ADPACE A-LIST

Measuring What Matters Most to People Living With Alzheimer's Disease and Care Partners: What Matters Most Qualitative Research

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BACKGROUND

- Understanding experiences and concepts important to people living with Alzheimer's disease (PLWAD) and to their care partners is critical to developing drugs and services that provide meaningful benefit.
- The Alzheimer's Disease Patient and Caregiver Engagement (AD PACE) What Matters Most (WMM) seminal research program aims to identify and measure treatment-related needs, preferences, and priorities of PLWAD and their care partners across the continuum of disease.
- The WMM research program previously evaluated the lived experience of Alzheimer's disease (AD) with PLWAD and their care partners and identified 42 WMM concepts encompassing treatment-related needs and preferences of PLWAD and their care partners.[1,2]
- Round 2 of this research builds upon previous WMM work through development of a conceptual model of disease to guide verification of WMM concepts identified as relevant, important, and meaningful to treat by extending to a more diverse population and interested parties, providing greater context for the lived experience of AD in consideration of stages across the AD continuum and refining the draft model as appropriate.

OBJECTIVES

- Evaluate the 42 WMM concepts among PLWAD and care partners across the full spectrum of disease to verify and identify any missing concepts among the broader population.
- Develop insights to refine the WMM survey to inform additional stakeholders and further contextualize WMM concepts.
- Refine a previously developed draft conceptual model of disease to provide aid in creating more comprehensive AD research tools.

METHODS

- We conducted a cross-sectional, single-visit observational study with PLWAD and care partners of PLWAD using semistructured, web-based interviews.
- To ensure that all needs, preferences, and priorities were assessed across the spectrum of disease, eligible participants were clinically confirmed and classified in 1 of 5 AD populations (Table 1), ranging from Group 1 (people with AD risk or pathology, or their care partners) to Group 5 (care partners of people with severe AD).
  - Additional participant eligibility criteria are presented in Table 1.
- Experienced qualitative researchers conducted individual interviews seeking to contextualize WMM concepts and determine how concepts can be prioritized.
- Interview data were systematically coded and evaluated using qualitative content analysis and thematic analysis methods.[3-6]
  - Important concepts and dominant trends were identified and compared across interviews.[7]
  - Descriptive statistics as appropriate (e.g., mean, standard deviation, range) were summarized for demographic and clinical data.

Table 1. AD Groups and Eligibility Criteria

AD Groups

- **Group 1:** Individuals with unimpaired cognition per self-report who have evidence of AD pathology (interviews with PLWAD or care partners of PLWAD)
  - Evidence of AD pathology determined by positive findings of amyloid positron emission tomography scan or cerebrospinal fluid lumbar puncture within in the past 6 months
- **Group 2:** Individuals with mild cognitive impairment and evidence of AD pathology (interviews with PLWAD or care partners of PLWAD)
  - Evidence of AD pathology as described above within in 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 dementia (interviews with PLWAD or care partners of PLWAD)
  - Evidence of mild AD as determined by a MMSE score of approximately 20-24,[8] a physician's assessment, or a comparable neuropsychological assessment within in the past 6 months
- **Group 4:** Individuals with a diagnosis of moderate AD dementia (interviews with care partners only)
  - Evidence of moderate AD as determined by an MMSE score of approximately 13-20,[8] a physician's assessment, or a comparable neuropsychological assessment within in the past 6 months
- **Group 5:** Individuals with severe AD dementia (interviews with care partners only)
  - Evidence of severe AD as determined by an MMSE score of 12 or less,[8] a physician's assessment, or comparable neuropsychological assessment within in the past 6 months

Inclusion Criteria

- At least 18 years of age
- Able to participate in a 1-hour interview
- Able to read, write, and understand English or Spanish

Exclusion Criteria

- PLWAD has a history of any other type of dementia
- PLWAD has a history of traumatic brain injury or cerebral vascular accident/stroke
- Any mental or other medical condition that the PLWAD's physician feels will interfere with the PLWAD's ability to engage in an interview

MMSE = Mini-Mental State Examination.

