



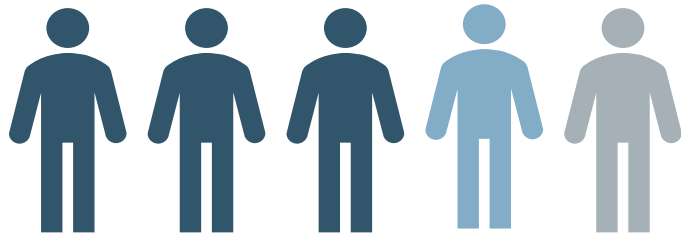
# Agitation Associated with Alzheimer's Dementia

Disease State Education: Disease State

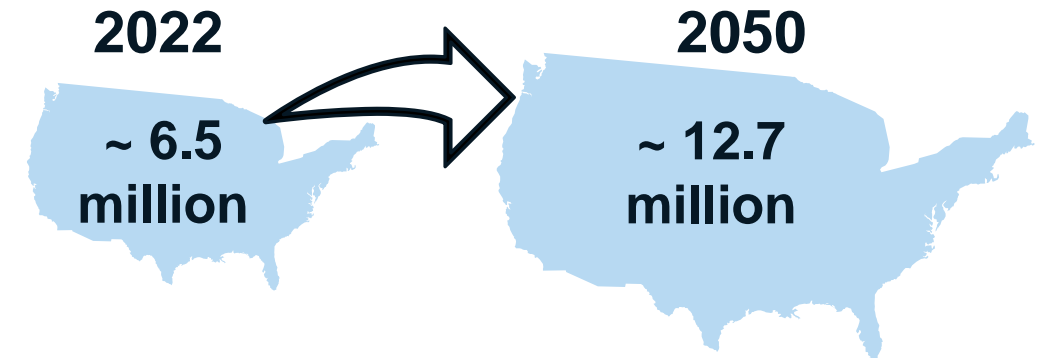
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Alzheimer's disease is highly prevalent, under-diagnosed, and predicted to increase significantly in the coming decades due to an aging population

