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Real-World Treatment Patterns and Clinical Management of Alzheimer's Disease Agitation

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Key Objective

This chart review was conducted to better understand characteristics, symptom presentation, and treatment patterns for patients with Alzheimer disease agitation in both long-term care and community settings

Introduction

- Agitation is a highly prevalent and debilitating neuropsychiatric symptom of Alzheimer disease (AD) that affects ~70% of patients over the course of the disease[1,2]
- AD agitation is characterized by a range of symptoms, including aggressive verbal and physical behaviors, emotional distress, disruptive irritability, and disinhibition, markedly worsening burden for patients and caregivers[1,2,3,4]
- While non-pharmacological interventions are recommended as first line treatment for neuropsychiatric symptoms like agitation[5], behavioral interventions are often difficult to implement and maintain[6]
- At the time of this survey, brexpiprazole, an atypical antipsychotic agent, was the only FDA–approved agent for agitation associated with dementia due to AD[7]
  - Antipsychotics have been associated with increased risk of cerebrovascular accidents and death in older people with dementia-related behavioral disturbances[8]
  - Dextromethorphan-bupropion (Auvelity®; AXS-05) was approved in April 2026 as the first non-antipsychotic to treat agitation associated with dementia due to AD[9]
- Pharmacologic treatments are also used off-label for AD agitation and include typical and atypical antipsychotics, anxiolytics, antidepressants, and antiepileptic agents[10]
  - These medications exhibit variable efficacy and are associated with considerable safety concerns[10]
- Real-world data from patients treated for AD agitation can help inform how this symptom presents and is managed across care settings to better optimize treatment and reduce patient and caregiver burden

References
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Disclosures
A Patel has served as a consultant and/or received speaker fees from Acadia, Alpha Cognition, Axsome Therapeutics, BMS, Neurocrine, Otsuka, and Teva. **C Zeni, M Tocco, G ML Eglit** and **Y Zhao** are employees of Axsome Therapeutics.

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Methods

Study Design

- An online quantitative survey was conducted (September to October 2024) among 285 US healthcare providers (HCPs) treating patients with AD agitation
  - HCPs treating ADA included a mix of physicians (e.g., primary care, neurologists, geriatricians), nurse practitioners and physician assistants across specialties treating AD agitation and those in long term care settings who interact daily with patients
- Each HCP reviewed two patient charts (one patient on first-line pharmacotherapy and one patient on second- or third-line pharmacotherapy) that fit the following criteria:
  - Possible or probable diagnosis of AD
  - Exhibits signs and/or symptoms of agitation associated with dementia due to AD
  - Receiving a pharmacologic treatment for agitation, even if they did not prescribe this treatment
  - Seen in a long-term care (LTC) or a community setting

Outcomes

- Patient demographics and clinical characteristics
- Initial agitation characteristics: time to first symptoms and symptom profile (eg, physical non-aggressive behaviors such as pacing and hoarding)
- Pharmacotherapy history for AD agitation
- Top reason for discontinuation of pharmacotherapy

Analysis

- Results were summarized across practice setting
- Continuous data was summarized with number of observations (n), mean, and standard deviation; categorical (discrete) data was presented as frequencies and percentages within each category

Study Population

n	Long-Term Care	Community	Overall
1st Line Patient	38	247	285
2nd Line Patient	18	125	143
3rd Line Patient	20	122	142
Total	76	494	570

Results

Patient Characteristics

	Long-Term Care (N = 76)	Community (N = 494)	Overall (N = 570)
Age			
n	66	444	510
Mean (SD)	82.3 (8.7)	78.2 (8.6)	78.8 (8.7)
Sex			
Female	50 (66%)	261 (53%)	311 (55%)
Caregiver Support			
Yes	49 (64%)	449 (91%)	498 (87%)
No	16 (21%)	24 (4.9%)	40 (7.0%)
Not known	11 (14%)	21 (4.3%)	32 (5.6%)
Time Since AD Diagnosis (Months)			
n	74	482	556
Mean (SD)	49.4 (32.4)	52.8 (47.3)	52.3 (45.6)
Comorbidities, n (%)			
Hypertension	46 (60.5)	302 (61.1)	348 (61.1)
High cholesterol	26 (34.2)	230 (46.6)	256 (44.9)
Depression	28 (36.8)	158 (32.0)	186 (32.6)
Arthritis	27 (35.5)	157 (31.8)	184 (32.3)
Anxiety	19 (25.0)	145 (29.4)	164 (28.8)
Diabetes	18 (23.7)	138 (27.9)	156 (27.4)
Obesity	12 (15.8)	89 (18.0)	101 (17.7)
Coronary heart disease	19 (25.0)	81 (16.4)	100 (17.5)
Heart disease	13 (17.1)	82 (16.6)	95 (16.7)
Osteoporosis	17 (22.4)	78 (15.8)	95 (16.7)
Chronic kidney disease	11 (14.5)	67 (13.6)	78 (13.7)
Thyroid disease	15 (19.7)	59 (11.9)	74 (13.0)