RESULTS

- The study population of 64 participants included 24 PLWAD (Table 2) and 40 care partners (Table 3) spanning experiences across the full AD spectrum, from at-risk through severe disease.
  - Both PLWAD and care partners were demographically diverse, representing a mix of sex, age, educational level, and race and ethnicity (Table 2 and Table 3).
- Participants endorsed the importance of all 42 original WMM concepts and their categorization within the hypothesized domains of thought processing , daily activity, emotion, independence, communication, and social life/activity (Figure 1).
  - Additionally, participants identified a few new candidate WMM concepts and suggested repositioning existing concepts to better describe the lived experience of AD (Figure 1, red shading).
  - Limited suggestions for recategorization or separating multi-dimensional concepts (e.g., "Awareness of date/time" and "Attending to date/time") were carried out to reduce ambiguity in the model.
- When asked to consider the descriptors "bother," "interference," and "impact" in describing WMM concepts,[9] both PLWAD and care partner respondents preferred "interference" over "bother" and "impact" over "interference" (Table 4, impact vs. interface shown) to best characterize the behavior of WMM concepts in daily life.
  - Respondents provided reasoning for their preferences, including PLWAD explaining their choice of "impact" in describing the lived AD experience on WMM concepts (Table 4).
- Participants prioritized concepts by selecting the concept of highest importance to them at the time of the interview - they or the person for whom they provide care did not have to be experiencing the sign, symptom, or impact. Participants consistently articulated most and least important items across multiple example questions and provided rationale for their choices.
  - Respondents were able to select "most" and "least" important concepts when presented with 2, 3, or 6 WMM concept options.
  - Thought processing was most frequently identified as the most important treatment benefit domain (55%, Figure 2a), though this decreased to 46% when PLWAD were analyzed separately (Figure 2b).
  - Treatment benefits affecting communication and independence were considered most important by more PLWAD (18% and 15%, respectively) than care partners (2% and 9%, respectively) (Figure 2b and Figure 2c).
  - Respondents provided reasoning reflecting the choice of thought processing by both PLWAD and care partners most frequently and the more frequent choice of communication and general independence by PLWAD (excerpts provided in Figure 2d).

Table 2. PLWAD Participant Characteristics Collected at Screening

Characteristic	AD classification Group 1 (n = 11)	 Group 2 (n = 7)	 Group 3 (n = 6)[a]	Overall PLWAD sample (n = 24)
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 assigned at birth, 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, Latin American, Latine, or Latinx	3	0	1	4 (17%)
White	3	5	3	11 (46%)
Highest level of education, n (%)				
High school diploma or equivalent (GED)	1	1	2	4 (17%)
Associate's degree/ technical school	1	0	0	1 (4%)
Some college	6	2	2	10 (42%)
College degree	3	4	1	8 (33%)
Graduate or professional degree	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%)
Divorced or separated	1	0	0	1 (4%)
Widowed/surviving partner	0	3	0	3 (13%)

SD = standard deviation.

Note: Group 4 and 5 data were collected from care partners of PLWAD only.

[a] 2 individuals with early-onset AD were included in the sample. Their responses were aligned with other respondents.

Table 3. Care Partner Participant Characteristics Collected at Screening

Characteristic	AD classification Group 1 (n = 5)	 Group 2 (n = 9)	 Group 3 (n = 10)	 Group 4 (n = 8)	 Group 5 (n = 8)	Overall care partner sample (N = 40)
Age (years)						
Mean (SD)	41.2 (12.6)	54.2 (17.3)	59.4 (16.5)	50.6 (4.3)	55.5 (8.2)	53.4 (13.7)
Range	20-53	29-74	24-79	44-57	41-68	20-79
Sex assigned at birth, 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, Latin American, Latine, or Latinx	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[a]						
Mean (SD)	25 (3.5)	20 (7.6)	21.4 (7.6)	27.8 (11.7)	23.5 (10)	23.4 (8.8)
Median	25	22.5	20	25	30	25
Range	20-30	10-30	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%)
Highest level of education, n (%)						
High school diploma or equivalent (GED)	0	0	1	0	1	2 (5%)
Associate's degree/ technical school	1	1	2	0	1	5 (13%)
Some college	1	3	3	1	2	10 (25%)
College degree	3	5	3	7	4	22 (55%)
Graduate or professional degree	0	0	1	0	0	1 (3%)

[a] Hours were collected as part of the study screener without explanation from participants for tasks considered in estimating. These estimates were also not a focus of the interviews. 11 respondents provided an estimate of hours such as 15+ or 30+ hours; the lowest end of the range of the estimate was used in these calculations. Note also that 2 care partner responses for hours were missing.