**Alzheimer's disease contributes to 60% to 80% of dementia cases**



**In the USA people  $\geq 65$  years with Alzheimer's dementia**

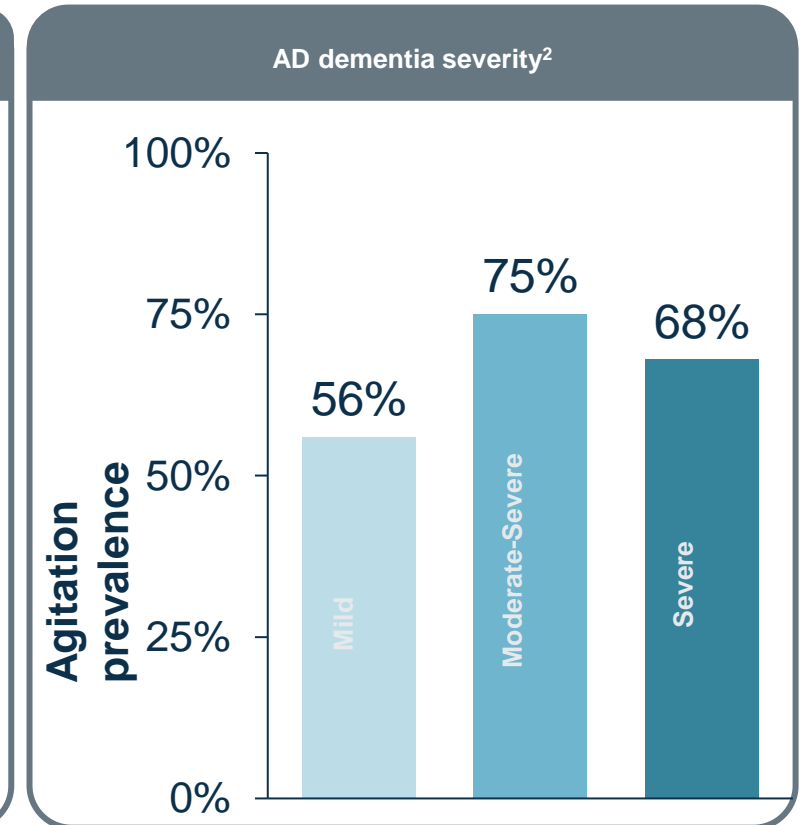
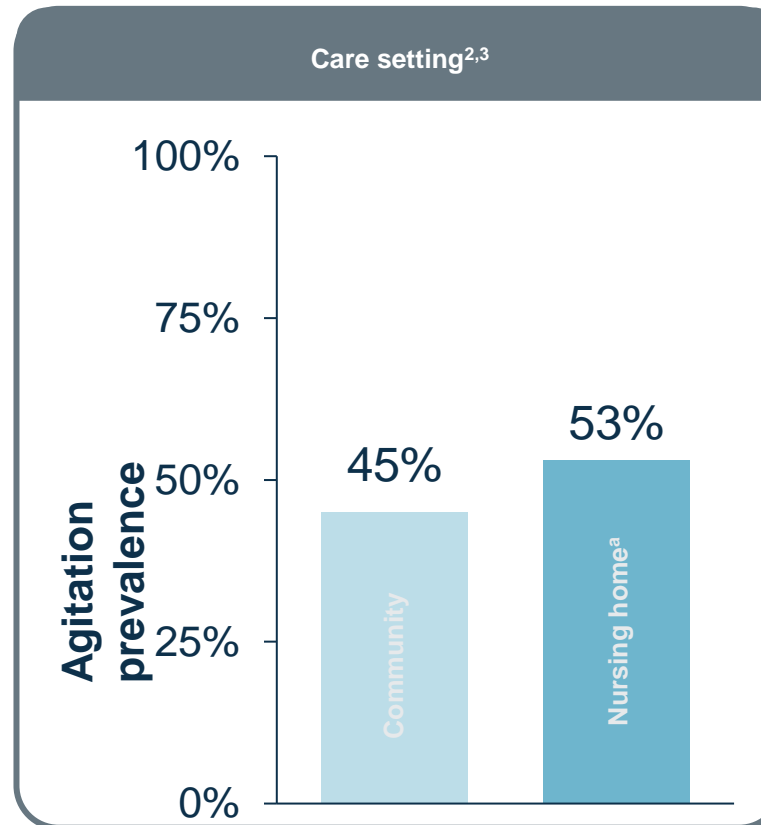


- Many people living with Alzheimer's disease are either undiagnosed or unaware of the diagnosis, with even higher rates among racial or ethnic minorities

1. Alzheimer's Association. (2022). 2022 Alzheimer's disease facts and figures. *Alzheimer's Dementia*, 18(4), 700-789. doi:10.1002/alz.12638.

# Agitation is a common neuropsychiatric symptom of Alzheimer's dementia and highly prevalent across patient settings and Alzheimer's disease severities

Manifestations of Alzheimer's dementia are not limited to cognitive symptoms and include a range of neuropsychiatric symptoms, including **agitation**, which when present are experienced alongside the hallmark disease characteristics of memory loss and cognitive decline<sup>1</sup>



<sup>a</sup>Nursing home percentage reported includes those with AD and other dementias. AD, Alzheimer's disease.

1. Kales, H. C., Gitlin, L. N., & Lyketsos, C. G. (2015). Assessment and management of behavioral and psychological symptoms of dementia. *BMJ*, 350.

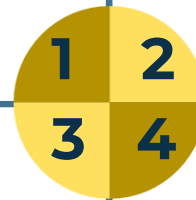
2. Halpern, R., Seare, J., Tong, J., Hartry, A., Oloay, A., & Aigbogun, M. S. (2019). Using electronic health records to estimate the prevalence of agitation in Alzheimer disease/dementia. *International Journal of Geriatric Psychiatry*, 34(3), 420-431.

