Priority Ranking:
What Matters Most to People Living with Alzheimer's Disease and Care Partners

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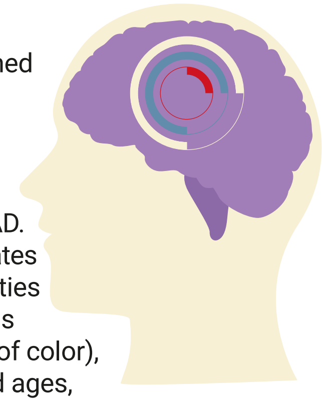
BACKGROUND

- The What Matters Most (WMM) in Alzheimer's disease (AD) research program—sponsored by the Alzheimer's Disease Patient and Caregiver Engagement (AD PACE) initiative of UsAgainstAlzheimer's—is a series of studies seeking to identify and measure treatment-related needs, preferences, and priorities of people at risk or living with Alzheimer's disease (PLWAD) and their care partners. This quantitative research is based on a refined draft conceptual model of disease, with 50 concepts within 6 hypothesized domains (Figure 1; Supplemental Figure S1).[1-4]
- A mixed-methods, prospective, observational survey-based study was conducted to qualitatively and quantitatively assess priorities and impacts and to evaluate the validity of the conceptual model among a large, diverse population of PLWAD and care partners across the full spectrum of AD severity.[5]

OBJECTIVES

- All WMM concepts have been previously endorsed as important by PLWAD and care partners.[1,3] This study aimed in part to:
  - Quantitatively assess priorities (ranking) among WMM concepts within hypothesized domains and between those domains from the perspective of a large population of PLWAD and care partners.
  - Understand whether prioritization varies for subgroups by race and ethnicity identity or disease stage.

METHODS



- The target survey population aimed to include ≥ 600 adults at risk or clinically diagnosed with mild cognitive impairment (MCI) or mild AD and care partners of people with moderate to severe AD. Individuals living in the United States (US) of varying races and ethnicities (≥ 50% respondents identifying as Black, Hispanic, or other person of color), a range of educational levels and ages, and approximately equal representation for each AD severity group were recruited (Table 1, Supplemental Table S1).
- Following pretesting to establish the ability of PLWAD and care partners to complete the activity, the web-based survey was conducted from June to December 2024. Separate versions of the survey were administered for PLWAD and for care partners taking the survey in consideration of a person living with moderate to severe AD and took approximately 30 minutes to complete; both versions were available in English and Spanish.
- Object-case best-worst scaling (BWS) (an experimental stated-preference method) was used to elicit ranked priorities within and between domains.[6,7]
  - Respondents answered 17 BWS questions, each asking them to identify the most and least important of a subset of 3 WMM concepts.
  - Responses were summarized descriptively and relative priority weights were calculated for PLWAD and care partner, AD severity, and race and ethnicity subgroups.
- Within each domain and for across-domain prioritization, relative priority weights totaled 100% to allow comparison, with greater values corresponding to relatively higher priorities.

