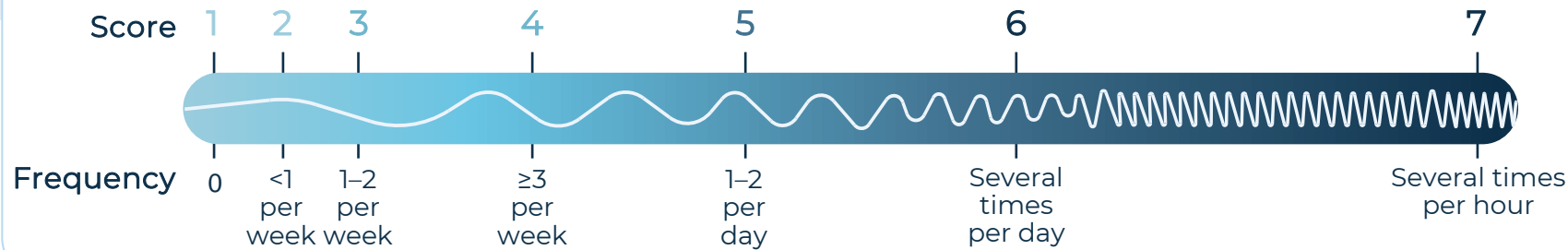
Reference:

1. Sano M, et al. *Int Psychogeriatr*. 2024;36(4):238-250.

Cohen-Mansfield Agitation Inventory (CMAI)

The CMAI is a clinically validated scale which quantifies the frequency of 29 agitated behaviors occurring within the previous 2 weeks^{1*}

Individual CMAI behaviors are scored on a 7-point scale:



Many of the CMAI behaviors can be grouped into 3 subscales, based on the IPA definition of agitation in cognitive disorders^{1,2}:



Excessive motor activity behaviors



Verbal aggression behaviors



Physical aggression behaviors

Total Score¹

No behaviors

29

More severe agitation

203

- Sum of individual behavior scores (ie, 29–203)
- Higher total score indicates more severe agitation
- A negative change in total score indicates improvement

*The CMAI can be administered by caregivers or completed by health care professionals.¹

IPA, International Psychogeriatric Association.

References:

1. Cohen-Mansfield J. Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). The Research Institute of the Hebrew Home of Greater Washington; 1991.
2. Sano M, et al. *Int Psychogeriatr*. 2024;36(4):238-250.

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The CMAI Measures A Broad Range Of Behaviors Of Agitation Consistent With The IPA Definition Of Agitation^{1,2}

29 CMAI Behaviors^{1,2}

Grouping CMAI items into types of behaviors—defined by IPA criteria—provides a framework for agitation and inappropriate behaviors in patients with dementia^{1,2}:

-  Excessive motor activity behaviors
-  Verbal aggression behaviors
-  Physical aggression behaviors
-  Other behaviors

Pacing and aimless wandering	Cursing or verbal aggression	Throwing things	Spitting	Hiding things
Inappropriate dressing or disrobing	Making verbal sexual advances	Biting	Making physical sexual advances or exposing genitals	Hoarding things
Trying to get to a different place	Constant unwarranted request for attention and/or help	Scratching	Hitting self or others	Eating or drinking inappropriate substances
Handling things inappropriately	Repetitive sentences and questions	Hurting self or others	Kicking	Making strange noises
Performing repetitious mannerisms	Complaining	Tearing things or destroying property	Grabbing people or things inappropriately	Intentional falling
General restlessness	Negativism		Pushing	
	Screaming			

CMAI, Cohen-Mansfield Agitation Inventory; IPA, International Psychogeriatric Association.

References:

- Cummings J, et al. *Int Psychogeriatr*. 2015;27(1):7-17.
- Cohen-Mansfield J. Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). Research Institute of the Hebrew Home of Greater Washington; 1991.