3. Fillit, H., Aigbogun, M. S., Gagnon-Sanschagrin, P., Cloutier, M., Davidson, M., Serra, E., Grossberg, G. (2021). Impact of agitation in long-term care residents with dementia in the United States. *International Journal of Geriatric Psychiatry*, 36(12), 1959-1969.

# The International Psychogeriatric Association (IPA) has developed a provisional consensus definition of agitation in patients with cognitive disorders

The consensus definition for agitation in cognitive disorders includes 4 definitions:

<p><b>Criteria for cognitive impairment or dementia syndrome</b></p> <p>Patients must meet criteria for a cognitive impairment or dementia syndrome including:</p> <ul style="list-style-type: none"> <li>• Alzheimer's disease</li> <li>• Mild cognitive impairment</li> <li>• Other dementias</li> </ul>	<p><b>Agitation behavior &amp; duration</b></p> <ul style="list-style-type: none"> <li>• Patient must exhibit <math>\geq 1</math> agitation behavior associated with emotional distress</li> <li>• Behavior must be persistent or frequently recurrent for <math>\geq 2</math> weeks</li> <li>• Must represent a change from the patient's usual behavior</li> </ul>
<p><b>Agitation behavior severity</b></p> <p>Behavior must be severe enough to produce excess disability, beyond that due to the cognitive impairment<sup>a</sup> and significantly impair <math>\geq 1</math> of the following:</p> <ul style="list-style-type: none"> <li>• Interpersonal relationships</li> <li>• Other aspects of social functioning</li> <li>• Ability to perform or participate in daily living activities</li> </ul>	<p><b>Agitation behavior cause</b></p> <p>Agitation cannot be attributable solely to:</p> <ul style="list-style-type: none"> <li>• Another psychiatric disorder</li> <li>• Suboptimal care conditions</li> <li>• Medical condition</li> <li>• Physiological effects of a substance</li> </ul>



<sup>a</sup>According to the clinician's opinion. IPA, International Psychogeriatric Association.

1. Cummings, J., Mintzer, J., Brodaty, H., Sano, M., Banerjee, S., Devanand, D., Lyketsos, C. G. (2015). Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *International Psychogeriatrics*, 27(1), 7-17.

# The IPA defines 3 agitation behavior domains associated with emotional distress

- The IPA defines agitation in Alzheimer's dementia as excessive motor activity, verbal aggression, or physical aggression. Examples of each include the following behaviors:

## 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

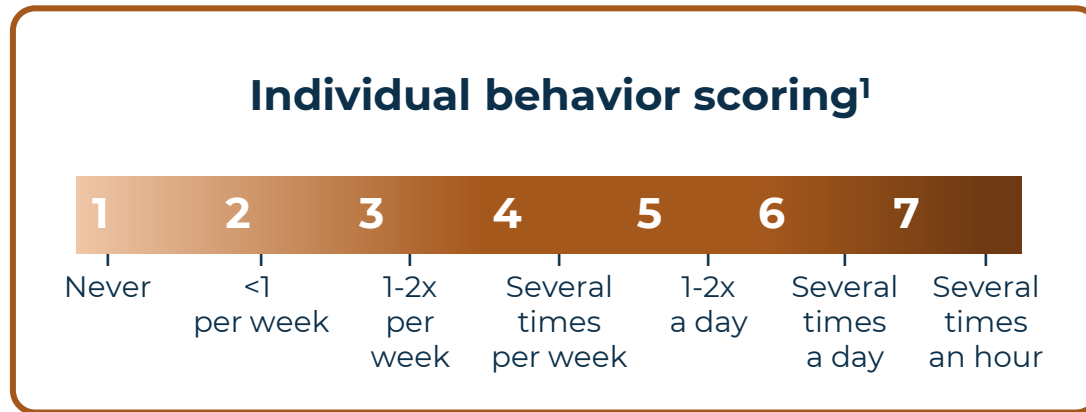


IPA, International Psychogeriatric Association.