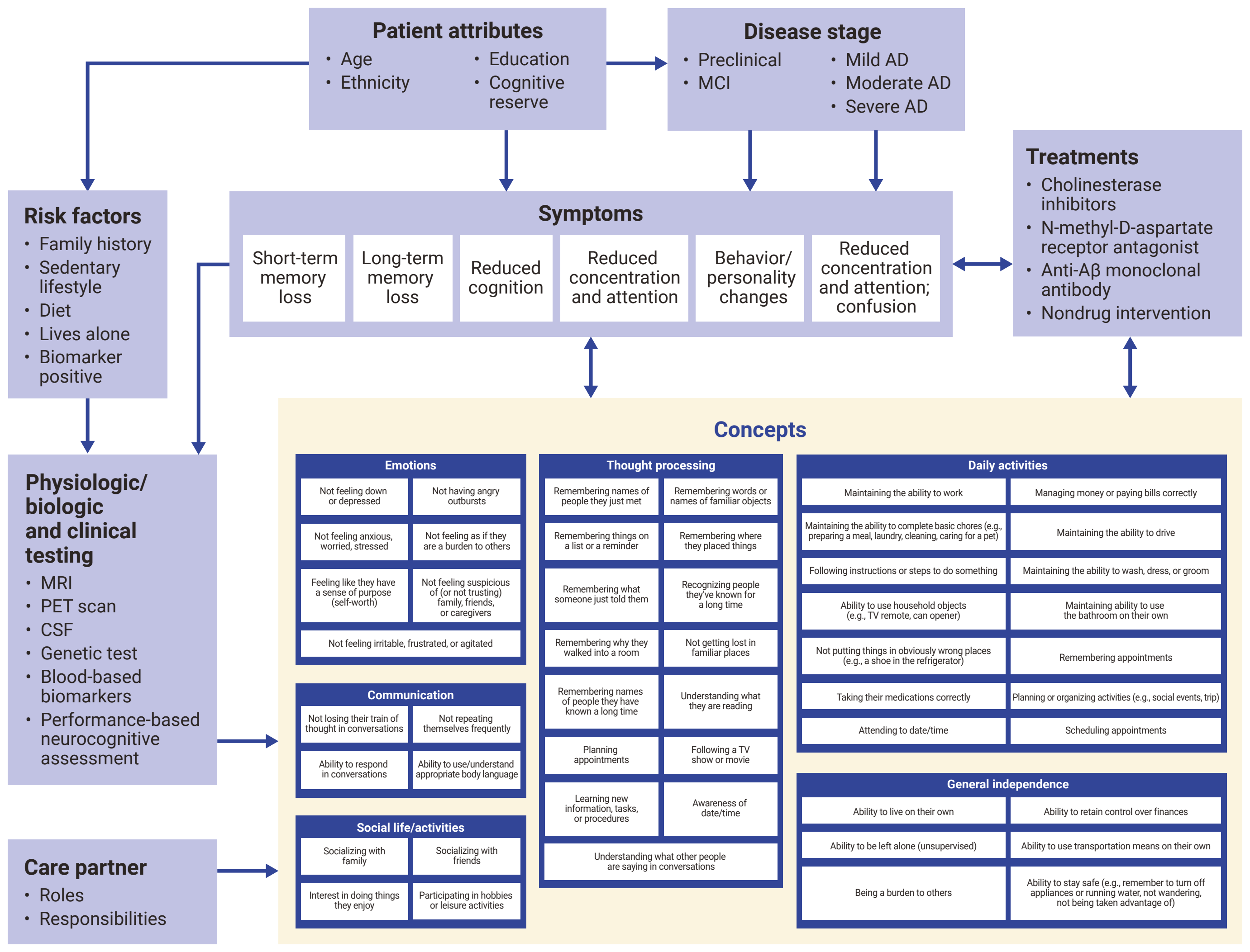
Table 1. **Survey Population Characteristics**

Survey population characteristic (N = 640)[a]	PLWAD participants Group 1 At risk/preclinical (n = 134)	 Group 2 MCI (n = 120)	 Group 3 Mild AD (n = 121)	Care partner participants Group 4 Moderate AD (n = 133)	 Group 5 Severe AD (n = 132)
Group description	Individuals with unimpaired cognition per self-report with evidence of AD pathology	Individuals with MCI due to AD	Individuals with mild AD dementia	Care partners of individuals with moderate AD dementia	Care partners of individuals with severe AD dementia
Age, mean (SD)	58.5 (13.2)	61.1 (14.0)	65.8 (10.5)	54.1 (15.1)	55.0 (16.8)
Sex assigned at birth, n (%)					
Female	79 (59.0)	66 (55.0)	63 (52.1)	37 (27.8)	54 (40.9)
Male	55 (41.0)	53 (44.2)	58 (47.9)	96 (72.2)	78 (59.1)
Intersex	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Race or ethnicity,[b] n (%)					
African American or Black	41 (30.6)	46 (38.3)	48 (39.7)	45 (33.8)	43 (32.6)
Alaska Native, American Indian, or Native American	4 (3.0)	3 (2.5)	2 (1.7)	3 (2.3)	2 (1.5)
Asian or Asian American	6 (4.5)	7 (5.8)	0 (0.0)	4 (3.0)	9 (6.8)
Hispanic, Latina/o, Latine, or Latinx	32 (23.9)	26 (21.7)	27 (22.3)	21 (15.8)	25 (18.9)
Middle Eastern and/or North African	0 (0.0)	1 (0.8)	2 (1.7)	0 (0.0)	1 (0.8)
Native Hawaiian or Pacific Islander	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
White	55 (41.0)	40 (33.3)	48 (39.7)	64 (48.1)	54 (40.9)
A race or ethnicity not listed	1 (0.7)	2 (1.7)	0 (0.0)	1 (0.8)	0 (0.0)
Highest grade or level of education,[c] n (%)					
High school diploma or equivalent (e.g., GED)	15 (11.2)	12 (10.0)	23 (19.0)	16 (12.0)	21 (15.9)
Associate's degree/technical school	11 (8.2)	10 (8.3)	9 (7.4)	16 (12.0)	11 (8.3)
Some college	30 (22.4)	28 (23.3)	31 (25.6)	24 (18.0)	28 (21.2)
College degree (e.g., BA, BS)	35 (26.1)	37 (30.8)	36 (29.8)	51 (38.3)	53 (40.2)
Graduate or professional degree (e.g., MS, MD, PhD, JD)	33 (24.6)	27 (22.5)	13 (10.7)	20 (15.0)	15 (11.4)