Table 4. Respondent Cognitive Debriefing on "Impact" Versus "Interfere" at First Mention

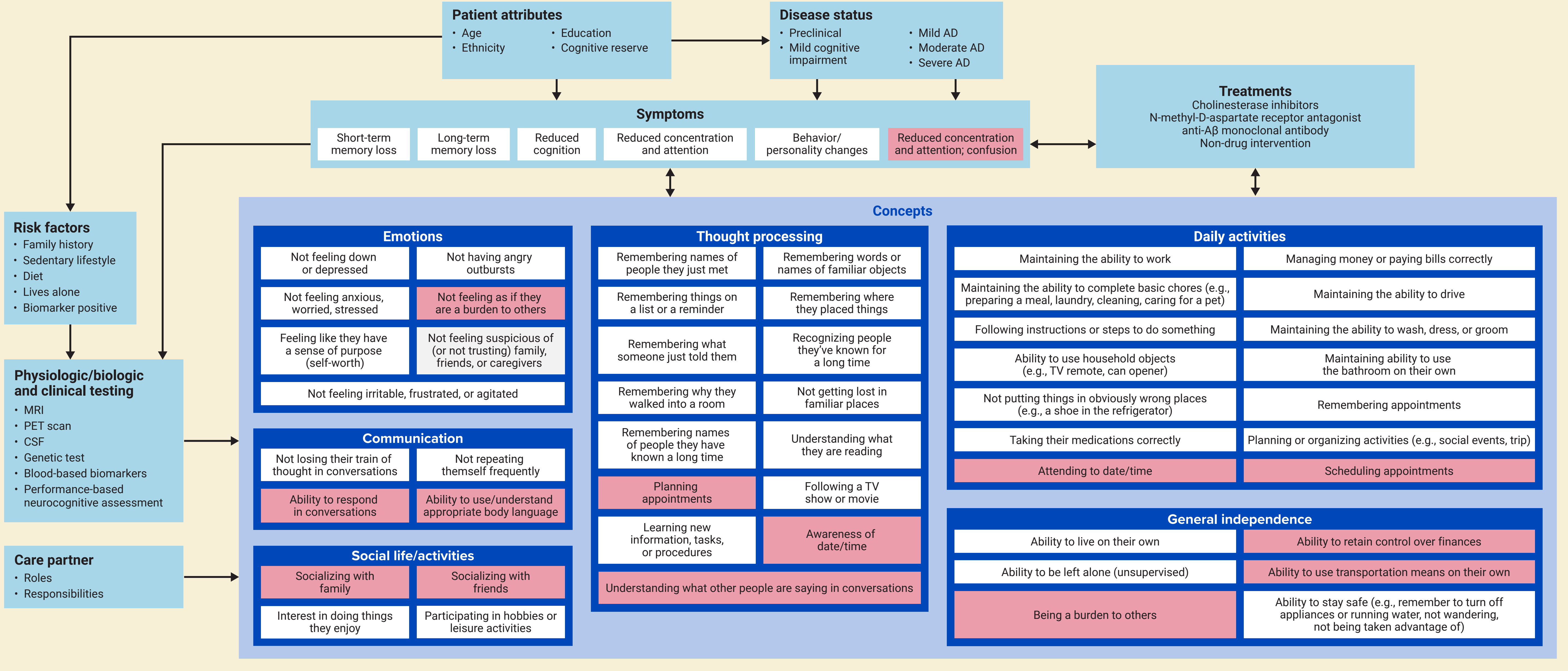
PLWAD						
	AD Classification					
Respondents (N)	Group 1 (N = 11)	Group 2 (N = 7[a])	Group 3 (N = 6)	Group 4 (N = 0)	Group 5 (N = 0)	Total (N = 24[a])
Prefer impact vs. interference (%)	9	2	4	N/A	N/A	15 (63%)
Care partners						
	AD Classification					
Respondents (N)	Group 1 (N = 5)	Group 2 (N = 9[b])	Group 3 (N = 10[b])	Group 4 (N = 8[b])	Group 5 (N = 8[b])	Total (N = 40[b])
Prefer impact vs. interference (%)	4	7	8	6	5	30 (75%)
Reasoning from PLWAD for choosing "impact" as a descriptor of the lived AD experience						
"It's different than bothered. Bothered means mad. How much are you upset? Bothered, impacted means changed. How much are you different now? I don't know." (IDI P15, G3)[c]						
"That's something that you know you're doing on a daily basis. So you feel that you say bother is like it's really irritating and getting on your nerves or something to me. But if you just say impacted, that's your life." (IDI P19, G1)[c]						
"Impact means…to me, it means to take away [from your life] by losing interest in what you're doing." (IDI P20, G1)[c]						

[a] 2 PLWAD (Group 2) did not respond to the impact vs. interfere question.

[b] 4 care partners (one each from Groups 2, 3, 4, and 5) did not respond to the impact vs. interfere question.

[c] Respondent identifier "P" indicates PLWAD participant number, and "G" indicates group number.