Despite The High Prevalence, Recognition Of Agitation Remains A Challenge That Delays Diagnosis And Treatment



Caregivers

- Often the **first to encounter** agitation symptoms¹
- **May not recognize** the full breadth of agitation symptoms²⁻⁴
- **May not understand** that treatment of agitation differs from treatment of Alzheimer's dementia²⁻⁴
- **May not readily talk** about agitation symptoms with HCPs until they become untenable, which can lead to underdiagnosis of agitation²⁻⁴



HCPs

- Often **rely on caregivers** to report agitation symptoms³
- **Agitation symptoms may not be easy to detect** in a clinical setting, especially when subtle³
- **Generally, may not educate** families about agitation early in Alzheimer's dementia²
- **May not be made aware** of agitation symptoms until burden becomes untenable for the caregiver²

Caregivers play a critical role in recognizing, assessing, and communicating agitation symptoms to HCPs.¹



Early Detection:

*Improving caregiver recognition and communication with HCPs may lead to **earlier diagnosis and timely management***³

Early detection by caregivers with tailored tools may:

- Improve recognition and overall management of agitation in patients with Alzheimer's dementia
- Encourage discussions with HCPs about agitation symptoms
- Assist HCPs in making a diagnosis of agitation associated with dementia due to Alzheimer's disease

HCP, healthcare provider.

References:

1. Clevenger C, et al. One minute to recognition: The Agitation in Alzheimer's Screener for Caregivers (AASC®). Presented at: Gerontological Society of America Annual Scientific Meeting; November 8-12, 2023; Tampa, FL.
2. Richler LG, et al. *Harv Rev Psychiatry*. 2023;31(1):22-27.

3. Stella F, et al. *Int J Geriatr Psychiatry*. 2015;30(12):1230-1237.

4. Gilmore-Bykovskyi A, et al. *Gerontologist*. 2020;60(5):896-904.

The Agitation In Alzheimer's Screener For Caregivers (AASC®)

The AASC® was developed based on the IPA definition to empower caregivers and HCPs in discussing, identifying, and reporting agitation in patients with Alzheimer's dementia

Goals of the AASC®

- To educate caregivers about agitation symptoms
- To facilitate caregiver-HCP conversations about agitation
- To help HCPs in screening for agitation in Alzheimer's

AASC®
Agitation in Alzheimer's Screener for Caregivers

A person with Alzheimer's dementia may become easily upset, frustrated, or angry. These feelings may be associated with agitation, a common symptom of Alzheimer's. The following questions ask about behaviors associated with agitation that you may have observed in the individual for whom you provide care.

Your answers to these questions can help you talk with your person's healthcare professional. Please select one response for each question.

Patient Name _____ Date _____

1. Are you noticing any of the following that represent a change from the individual's usual or past behavior?

	Yes	No
a. Repeating motions or behaviors (e.g., rocking, raising fist, pointing finger)	<input type="checkbox"/>	<input type="checkbox"/>
b. Pacing or restlessness (cannot be still)	<input type="checkbox"/>	<input type="checkbox"/>
c. Cursing/using profanity or talking out verbally	<input type="checkbox"/>	<input type="checkbox"/>
d. Raising voice or yelling or screaming	<input type="checkbox"/>	<input type="checkbox"/>
e. Resisting assistance or care	<input type="checkbox"/>	<input type="checkbox"/>
f. Throwing or hitting or breaking things	<input type="checkbox"/>	<input type="checkbox"/>
g. Trying to hurt self or others (e.g., grabbing, kicking, hitting, biting)	<input type="checkbox"/>	<input type="checkbox"/>

2. Do any of these behaviors make the individual's day-to-day activities or interactions with others more challenging?

	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>

Disclaimer: This screener was developed by Otsuka Global Medical Affairs, along with a panel of multidisciplinary experts and was funded by Otsuka Pharmaceutical Development & Commercialization, Inc. The AASC® is a screening tool and is not a diagnostic tool.

Agitation criteria based on the International Psychogeriatric Association (IPA) definition (Sano et al., 2020).

References: 1. Clevenger C, et al. Validation of the Agitation in Alzheimer's Screener for Caregivers (AASC®), a Novel Clinical Tool to Screen for Agitation in Alzheimer's Dementia. The American Association of Geriatric Psychiatry (AAGP) Annual Meeting, March 14-17, 2023, Phoenix, AZ.
2. Sano M, Clevenger C, Auer S, et al. *Int Psychogeriatr*. 2023;35:1-5.