1. Cummings, J., Mintzer, J., Brodaty, H., Sano, M., Banerjee, S., Devanand, D., Lyketsos, C. G. (2015). Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *International Psychogeriatrics*, 27(1), 7-17.

# The CMAI measures the frequency of manifestations of a broad range of agitated behaviors

- The Cohen-Mansfield Agitation Inventory (CMAI) questionnaire quantifies the frequency of 29 agitated behaviors within the previous 2 weeks, rated on a 7-point scale<sup>1</sup>
- The questionnaire can be self-administered by caregivers or completed by healthcare practitioners<sup>1,2</sup>



- Point changes within the CMAI scale should be compared and interpreted with care: a change from “never” to “once or twice a week” (2 points) may not represent an equivalent overall change in impact as “once or twice a day” to “several times an hour” (2 points); the nature of a particular behavior should also be considered

CMAI, Cohen-Mansfield Agitation Inventory.

1. Cohen-Mansfield, J. (1991). Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). *Research Institute of the Hebrew Home of Greater Washington*.

2. Sano, M., Soto, M., Carrillo, M., Cummings, J., Hendrix, S., Mintzer, J., Touchon, J. (2018). Identifying better outcome measures to improve treatment of agitation in dementia: a report from the EU/US/CTAD Task Force. *The Journal of Prevention of Alzheimer's Disease*, 5(2), 98-102.

# The CMAI measures a broad range of behaviors of agitation and consists of 4 factors

- The CMAI scale consists of 4 factors, including:<sup>1</sup>

Aggressive behavior	Physically non-aggressive behavior
Verbally agitated behavior	Hiding and hoarding

- By grouping CMAI items into defined factors representing types of behaviors, the concept and reporting of agitation is made more streamlined and accessible to healthcare professionals and caregivers/family<sup>1</sup>

29 CMAI behaviors <sup>1,2</sup>				
Pacing and aimless wandering	Hiding things	Throwing things	Spitting	Making physical sexual advances or exposing genitals
Inappropriate dressing or disrobing	Hoarding things	Screaming	Cursing or verbal aggression	Eating or drinking inappropriate substances
Trying to get to a different place	Constant unwarranted request for attention/help	Biting	Hitting (including self)	Making strange noises
Handling things inappropriately	Repetitive sentences/questions	Scratching	Kicking	Intentional falling
Performing repetitious mannerisms	Complaining	Hurting self or others	Grabbing people or things inappropriately	Making verbal sexual advances
General restlessness	Negativism	Tearing things or destroying property	Pushing	

CMAI, Cohen-Mansfield Agitation Inventory.

- Rabinowitz, J., Davidson, M., De Deyn, P. P., Katz, I., Brodaty, H., & Cohen-Mansfield, J. (2005). Factor analysis of the Cohen-Mansfield Agitation Inventory in three large samples of nursing home patients with dementia and behavioral disturbance. *The American Journal of Geriatric Psychiatry*, 13(11), 991-998.
- Cohen-Mansfield, J. (1991). Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). *Research Institute of the Hebrew Home of Greater Washington*.



# The CMAI measures a broad range of behaviors of agitation consistent with the IPA consensus definition of agitation

- Many of the behaviors in the CMAI scale are relevant to the 3 domains of the IPA definition of agitation, which include:<sup>1,2</sup>



Excessive motor activity



Verbal aggression



Physical aggression



Excessive motor activity



Verbal aggression



Physical aggression

29 CMAI behaviors <sup>2,3</sup>				
Pacing and aimless wandering	Hiding things	Throwing things	Spitting	Making physical sexual advances or exposing genitals
Inappropriate dressing or disrobing	Hoarding things	Screaming	Cursing verbal aggression	Eating or drinking inappropriate substances
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CMAI, Cohen-Mansfield Agitation Inventory; IPA, International Psychogeriatric Association.