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



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
- Reduced concentration and attention; confusion

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
- Understanding what other people are saying in conversations

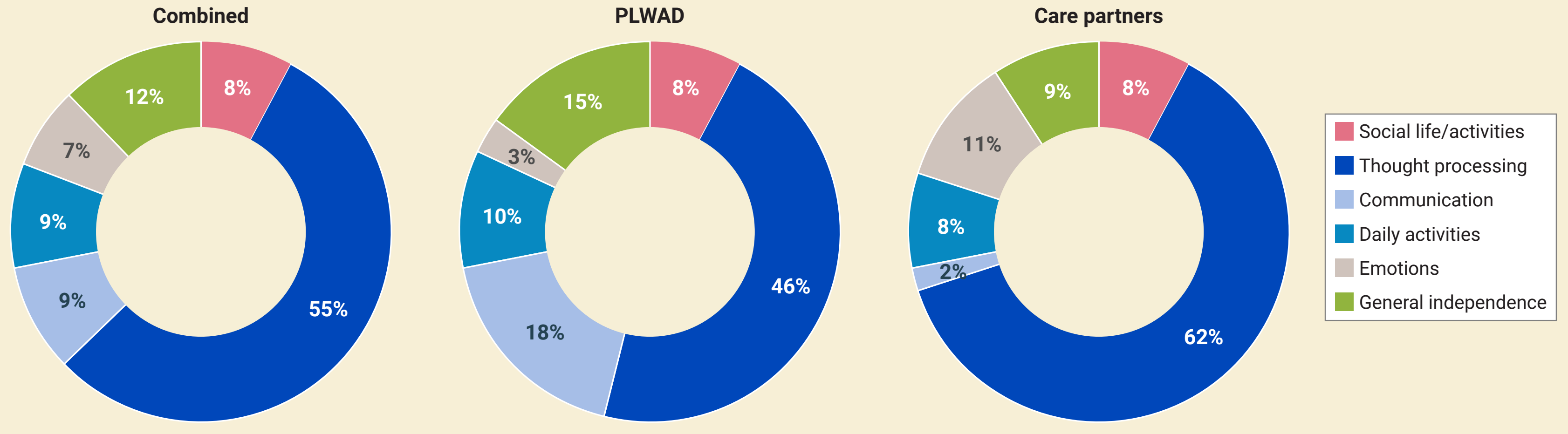
Daily activities
- Maintaining the ability to work
- Managing money or paying bills correctly
- Maintaining the ability to complete basic chores (e.g., preparing a meal, laundry, cleaning, caring for a pet)
- Maintaining the ability to drive
- Following instructions or steps to do something
- Maintaining 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)

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

Note: Red shading indicates new, refined, or repositioned concepts within the conceptual disease model.

Figure 2. Most Meaningful Treatment Benefit Domain



Respondent	Most Meaningful Treatment Benefit	Response
PLWAD (IDI P22, G1)	Thought processing	"I would first go to **thought processing**. […] remembering names, words and names of familiar object, and recognizing people, getting lost in familiar places, […] remember what someone just told you. I mean, it's just terrifying when I think of these things, that not being able to comprehend, it's very difficult."
PLWAD (IDI P3, G1)	Communication	"Well, the most important to me is my family and my friends and not forgetting them. I say my memory of not forgetting the people that I love. Yeah, **communicating** with them and not being a burden to them."
PLWAD (IDI P16, G1)	General independence	"For me personally, I think **independence** is probably the most important […]. But as somebody who is very **independent**, it's very hard to ask for help, and it's very hard to accept help."
Care Partner (IDI CP39, G2)	Thought processing	"It would be losing **train of thought**. I think if that is solved, a lot of the other ones will be solved."

CONCLUSIONS

- WMM research has developed a robust qualitative dataset describing the lived experience of AD from PLWAD and care partner perspectives
- This phase of the WMM research program demonstrated endorsement of previously identified WMM concepts and refined domain placement and concept presentation in a conceptual disease model, and greater characterization of WMM by participants representing PLWAD and care partners across the AD continuum.
  - The model was refined to include a limited number of WMM concepts that were added or reworded to reduce each to a unidimensional concept.
  - Respondents were able to articulate clear preferences for a single most important treatment benefit among the WMM concepts and domains, and qualitatively-defined differences between patients and care partners were identified.
- These findings provide context for understanding WMM in the lived AD experience and allowed for refinement of the conceptual disease model.
  - This model may serve as a useful roadmap to identify best-fit clinical outcome assessments and guide future clinical studies.
- Our WMM research will inform development of a refined WMM survey for additional stakeholders, including clinicians, payers, and policymakers.
- WMM research has developed a robust qualitative dataset describing the lived experience of AD from PLWAD and care partner perspectives.

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