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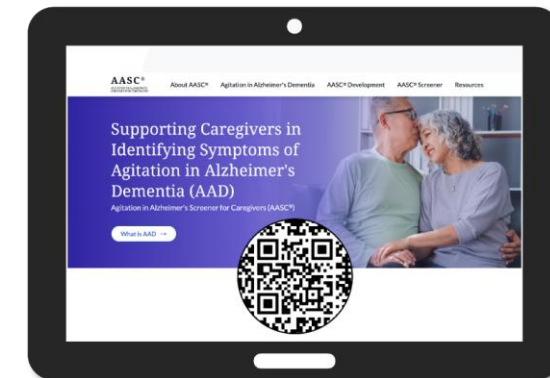
The AASC® is the first clinical tool based on IPA criteria

Items screen for both the presence and impact of agitation symptoms

Can be completed in <1 minute

Simple to score

Use the digital version or download and print the AASC® at www.theaasc.com



HCP, healthcare provider; IPA, International Psychogeriatric Association.

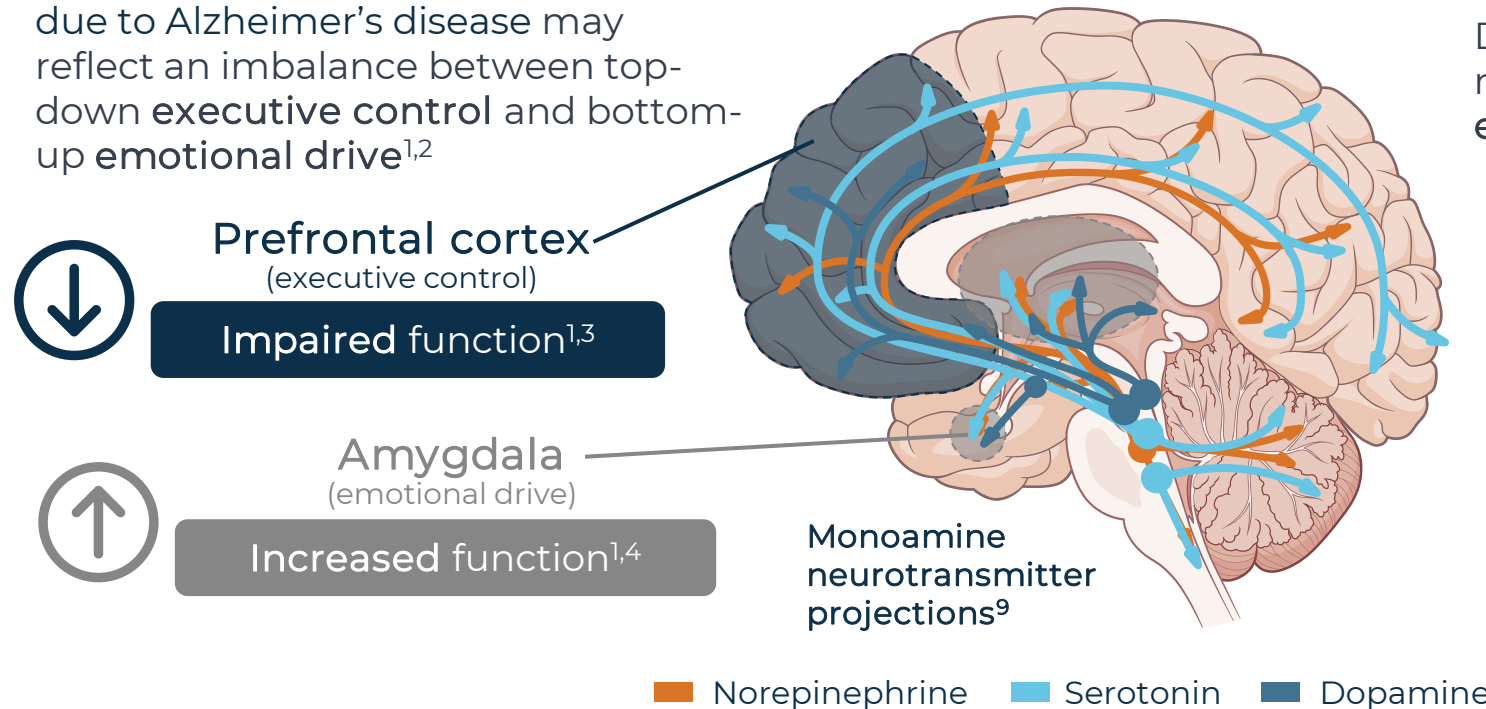
Reference:

1. Clevenger C, et al. One minute to recognition: The Agitation in Alzheimer's Screener for Caregivers (AASC™). Presented at: Gerontological Society of America Annual Scientific Meeting; November 8-12, 2023; Tampa, FL.

Brain Pathology and Monoaminergic Dysfunction

Imbalance between executive control and emotional drive may arise from the accumulation of tau pathology and neurodegeneration within key brain regions. A consequence of this pathology is the dysfunction of the monoamine/NSD neurotransmitter systems¹

Agitation associated with dementia due to Alzheimer's disease may reflect an imbalance between top-down **executive control** and bottom-up **emotional drive**^{1,2}



Dysfunction of NSD neurotransmitter system may contribute to imbalance between **executive control** and **emotional overdrive**^{1,5-8}



Norepinephrine system^{1,5}

Increased activity



Serotonin system^{1,7}

Decreased activity



Dopamine system^{1,8}

Dysregulation

NSD, norepinephrine, serotonin, and dopamine.

References:

1. Cummings JL, et al. *CNS Spectr*. 2024;1-10.
2. Rosenberg PB, et al. *Mol Aspects Med*. 2015;43-44:25-37.
3. Banno K, et al. *Neuropsychiatr Dis Treat*. 2014;10:339-348.

4. Wright CI, et al. *Biol Psychiatry*. 2007;62(12):1388-1395.
5. Jacobs HI, et al. *Mol Psychiatry*. 2021;26(3):897-906.
6. Arnsten AFT, et al. *Neurobiol Stress*. 2015;1:89-99.
7. Lancôt KL, et al. *J Neuropsychiatry Clin Neurosci*. 2001;13(1):5-21.

8. Lindenmayer JP. *J Clin Psychiatry*. 2000;61(Suppl 14):5-10.
9. Carandini T, et al. *Neuroimage Clin*. 2021;30:102587.

Agitation Can Worsen The Impact Of An Already Devastating And Burdensome Disease

Overall, agitation versus no agitation in patients with Alzheimer's dementia has been associated with¹⁻⁷:



Accelerated
disease
progression



Functional
decline



Decreased
quality of life



Greater
comorbidities



Increased use
of concomitant
therapies



Earlier
death



Increased
risk of
hospitalization/
institutionalization

In the LTC setting, agitation versus no agitation has been associated with a significantly increased risk of¹:



Falls



Fractures



Infections



Higher medication use



Other NPS*

*Includes depression, anxiety, delusion, and hallucinations.
LTC, long-term care; NPS, neuropsychiatric symptoms.

References:

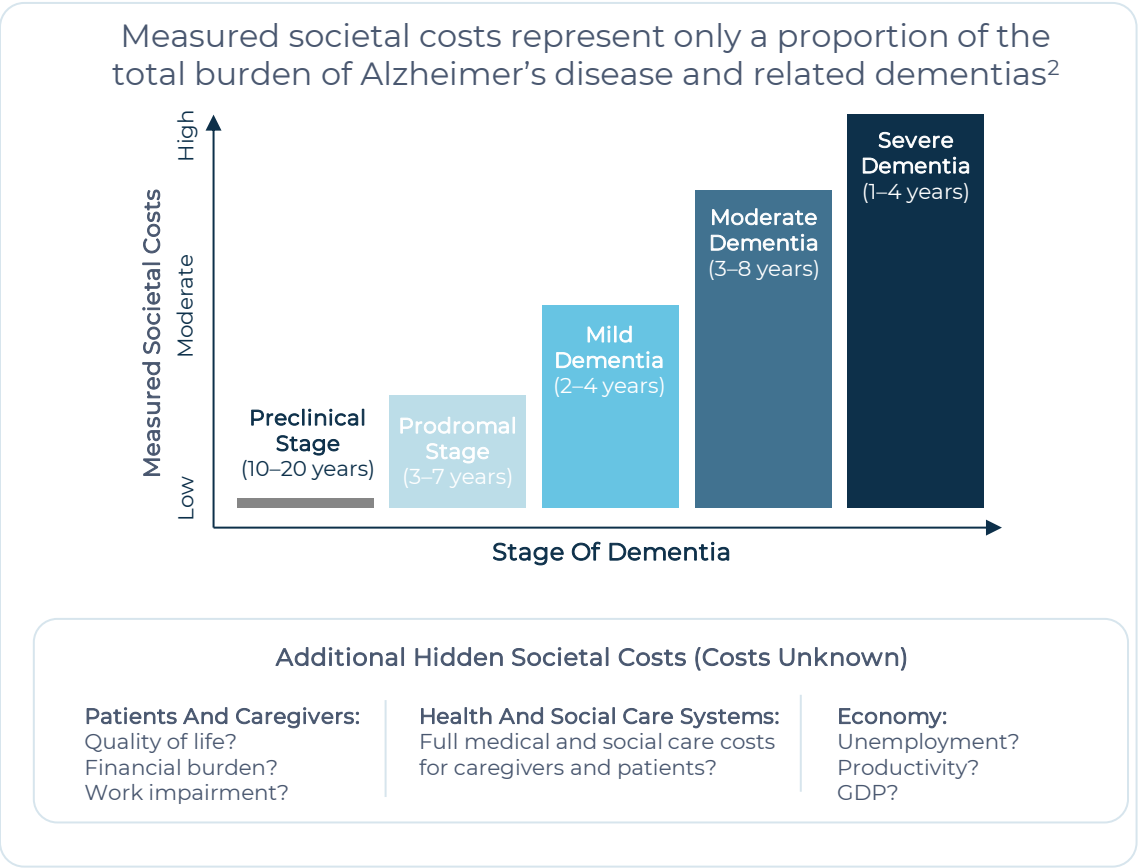
1. Fillit H, et al. *Int J Geriatr Psychiatry*. 2021;36(12):1959-1969.
2. Jones E, et al. *J Alzheimers Dis*. 2021;83(1):89-101.
3. Halpern R, et al. *Int J Geriatr Psychiatry*. 2019;34(3):420-431.
4. Koenig AM, et al. *Curr Psychiatry Rep*. 2016;18(1):3.
5. Peters ME, et al. *Am J Psychiatry*. 2015;172(5):460-465.
6. Scarmeas N, et al. *Arch Neurol*. 2007;64(12):1755-1761.
7. Banerjee S, et al. *J Neurol Neurosurg Psychiatry*. 2006;77(2):146-148.

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Agitation Is Associated With An Increased Economic Burden For Both Individuals And Healthcare Systems