SD = standard deviation.

[a] "Missing" or "prefer not to answer" not reported; responses may not add to 100%. [b] Respondents could select all that apply; responses may exceed 100%. [c] Responses reported by ≥ 5% of at least one Group shown.

Figure 1. **What Matters Most Conceptual Model of Disease**



Patient attributes
- Age
- Ethnicity
- Education
- Cognitive reserve

Disease stage
- Preclinical
- MCI
- Mild AD
- Moderate AD
- Severe AD

Risk factors
- Family history
- Sedentary lifestyle
- Diet
- Lives alone
- Biomarker positive

Symptoms
- Short-term memory loss
- Long-term memory loss
- Reduced cognition
- Reduced concentration and attention
- Behavior/ personality changes
- Reduced concentration and attention; confusion

Treatments
- Cholinesterase inhibitors
- N-methyl-D-aspartate receptor antagonist
- Anti-Aβ monoclonal antibody
- Nondrug intervention

Physiologic/ biologic and clinical testing
- MRI
- PET scan
- CSF
- Genetic test
- Blood-based biomarkers
- Performance-based neurocognitive assessment

Care partner
- Roles
- Responsibilities

Concepts

Emotions
- Not feeling down or depressed
- Not having angry outbursts
- Not feeling anxious, worried, stressed
- Not feeling as if they are a burden to others
- Feeling like they have a sense of purpose (self-worth)
- Not feeling suspicious of (or not trusting) family, friends, or caregivers
- Not feeling irritable, frustrated, or agitated

Communication
- Not losing their train of thought in conversations
- Not repeating themselves frequently
- Ability to respond in conversations
- Ability to use/understand appropriate body language

Social life/activities
- Socializing with family
- Socializing with friends
- Interest in doing things they enjoy
- Participating in hobbies or leisure activities

Thought processing
- Remembering names of people they just met
- Remembering words or names of familiar objects
- Remembering things on a list or a reminder
- Remembering where they placed things
- Remembering what someone just told them
- Recognizing people they've known for a long time
- Remembering why they walked into a room
- Not getting lost in familiar places
- Remembering names of people they have known a long time
- Understanding what they are reading
- Planning appointments
- Following a TV show or movie
- Learning new information, tasks, or procedures
- Awareness of date/time
- Understanding what other people are saying in conversations

Daily activities
- Maintaining the ability to work
- Managing money or paying bills correctly
- Maintaining the ability to complete basic chores (e.g., preparing a meal, laundry, cleaning, caring for a pet)
- Maintaining the ability to drive
- Following instructions or steps to do something
- Maintaining the ability to wash, dress, or groom
- Ability to use household objects (e.g., TV remote, can opener)
- Maintaining ability to use the bathroom on their own
- Not putting things in obviously wrong places (e.g., a shoe in the refrigerator)
- Remembering appointments
- Taking their medications correctly
- Planning or organizing activities (e.g., social events, trip)
- Attending to date/time
- Scheduling appointments

General independence
- Ability to live on their own
- Ability to retain control over finances
- Ability to be left alone (unsupervised)
- Ability to use transportation means on their own
- Being a burden to others
- Ability to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)

Aβ = amyloid beta; CSF = cerebrospinal fluid; MRI = magnetic resonance imaging; PET = positron emission tomography.
Note: The conceptual model of disease was previously presented at the Clinical Trials on Alzheimer's disease (CTAD) meeting held 24-27 October 2023 in Boston, MA, United States.[4]

RESULTS

Respondent Characteristics

- Respondents (n = 640) represented diverse race and ethnicity, AD severity, and educational status groups, similar to those living with AD in the US (Table 1, Supplemental Tables S2-S3).
  - For PLWAD, mean age increased with increasing disease severity, the majority were female, and most were living with spouses/partners or alone in their own house.
  - For care partners of a person living with moderate to severe AD, most were in their 50s, most were male, and most were the child, spouse, or family member of the PLWAD.