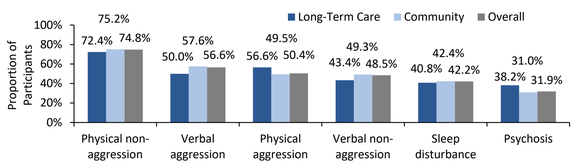
AD, Alzheimer's Disease; SD, standard deviation.

- Most patients demonstrated comorbidities, consistent with an elderly population[11]
- Overall, 32.6% of the participants had comorbid depression (LTC: 36.8%, Community: 32.0%) and 28.8% had comorbid anxiety (LTC: 25.0%, Community: 29.4%)

Initial Agitation Characteristics

- The mean time from AD diagnosis to reporting agitation symptoms was 29.2 months (LTC: 25.0 months, Community: 29.8 months)
- At initial agitation presentation, patients reported a mean of 5.42 symptoms (LTC: 5.99 symptoms, Community: 5.34 symptoms)

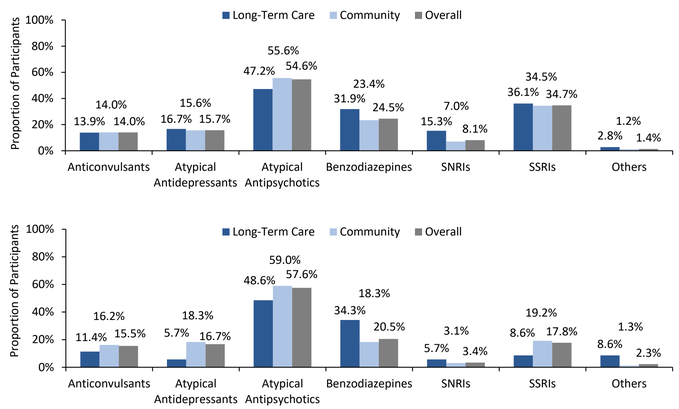
Figure 1. Agitation Symptom Categories at Initial Presentation



- Overall, physical non-aggression symptoms were the most commonly reported at initial agitation presentation (74.8%), followed by verbal aggression (56.6%), and physical aggression (50.4%)

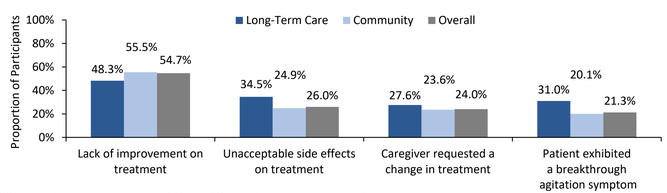
Treatment History and Reasons for Discontinuation

Figure 2. AD Agitation-Related Medication Use in (A) First-Line and (B) Second- or Third-Line



- Atypical antipsychotics were the most commonly used medication across treatment lines (first-line: 54.6%, second- or third-line 57.6%), followed by SSRIs in the first-line setting and benzodiazepines in the second-line setting
- Across treatment lines, LTC patients were more likely to be prescribed benzodiazepines and SNRIs vs community patients; community patients were more likely to be prescribed atypical antipsychotics vs LTC patients
- SSRIs and SNRIs were less likely to be used as a second- or third-line treatment vs a first-line treatment

Figure 3: Top Reasons for Discontinuation of Medications



SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors.

- The most common reasons for discontinuation overall were lack of improvement on treatment, followed by caregiver requesting a change and exhibition of a breakthrough agitation symptom

Conclusions

- In this chart review, agitation was initially reported at an average of over 2 years after AD diagnosis
- Approximately one-third of patients had comorbid depression or anxiety, with similar patterns observed across LTC and community settings
- The 3 most frequently reported initial agitation symptoms were physical non-aggression, verbal aggression, and physical aggression
- Atypical antipsychotics were the most prescribed treatment; lack of improvement was the primary reason for discontinuation across all medications
- These findings highlight the need for additional treatment options across care settings and may inform future approaches to optimizing care for patients with AD agitation