- Cummings, J., Mintzer, J., Brodaty, H., Sano, M., Banerjee, S., Devanand, D., Lyketsos, C. G. (2015). Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *International Psychogeriatrics*, 27(1), 7-17.
- Cohen-Mansfield, J. (1991). Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). *Research Institute of the Hebrew Home of Greater Washington*.
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# Additional slides

# The NPI evaluates 12 neuropsychiatric symptoms, including agitation

- **The Neuropsychiatric Inventory (NPI)** evaluates 12 neuropsychiatric symptoms common in dementia including:<sup>1</sup>
  - Delusions
  - Hallucinations
  - Agitation
  - Dysphoria
  - Anxiety
  - Apathy
  - Irritability
  - Euphoria
  - Disinhibition
  - Aberrant motor behavior
  - Night-time behavior disturbances
  - Appetite and eating abnormalities
- **The Neuropsychiatric Inventory – Nursing Home version (NPI-NH)** rating scale is a screening instrument for neuropsychiatric symptoms in patients with dementia residing in a nursing home<sup>2</sup>
  - The NPI-NH adapts the original NPI scale by rephrasing the questions and changing the caregiver distress scale to an occupational disruptiveness scale that captures the impact of the behavioral changes on daily life and the effectiveness of the professional caregiver<sup>3</sup>
  - Used to characterize the frequency and severity of symptoms<sup>2</sup>

NPI, Neuropsychiatric Inventory; NPI-NH, Neuropsychiatric Inventory – Nursing Home version.

1. Cummings, J. L. (1997). The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology*, 48(5 Suppl 6), 10S-16S.

2. Cummings JL. (2009) *Neuropsychiatric Inventory Nursing Home Version (NPI-NH) Instructions for Use and Administration*. Retrieved from [https://www.dementiaresearch.org.au/wp-content/uploads/2016/01/NPI-NH\\_cr.pdf](https://www.dementiaresearch.org.au/wp-content/uploads/2016/01/NPI-NH_cr.pdf).

3. Cummings, J. (2020). The neuropsychiatric inventory: development and applications. *Journal of Geriatric Psychiatry and Neurology*, 33(2), 73-84.

# Other clinically validated rating scales used in agitation in Alzheimer's dementia research studies

- **The Mini-Mental State Examination (MMSE)** is an important, clinically validated 30-point questionnaire that is widely used to test cognitive function among the elderly and to assess severity of cognitive impairment in patients with Alzheimer's dementia<sup>1</sup>

## The Clinical Global Impression (CGI) scale<sup>2</sup>

### CGI – Severity (CGI-S) scale

Provides an assessment of the clinician's view of the severity of the patient's global functioning prior to and after initiating a study medication<sup>2</sup>

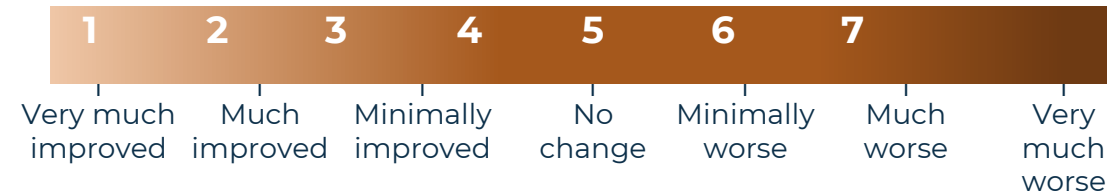
CGI-S



### CGI – Improvement (CGI-I) scale

Compares the patient's baseline condition (prior to initiation of treatment) with their current state<sup>2</sup>

CGI-I



CGI-I, Clinical Global Impression – Improvement; CGI-S, Clinical Global Impression – Severity; MMSE, Mini-Mental State Examination.

1. Creavin, S. T., Wisniewski, S., Noel-Storr, A. H., Trevelyan, C. M., Hampton, T., Rayment, D., Milligan, R. (2016). Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database of Systematic Reviews* (1).
2. Busner, J., & Targum, S. D. (2007). The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)*, 4(7), 28.

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