Priority Ranking: Full Sample

- As supported by survey pretesting, results indicated care partners and PLWAD—including those who at risk or are in the earlier clinical stages of disease (Groups 1 [at risk], 2 [MCI], and 3 [Mild AD])—were able to engage in the BWS ranking activity.
- PLWAD and care partners *can* and *do* prioritize among the WMM concepts and domains (Figure 2; Supplemental Figure S2).

PLWAD and Care Partner Cohorts

- PLWAD and care partners may have different priorities in terms of treatment outcomes (Figure 3).
  - PLWAD selected the General Independence domain as the highest priority, whereas care partners selected Communication.
  - Care partners also placed higher priority on Daily Activities and Emotions domains than PLWAD.

AD Severity and Race and Ethnicity Subgroups

- Prioritization of domains differed across the disease continuum (Figure 4).
  - The priority weights for the General Independence domain decreased as AD severity increased. Priority weights for the Communication and Emotions domains tended to increase as AD severity increased.
- There were differences and similarities in domain prioritization by race and ethnicity subgroups (Figure 5). For example:
  - The Thought Processing domain had the greatest priority weight for multiracial participants and was approximately 2 times that for White participants.
  - The priority of the General Independence domain was greater for Hispanic and White participants than for Black and multiracial participants.

Figure 2. **WMM Ranking by Full Sample**

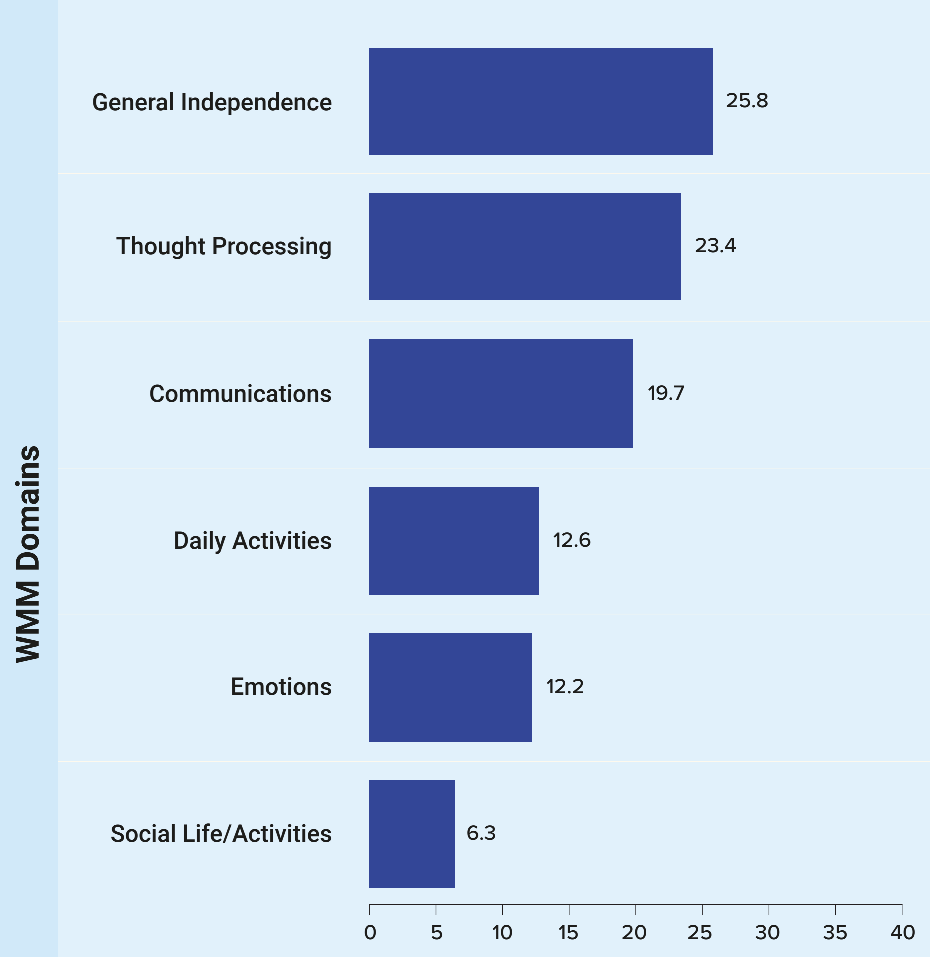


Figure 3. **WMM Ranking by PLWAD and Care Partners**

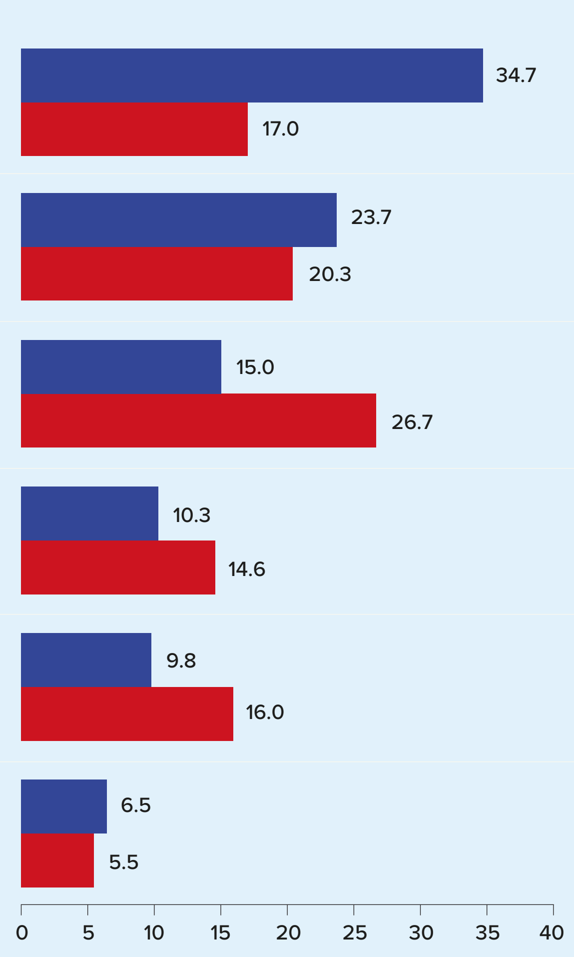


Figure 4. **WMM Ranking by AD Severity Groups**

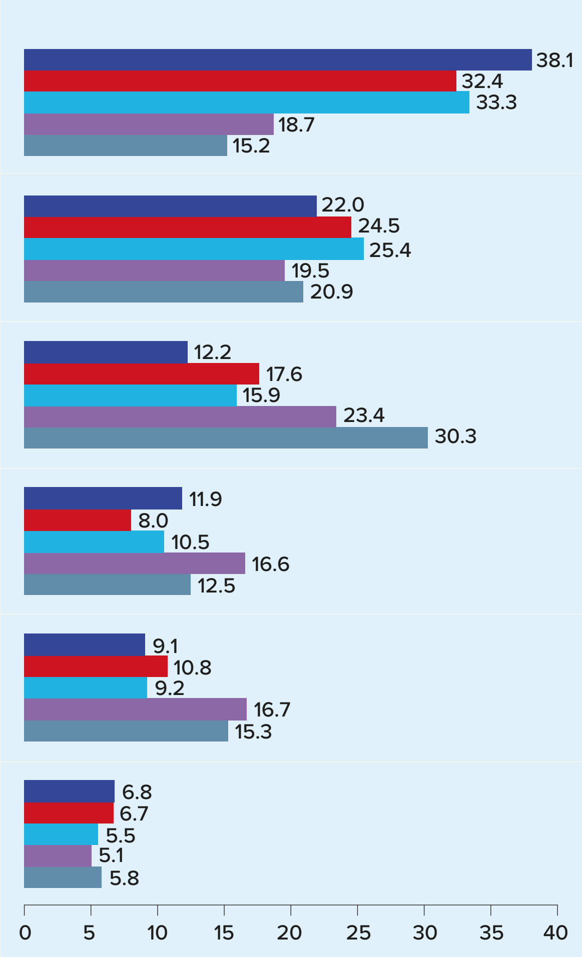
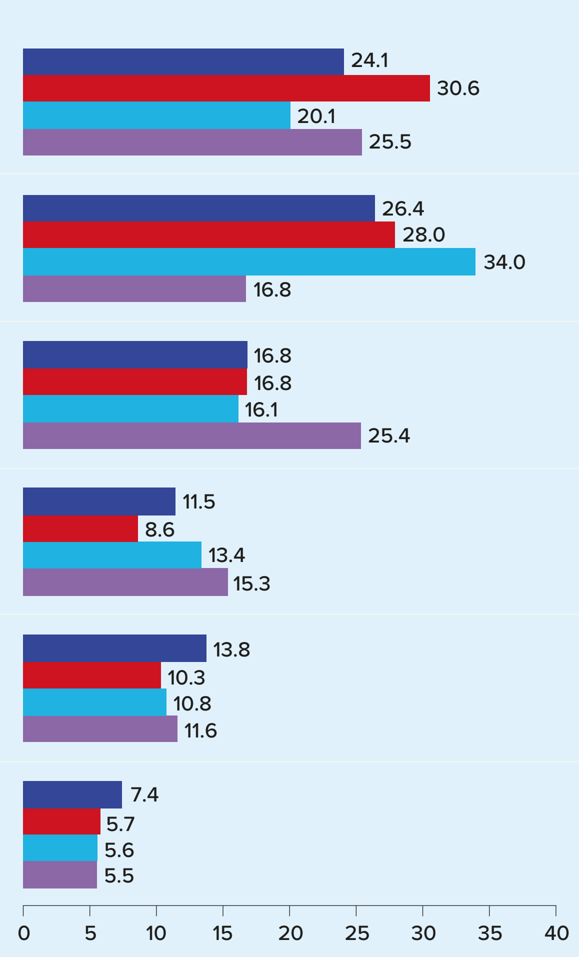


