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Enclosure:

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Validation of the Agitation in Alzheimer's Screener for Caregivers (AASC®), a Novel Clinical Tool to Screen for Agitation in Alzheimer's Dementia

George Grossberg[1]; W. Clay Jackson[2]; Malaak Brubaker[3]; Iwona Bucior[3]; T. Michelle Brown[4]; Emily Bratlee-Whitaker[4]; Sheri Fehnel[4]; Anton M. Palma[3]; Mehul Patel[3]; Sue Peschin[5]; Jared Stroud[6]; Carolyn Clevenger[7]

[1]Saint Louis University, Saint Louis, MO; [2]University of Tennessee College of Medicine, Memphis, TN; [3]Otsuka Pharmaceutical Development & Commercialization, Princeton, NJ; [4]RTI Health Solutions, Research Triangle Park, NC; [5]Alliance for Aging Research, Washington, DC; [6]OhioHealth, Columbus, OH; [7]Emory University, Atlanta, GA.

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Introduction

- Agitation, a common neuropsychiatric symptom of Alzheimer's dementia, is complex and burdensome[1,2]; often left unrecognized, underreported, and untreated, agitation in Alzheimer's dementia may become more severe over time, increasing the potential for patient harm, caregiver burnout, and nursing home placement.[3-5]
- There is an urgent, unmet clinical need for a validated, quick, easy-to-use screener tool to support caregivers and healthcare professionals (HCPs) in the identification of agitation in Alzheimer's dementia.[6]
- The Agitation in Alzheimer's Screener for Caregivers (AASC®), based on the International Psychogeriatric Association (IPA) definition of agitation in cognitive disorders (**Table 1**), was developed with input from multidisciplinary experts and refined after qualitative evaluation with caregivers.[7,8]

The objective of this study was to assess the predictive validity of the AASC® against the IPA agitation criteria further to support its value and utility in clinical practice.

Table 1. International Psychogeriatric Association Definition of Agitation in Cognitive Disorders.

1.	The patient meets criteria for a cognitive impairment or dementia syndrome (eg, 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)
2.	The patient exhibits at least one of the following agitation behaviors that are associated with observed or inferred evidence of emotional duress (eg, rapid changes in mood, irritability, outbursts). The behavior has been persistent or frequently recurrent for a minimum of two weeks or the behavior represents a dramatic change from the patient's usual behavior* a. Excessive motor activity (eg, pacing, rocking, gesturing, pointing fingers, restlessness, performing repetitious mannerisms) b. Verbal aggression (eg, yelling, speaking in an excessively loud voice, using profanity, screaming, shouting) c. Physical aggression (eg, grabbing, shoving, pushing, resisting, hitting others, kicking objects or people, scratching, biting, throwing objects, hitting self, slamming doors, tearing things, and destroying property)
3.	Behaviors are severe and associated with excess distress or produce disability, which in the clinician's opinion is beyond that due to 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
4.	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 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.

Adapted from International Psychogeriatric Association. Defining Agitation. Accessed February 14, 2025. https://www.ipa-online.org/news-and-issues/defining-agitation.

Methods

- This cross-sectional, observational, multisite, single-visit study was conducted in the US in 2 phases:
  - Phase 1 assessed the agreement/predictive metrics of the AASC® and whether further refinement was needed.
  - Phase 2 included final analyses to evaluate the predictive validity of the final, improved tool.
- Patient, caregiver, and HCP eligibility criteria are shown in **Table 2**.

Table 2. Key Eligibility Criteria.

Patients
• Community-dwelling (ie, does not live in a residential or long-term-care setting)
• Has a recorded diagnosis of Alzheimer's disease/dementia[a]
• Not currently in a state of delirium
• Not diagnosed with schizophrenia, bipolar disorder, or any potentially confounding condition
Caregivers
• Provides care and assistance to the patient with Alzheimer's disease for ≥10 hours in a typical week
• Aged 18 to 85 years and able to speak, read, and comprehend English
Healthcare professionals
• Current caseload includes ≥10% of patients with any form of dementia
• Willing to complete IPA criteria training

IPA, International Psychogeriatric Association.

[a]Precludes rule-out and differential diagnoses, including other forms of dementia (eg, vascular dementia, Lewy Body dementia, dementia related to Huntington's disease, dementia related to Parkinson's disease, and Pick's dementia); imaging or biomarker confirmation of Alzheimer's disease is not required.

- Quantitative evaluation analyses were conducted using data from caregiver–healthcare professional (HCP) dyads.
- Caregivers completed the AASC® (**Figure 1**); ≥1 endorsed (yes) agitation behavior (item 1) paired with the endorsement (yes) of negative impact (item 2) would indicate a positive screen
- HCPs applied the IPA criteria by answering the question: "Based on the IPA definition of agitation in cognitive disorders, in your judgment, does this patient have agitation due to Alzheimer's?"
  - Yes, meets IPA criteria
  - No, has agitation attributable solely to another psychiatric or medical condition
  - No, does not meet IPA criteria for another reason (eg, not displaying agitated behavior)
- The predictive metrics of the final optimized AASC® were analyzed using percent agreement, sensitivity, specificity, Cohen's kappa coefficient, and the weighted average of precision and recall (F1 score).

Figure 1. Final AASC® Items.

ITEM	RESPONSE
1 **Are you noticing any of the following that represent a change from the individual's usual or past behavior?**	
Repeating motions or behaviors (eg, rocking, raising fist, pointing finger)	YES NO
Pacing or restlessness (cannot be still)	YES NO
Cursing/using profanity or lashing out verbally	YES NO
Raising voice or yelling or screaming	YES NO
Resisting assistance or care	YES NO
Throwing or hitting or breaking things	YES NO
Trying to hurt self or others (eg, grabbing, kicking, hitting, biting)	YES NO
2 **Do any of these behaviors make the individual's day-to-day activities or interactions with others more challenging?[a]**	YES NO

AASC®, Agitation in Alzheimer's Screener for Caregivers.

