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Measuring “What Matters Most” to People Living With Alzheimer’s Disease and Care Partners: A Next Generation Conceptual Model of Alzheimer’s Disease

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BACKGROUND

- The Alzheimer’s Disease Patient and Caregiver Engagement Initiative’s What Matters Most (WMM) Research Program includes seminal studies to identify and measure treatment-related needs, preferences, and priorities of people living with Alzheimer’s disease (PLWAD) and their unpaid care partners.
- The first set of WMM studies[1-3] explored what is important to PLWAD and care partners.
- This early WMM research initially identified 42 concepts[2] deemed to be of highest importance in treatment-related needs across the Alzheimer’s disease (AD) spectrum, ranging from preclinical to severe AD. The process of identifying and contextualizing concepts is an iterative process that will involve continuous learning from PLWAD and their caregivers.
- Now we are conducting the WMM Next Generation Studies to generate data that can contextualize findings through a conceptual model of disease, verify previously identified concepts, and learn by assessing new emerging concepts from a more representative and inclusive study sample.

OBJECTIVE

- Verify WMM concepts across a more diverse, inclusive, and thereby a more representative study population
  - Identify any missing concepts
- Develop and refine a draft conceptual model of disease
  - Determine usefulness within the roadmap to inform identification of fit-for-purpose clinical outcome assessment
- Broaden the context of the initial WMM survey to inform additional stakeholders, including health economic evaluations, across the AD research field.

METHODS

- First, a draft conceptual model of disease was developed expanding upon an existing AD model[4] structure after careful examination of previously collected WMM data.
- Then we conducted a prospective, single-visit, observational study among clinically confirmed PLWAD and care partners across the spectrum of disease.
  - Eligibility criteria and definitions for the 5 AD populations are presented in Table 1.
  - Interview participants were demographically representative and were targeted to ensure a mix of sexes, ages, education levels, races, and ethnicities.
- Experienced qualitative researchers conducted a series of in-depth interviews with PLWAD and/or care partners across a continuum of AD stages to confirm findings from the original WMM work and to inform refinement of a draft conceptual model and WMM survey.
- Using field notes and transcripts, qualitative content analysis and thematic analysis methods were used to analyze the interview data.[5-8]
- Important concepts and dominant trends were identified in each interview and compared across interviews to enable the assessment of patterns in participants’ responses.[9]
- Descriptive statistics (e.g., mean, standard deviation, range), including those for the frequency (e.g., number, percentages) of select items, were calculated as appropriate.

Table 1. Eligibility Criteria and AD Groups

Inclusion criteria
• Aged at least 18 years • Resided in the United States • Documented evidence for classification into 1 of the 5 AD groups • Able to read, write, and understand English or Spanish • Able to participate in a 1-hour, in-person interview
Exclusion criteria
• PLWAD has a history of any other type of dementia • PLWAD has a history of traumatic brain injury, cerebral vascular accident/stroke • Any mental or other medical condition that the PLWAD’s physician feels would interfere with the PLWAD’s ability to engage in an interview
AD groups
• **Group 1:** Individuals with unimpaired cognition per self-report who have evidence of AD pathology – Evidence of AD pathology determined by positive findings of amyloid positron emission tomography scan or cerebrospinal fluid lumbar puncture within the past 6 months • **Group 2:** Individuals with mild cognitive impairment and evidence of AD pathology – Evidence of AD pathology as described above within the past 6 months and complaints of memory problems, losing or misplacing things, forgetting events or appointments, word-finding difficulties, etc. (based on chart notes or patient self report) • **Group 3:** Individuals with a diagnosis of mild AD – Evidence of mild AD as determined by a MMSE score of approximately 20-24,[10] a physician’s assessment, or a comparable neuropsychological assessment within the past 6 months • **Group 4:** Individuals with a diagnosis of moderate AD (interview with care partner only) – Evidence of moderate AD as determined by an MMSE score of approximately 13-20,[10] a physician’s assessment, or a comparable neuropsychological assessment that can be used for AD staging within in the past 6 months • **Group 5:** Individuals with severe AD (interview with care partner only) – Evidence of severe AD as determined by an MMSE score of 12 or less,[10] a physician’s assessment, or comparable neuropsychological assessment within the past 6 months

MMSE = Mini-Mental State Examination.