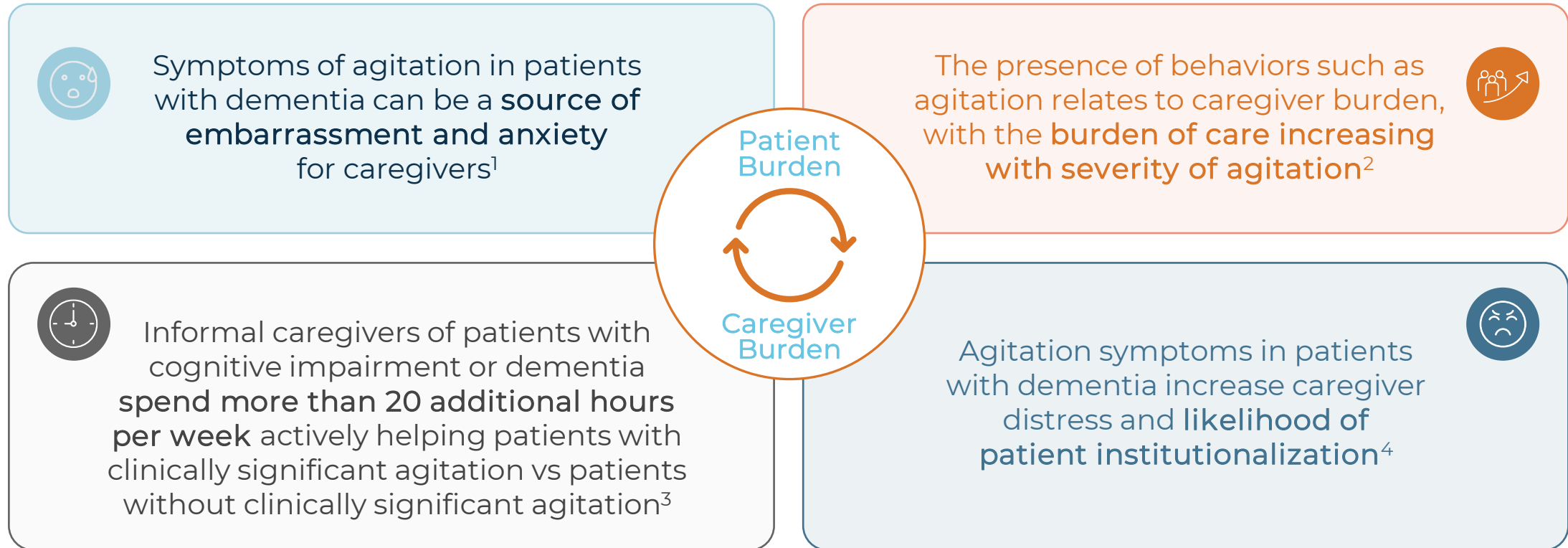
In a real-world study of 1,349 patients with early cognitive impairment or Alzheimer’s dementia, patients identified as having **agitation** demonstrated significantly **higher health care resource utilization** and costs than patients without agitation¹

	Non-Agitated Patients	Agitated Patients
Percentage institutionalized	3.2%	11.9%
Mean number of hospitalizations for any reason in the past 12 months	0.2	0.4
Mean number of consultations with any health care provider in the past 12 months	4.3	6.5
Mean total direct health care costs in the past 12 months	\$9,243	\$20,041
Mean professional caregiver time/week (hours)	10.6	27.2
Mean non-professional caregiver time/week (hours)	33.3	48.0



References:
1. Jones E, et al. *J Alzheimers Dis.* 2021;83(1):89-101.
2. El-Hayek YH, et al. *J Alzheimers Dis.* 2019;70(2):323-341.

Agitation Associated With Dementia Due To Alzheimer's Dementia Is Associated With High Caregiver Burden



AD, Alzheimer's dementia.

References:

1. Cohen-Mansfield J. *J Psychiatr Res*. 2008;43(1):64-69.
2. Schein J, et al. *J Alzheimers Dis*. 2022;88(2):663-677.

3. Okura T, Langa KM. *Alzheimer Dis Assoc Disord*. 2011;25(2):116-121.
4. Fillit H, et al. *Int J Geriatr Psychiatry*. 2021;36(12):1959-1969.

Current Treatment Paradigm For A Comprehensive Management Plan¹

American Psychiatric Association Practice Guideline On The Use Of Antipsychotics To Treat Agitation Or Psychosis In Patients With Dementia



Differential diagnosis

General medical, psychiatric, environmental, or psychosocial problems



Individualize

Understand individual circumstances and triggers



Nonpharmacologic intervention

First-line treatment



Pharmacologic intervention

If nonpharmacologic measures are unsuccessful or behaviors are dangerous or distressing

Reference:

1. Reus VI, et al. *Am J Psychiatry*. 2016;173(5):543-546.

Nonpharmacologic Interventions to Treat Patients With Agitation Associated With Dementia Due To Alzheimer's Disease