Figure 5. **WMM Ranking by Race and Ethnicity Groups**



Standardized priority weights sum to 100%

Note: Subgroups were defined by the respondent's self-reported racial and ethnic identity (for care partners, their self-reported race/ethnicity, not that for the PLWAD for whom they care, was used) and consisted of respondents identifying solely as Black or African American (n = 209); solely as Hispanic, Latina/o, Latine, or Latinx (n = 121); multiracial or another race or ethnicity, including Alaska Native, American Indian, Native American, Asian, Asian American, Middle Eastern, North African, Native Hawaiian, or Pacific Islander, or a race or ethnicity not listed in the survey (n = 61); or solely as White (n = 249).

Figure 3
- 🟦 PLWAD (n = 375)
- 🟥 Care partner (n = 265)

Figure 4
- 🟦 Group 1: Non-clinically impaired AD (n = 134)
- 🟥 Group 2: MCI AD (n = 120)
- 🟦 Group 3: Mild AD (n = 121)
- 🟪 Group 4: Moderate AD (n = 133)
- 🟦 Group 5: Severe AD (n = 132)

Figure 5
- 🟦 Black or African American (n = 209)
- 🟥 Hispanic, Latina/o, Latine, or Latinx (n = 121)
- 🟦 Multiracial or Other Race or Ethnicity (n = 61)
- 🟪 White (n = 249)

CONCLUSIONS

- Overall, this survey study provides unique information on meaningful treatment goals across the full spectrum of disease severity, in addition to health-related quality of life data and utility assessment relevant for health economic assessment.
- This dataset is novel for several reasons, including the large sample size across the disease severity spectrum, diverse demographic composition of the sample, and use of clinical diagnosis to facilitate recruitment. The results reported here quantify prioritization of key concepts by those with lived experience of disease, demonstrating:
  - PLWAD and care partners *can* and *do* prioritize among the concepts.
  - Although all What Matters Most concepts are important to the lived experience, individuals *prioritize* concepts differently based on disease stage and status as a PLWAD or care partner.
  - Differing prioritization among race and ethnicity subgroups underscores the importance of ensuring cultural appropriateness of measure selection.
- In addition to prioritization, survey results not presented here demonstrate:
  - The What Matters Most concepts reflect aspects of the Alzheimer's lived experience that are *impactful* to PLWAD and care partners across the spectrum of disease severity.
  - A *single* What Matters Most conceptual model of disease is applicable across the full spectrum of disease.
- These results support use of What Matters Most concepts to guide clinical care regarding impact of disease.
- Additionally, results provide the basis for measurement of disease within interventional and observational trials, aligning with best practice for assessing meaningful clinical benefit.[8]
- These data inform the selection of relevant patient-centric outcome measures and the development of study endpoints to better guide the development and evaluation of AD treatments and services.

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Presented at: Alzheimer's Association International Conference; 27-31 July 2025; Toronto, Canada