RESULTS

- For model development, 42 WMM concepts were categorized across 6 hypothesized domains of thought processing (14), communication (3), mood/emotions (6), daily activities (12), social life/activities (3), and independence (4) to form a draft conceptual model of disease.
- Data were collected from 64 interviews with WMM Next Generation Studies participants that included spontaneous concept elicitation about the lived experience of AD, discussion of the draft conceptual disease model, and contextualization of the WMM concepts in terms of bother, interference, and impact with participants who spanned the full spectrum of AD, including at-risk (Group 1) through care partners of individuals living with severe AD (Group 5).
  - Interview participants were demographically representative and represented a mix of sexes, ages, educational levels, races, and ethnicities (Table 2, Table 3).
- The draft conceptual disease model was reviewed with all participants, and content was endorsed by all participants.
  - All WMM concepts were consistently deemed as important by study participants.
  - Participants also frequently distinguished the concepts of importance and relevancy, indicating where a concept was:
    - Important (mattered regarding the lived experience of the disease or a treatment preference)
    - Currently relevant (was part of the respondent’s personal experience)
    - Relevant in terms of others (family or friends, others living with AD) if not relevant or currently relevant to a participant’s own lived experience
  - A small number of candidate WMM concepts were added or split across domains to better align with participant descriptions of the lived experience of each concept (Figure 1).
- Importantly, respondents also identified priorities among the concepts grouped within and between domains.
  - Notably, all PLWAD and care partners were able to successfully rank each of the concepts and were able to offer a rationale to support selection.
- These results reaffirmed the 42 original WMM concepts, informed a refinement of the model structure, and identified a limited number of candidate WMM concepts.

Table 2. PLWAD Demographic Characteristics Collected at Screening

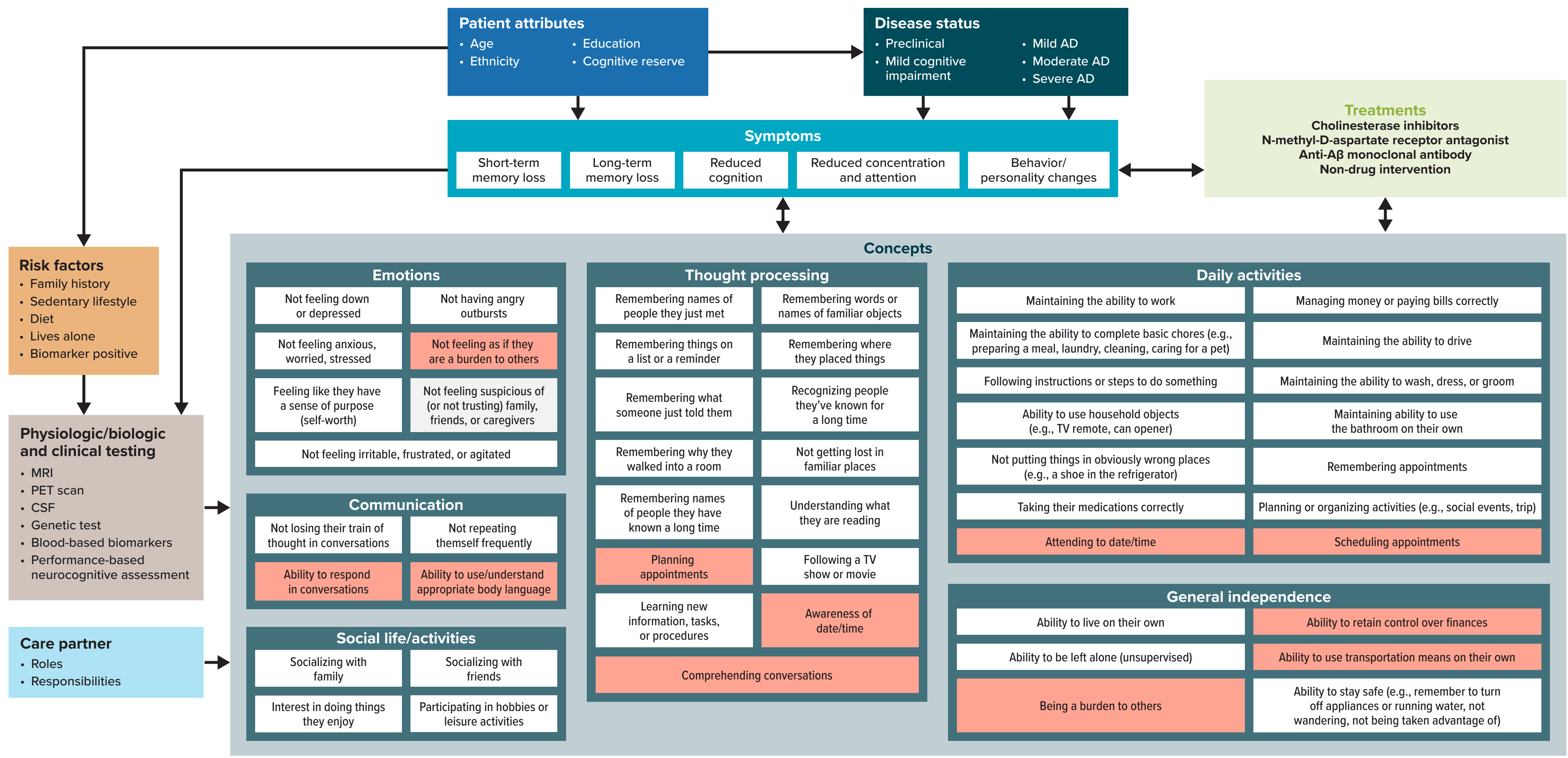
Characteristic	AD classification			Overall PLWAD Sample (N = 24)
	Group 1 (n = 11)	Group 2 (n = 7)	Group 3 (n = 6)	
Age (years)				
Mean (SD)	52.7 (5.7)	74.1 (5.4)	67.8 (10.6)	62.8 (11.8)
Range	47-66	64-81	52-80	47-81
Sex, n (%)				
Female	10	5	3	18 (75%)
Male	1	2	3	6 (25%)
Race and ethnicity, n (%)				
African American or Black	5	1	2	8 (33%)
Asian or Asian American	0	1	0	1 (4%)
Hispanic	3	0	1	4 (17%)
White	3	5	3	11 (46%)
Current employment status, n (%)				
Employed full-time	3	0	1	4 (17%)
Employed part-time	7	0	0	7 (29%)
Retired	1	7	4	12 (50%)
Disabled	0	0	1	1 (4%)
Current marital status, n (%)				
Single	1	1	1	3 (13%)
Married	6	3	5	14 (58%)
Living with partner	3	0	0	3 (13%)