[a]Item 2 was revised from "Do any of these behaviors negatively affect the individual's relationships, activities, or willingness to receive care?" in Version 1.

Results

- Data were collected from 226 caregiver-HCP dyads across 12 US clinical sites between 18 Jun 2024 through 5 Dec 2024. These data were used to assess the predictive metrics of the AASC® against the IPA criteria in recognizing agitation in Alzheimer's dementia.
- Patients and caregivers were primarily female (59%, 62%), White (64%, 60%), and ~76 and 61 years of age, respectively (**Table 3**).
- Caregivers spent an average of 60 hours (range, 9 hours to 168 hours) per week providing care.

Table 3. Caregiver Characteristics (Screener Self-Report).

	Total (N = 226)	
Characteristics[a]	Caregiver	Patient
Age in years, mean (range)	60.7 (18−90)	75.5 (52−93)
Female, n (%)	140 (61.9)	133 (58.9)
Relationship to person with Alzheimer's dementia, n (%)		
Spouse/partner	104 (46.0)	–
Adult child	26 (11.5)	–
Other family member	28 (12.4)	–
Nonfamily member[b]	68 (30.1)	–
Hours of care provided per week, mean (range)	59.9 (9−168)	–
Race and ethnicity, n (%)[c]		
White	139 (61.5)	145 (64.2)
Hispanic, Latin American, or Latinx	41 (18.1)	36 (15.9)
African American or Black	30 (13.3)	30 (13.3)
Asian American	10 (4.4)	9 (4.0)
Middle Eastern and/or North African	3 (1.3)	2 (0.9)
Native Hawaiian and/or Pacific Islander	1 (0.4)	–
Education level, n (%)		
Less than high school	7 (3.1)	25 (11.1)
High school or equivalent	71 (31.4)	83 (36.7)
Some college/associate's degree	73 (32.3)	48 (21.2)
Bachelor's degree	27 (11.9)	41 (18.1)
Some graduate school	13 (5.8)	–
Professional/advanced degree	35 (15.5)	27 (11.9)

[a]Percentages may not sum to 100% due to missing data or unlisted responses. [b]Most nonfamily caregivers were paid caregivers and associated with a single clinical study site. [c]Multiple response item; participants who identified as more than one race/ethnicity were counted in each category they selected.

- The false negative rate from phase 1 analyses (n = 121 dyads) was 33.1%, primarily due to caregivers' lack of endorsements of the impact of agitation, which prompted a final refinement of item 2.
- In the final phase of the quantitative evaluation of the improved AASC® against the IPA criteria, percentage agreement was 73.3% (rate of false negatives was 9.5%), sensitivity was 0.77, specificity was 0.70, and kappa and F1 scores were 0.47 and 0.71, respectively (**Table 4**).

Table 4. Predictive Validity of the Improved AASC® Against the IPA Criteria.

Parameter	Results (n = 105)	
Agreement, %[a]	73.3	
Sensitivity (95% CI)	0.77 (0.65−0.90)	
Specificity (95% CI)	0.70 (0.59−0.82)	
Positive predictive value (95% CI)	0.65 (0.52−0.78)	
Negative predictive value (95% CI)	0.81 (0.71−0.92)	
Cohen's kappa coefficient, κ (95% CI)	0.47 (0.29−0.63)	
F1 Score	0.71	
C-index	0.74	
Classification matrix	True positives, n = 34	False positives, n = 18
	True negatives, n = 43	False negatives, n = 10

AASC®, Agitation in Alzheimer's Screener for Caregivers; F1, weighted average of precision and recall; HCP, healthcare professionals; IPA, International Psychogeriatric Association.

[a]Agreement = (true positives + true negatives) / total sum. [b]Based on caregiver judgement using the optimized AASC®. [c]Based on HCP judgement using the IPA criteria.

CONCLUSIONS

The AASC® includes 2 items, which are succinctly worded using caregiver-friendly language, to screen for agitation in Alzheimer's dementia at home, in a waiting room, or at a doctor's office.

In this study, the AASC® screener tool (self-adm inistered by caregivers) was quantitatively evaluated against HCPs' assessments of agitation using the IPA criteria.

The AASC® can facilitate communication between caregivers and HCPs, elevate awareness and knowledge of agitation, and support identification of agitation in Alzheimer's dementia.

The AASC® combines pragmatism and accuracy to maximize its use in a busy clinical practice, ultimately assisting HCPs in making a diagnosis and managing agitation in Alzheimer's dementia.

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Ethics

This study was reviewed and deemed exempt by Advarra, a central institutional review board (IRB).

Disclosures

GG: Recipient of consulting fees from Acadia, Avanir, Biogen, BioXcel, Genentech, Karuna, Lundbeck, Otsuka, Roche, and Takeda.
WCJ: Recipient of funds for consulting and travel to advisory meetings for Otsuka and member of the advisory board for the Tennessee Governor's Opioid Abatement Council.
MB, IB, AMP, and MP: Full-time employees of Otsuka Pharmaceutical Development & Commercialization, Inc.
SF, TMB, and EBW: Employees of RTI Health Solutions, an independent nonprofit research organization retained by Otsuka to conduct this research, which is the subject of this poster.
SP: President and CEO of The Alliance for Aging Research, which receives funding from the study sponsor (Otsuka) for nonbranded health education and advocacy on neuropsychiatric symptoms of dementia.
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