Caregiver interventions¹

Caregiver education and support, connection to external organizations and services



Remove stressors^{2,3}

Separate the patients from stimuli and environments that worsen symptoms, assess medication effects



Sensory enhancement/relaxation^{1,4,5}

Hand massage, individualized music or art, sensory modulation, multisensory environments, supportive interactions, orienting stimuli



Improve environment¹

Control temperature, facilitate and simplify activities, decrease environmental noise



Purposeful activity^{1,4}

Helping tasks/volunteer roles, inclusion in group activity programs, access to outdoors, physical activity



Social contact⁴

Pet therapy, one-to-one visits

Treatment goals of nonpharmacologic approaches include prevention, management, reduction, or elimination of behavioral occurrences (frequency, severity); reduction of caregiver distress; and/or prevention of adverse consequences including harm to caregiver or patient¹

References:

1. Gitlin LN, et al. *JAMA*. 2012;308(19):2020-2029.
2. Desai A. *J Gerontol Nurs*. 2017;43(2):9-17.
3. Carrarini C, et al. *Front Neurol*. 2021;12:644317.
4. Abraha I, et al. *BMJ Open*. 2017;7(3):e012759.
5. James IA, et al. *Clin Interv Aging*. 2023;18:219-230.

Pharmacologic Interventions to Treat Agitation Associated With Dementia Due To Alzheimer's Dementia

If nonpharmacologic measures are unsuccessful or symptoms are severe, dangerous, and/or cause significant distress, then judicious pharmacologic intervention is recommended¹



There is only one FDA-approved drug for treatment of agitation associated with dementia due to Alzheimer's disease, and it is classified as an atypical antipsychotic²

However, clinicians may prescribe other unapproved pharmacologic treatments, including^{1,3-6}:

- Antipsychotics (typical and atypical)
- Anticonvulsants
- Anxiolytics or sedative-hypnotics
- Antidepressants
- Other medications

Pharmacologic treatments can be associated with adverse events^{1,4,5,7,8}:



Sedation*



Extrapyramidal symptoms



Orthostatic hypotension



Cognitive worsening



Fractures and falls



Cerebrovascular and cardiovascular complications





*Some family caregivers of patients with Alzheimer's disease and other forms of dementia find sedative effects distressing and unhelpful.⁸

FDA, Food and Drug Administration.

References:

1. Rabins PV, et al. *Am J Psychiatry*. 2007;164(12 Suppl):5-56.
2. Lee D, et al. *JAMA Neurol*. 2023;80(12):1307-1316.
3. Aigbogun MS, et al. *J Alzheimers Dis*. 2020;77(3):1181-1194.
4. Schneider LS, et al. *Am J Geriatr Psychiatry*. 2006;14(3):191-210.
5. Porsteinsson AP, et al. *JAMA*. 2014;311(7):682-691.
6. Caraci F, et al. *F1000Res*. 2020;9:F1000 Faculty Rev-686.
7. Marcinkowska M, et al. *CNS Drugs*. 2020;34(3):243-268.
8. Harding R, et al. *Med Law Rev*. 2013;21(2):243-277.

Summary

-  Agitation in Alzheimer's dementia, a prevalent and burdensome condition, is often difficult to recognize
-  The IPA criteria provides a foundation for recognizing agitation in cognitive disorders, while the CMAI measures a broad range of agitated behaviors consistent with that IPA definition
-  Improving caregiver recognition and communication with HCPs may support earlier detection of agitation associated with dementia due to Alzheimer's disease and may improve overall management of symptoms
-  The current treatment paradigm for agitation associated with dementia due to Alzheimer's disease calls for a comprehensive management plan that involves non-pharmacological interventions and potentially, pharmacological interventions

CMAI, Cohen-Mansfield Agitation Inventory; HCP, health care provider; IPA, International Psychogeriatric Association.

For more information or to request a more detailed live presentation on this topic from your local Medical Science Liaison, please visit www.PsychU.org/contact

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