SD = standard deviation.

Table 3. Care Partner Demographic Characteristics Collected at Screening

Characteristic	AD classification					Overall Care Partner Sample (N = 40)
	Group 1 (n = 5)	Group 2 (n = 9)	Group 3 (n = 10)	Group 4 (n = 8)	Group 5 (n = 8)	
Age (years)						
Mean (SD)	41.2 (12.6)	54.2 (17.3%)	59.4 (16.5%)	60.6 (4.3)	55.5 (8.2)	53.4 (13.7)
Range	20-53	29-74	24-79	44-57	41-68	20-79
Sex, n (%)						
Female	5	5	6	6	6	28 (70%)
Male	0	4	4	2	2	12 (30%)
Race and ethnicity, n (%)						
African American or Black	3	2	3	2	1	11 (28%)
Asian or Asian American	0	1	0	0	1	2 (5%)
Hispanic	2	0	2	3	1	8 (20%)
White	0	6	5	3	5	19 (48%)
Relationship to PLWAD, n (%)						
Parent	0	0	1	1	1	3 (8%)
Another family member	5	9	9	7	6	36 (90%)
Friend or another nonpaid professional caregiver	0	0	0	0	1	1 (3%)
Hours spent providing direct care to PLWAD in a typical week						
Mean (SD)	23.8 (2.5)	18.6 (6.9)	18.8 (8.5)	27.0 (13.3)	19.6 (11.1)	21.5 (9.4)
Range	20-25	10-25	10-30	10-45	4-30	4-45
Current employment status, n (%)						
Employed full-time	4	2	6	7	4	23 (58%)
Employed part-time	1	2	1	0	1	5 (13%)
Retired	0	3	3	0	1	7 (18%)
Unemployed	0	2	0	1	2	5 (13%)

Figure 1. Updated Full Conceptual Model of Disease: What Matters Most Next Generation



Patient attributes
- Age
- Ethnicity
- Education
- Cognitive reserve

Disease status
- Preclinical
- Mild cognitive impairment
- Mild AD
- Moderate AD
- Severe AD

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

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

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

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 themself 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
- Comprehending 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)

CSF = cerebrospinal fluid; MRI = magnetic resonance imaging; PET = positron emission tomography.

Note: Red shading indicates candidate new or reallocated/refined concepts to the conceptual model of disease.

CONCLUSIONS

- PLWAD and care partners reported AD as both highly symptomatic and impactful and can readily describe the lived experience.
- Importance of the previously identified 42 WMM concepts was verified in a more representative patient population.
- The structure of a draft conceptual model was refined and optimized.
  - All WMM concepts collected in previous research efforts were easily defined and endorsed based on importance and relevance to this broad and representative study population.
  - A few new WMM concepts were identified, and the conceptual disease model was updated to accommodate these changes.
  - Respondents were also able to contextualize the WMM concepts more fully in terms of “bother,” “interference,” or “impact,” with the descriptor of impact most frequently selected as the best method for describing the AD experience upon the concept.
- WMM concepts contextualized by domains offer a roadmap to support future clinical trials seeking to measure clinically meaningful outcomes and patient-centric endpoints.
- The next steps for WMM Next Generation research include the following:
  - Quantitative WMM Next Generation survey data collection will enhance the robustness of findings to further contextualize WMM and some health economic evaluations to inform additional stakeholders.
  - The conceptual model will be refined continuously throughout the WMM Research Program.

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The power of **knowledge.**
The value of **understanding.**

Presented at: Alzheimer’s Association International Conference; 16-20 July 2023; Amsterdam, Netherlands