

Identifying What Matters to People with and at Risk for Alzheimer's Disease and Their Care Partners: Concept Elicitation and Item Development

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Introduction:

Recent guidance from the US Food and Drug Administration (FDA) stresses the importance that outcome measures used to assess treatment effect in early Alzheimer's disease (AD) represent clinically meaningful changes (FDA, 2018; Edgar et al., 2019). Researchers have taken different approaches to defining "meaningful changes," including eliciting what matters to individuals with or at risk for AD and their care partners. While several studies have examined concepts important AD patients and their care partners, these studies cannot be broadly generalized due to their limited focus on either specific AD symptoms or AD severity. Prior studies include reviewing existing instruments to develop conceptual models of patient-relevant concepts (e.g., Hartry et al., 2018); conducting qualitative interviews and instrument reviews to develop composite measures of patient-relevant changes in early AD (e.g., Ropacki et al., 2017; Gordon et al., 2016); and developing instruments to measure progression from normal aging to dementia (Jutten et al., 2017).

The Alzheimer's Disease Patient and Caregiver Engagement (AD PACE) What Matters Most (WMM) study was designed to understand and assess treatment-related needs, preferences, and priorities among individuals with or at risk for AD and their care partners, across the continuum of disease. This two-phase study involved in-depth interviews with 5 groups comprising 60 individuals and care partners (Table 1) to elicit all notable disease-related symptoms and impacts on the lives of individuals with AD and their care partners (Phase 1) (Vradenburg et al., 2019). Phase 2 quantitatively estimated the relative importance of each disease impact identified in Phase 1 and which potential treatment symptoms or impacts are likely to matter most to these populations.

Objective:

Building from the results of the qualitative interviews from Phase 1 of the WMM Study, determine which notable disease-related symptoms and impacts, or concepts of interest, are most important to people with or at risk for AD and their care partners, to inform the WMM Quantitative Study (Phase 2) and additional research.

Methods:

Qualitative Interviews

In-depth interviews were conducted with 60 clinician-referred individuals and care partners across a continuum of 5 AD stages (n=12 each). A description of each participant group is provided in Table 1.

AD Stage	Description	Participants
Group 1	Individuals with unimpaired cognition but with evidence of AD pathology	Participants in Groups 1, 2, and 3 were interviewed directly and self-reported their symptoms as well as impacts, and desired treatment outcomes.
Group 2	Individuals with mild cognitive impairment (MCI) and evidence of AD pathology	
Group 3	Individuals with a diagnosis of mild AD	
Group 4	Individuals with a diagnosis of moderate AD and their care partners (dyads interviewed together)	Patients were interviewed together with their care partners (as a dyad) and, when able, were asked to self-report on their symptoms, impacts, and desired treatment outcomes.
Group 5	Care partners of individuals with a diagnosis of severe AD	Care partners of individuals with severe AD were interviewed.

Patients in Groups 1-3 reported on symptoms they experienced, worries, and impacts to their lives, and what they desired in treatment outcomes. Care partners in both Groups 4 and 5 reported on symptoms they observed in their care recipients, their own worries, and impacts to their lives, and what care partners desired in treatment outcomes. All interviews followed semi-structured interview guides. The purpose of the interview guides was to ensure that data were collected in a systematic and consistent way and that the interview objectives were met, while also encouraging spontaneity of responses and a conversational tone throughout the interviews. Interviews were conducted in five locations: Chicago, IL; St. Louis, MO; St. Paul, MN; New Orleans, LA; and Raleigh, NC.

Interviews were recorded and transcribed for analysis. Qualitative data analysis included identification of dominant trends in each interview and comparison across subsequent interviews to generate themes or patterns in the description of AD symptoms, impacts, and desired treatment outcomes.

Concept Synthesis from Interviews and Published Literature

Fifty unique concepts from the WMM Phase 1 interviews were compiled. These concepts were then examined in addition to:

- Fifty-six concepts from Hartry et al. (2018) identified from the conceptual model presented, the concept matrix presented in the supplementary material, and the lists of bothers and items of importance in the survey instrument;
- Twenty-six concepts from Gordon et al. (2016) identified from the Cognition Initiative Instrument; and
- Seventeen unique concepts from Jutten et al. (2017) from the Amsterdam IADL Questionnaire.

Removing redundancies and overlapping concepts, this list was reduced to a total of 83 concepts for potential inclusion in the WMM Phase 2 interviews.

Concept Reduction and Item Creation

1. We then examined the 83 concepts, divided "double-barreled" concepts into simpler concepts, and streamlined remaining concepts.
2. Further reduction and revisions were based on consensus of two researchers who conducted the WMM interviews and reviewed by a third researcher not involved in the WMM interviews, resulting in a total of 57 distinct concepts.
3. Following further iterative rounds of review and streamlining, items were developed for 45 concepts that were identified as sufficiently distinct and retained for pretest interviews.

Pretest Interviews

Forty-five items were pretested in in-person interviews with 8 patients and 7 care partners across the 5 groups. An iterative interview process was further applied to streamline the items and create a list of 42 unique items reflecting "what matters most" as determined in these interviews. Based on feedback across all participants, four items were removed from the list of 45 items, two items were combined to create a new item, and two new items were developed. Details of these changes are presented in Table 2.

Original Item	Feedback from Interview Participants	Revision
Needing to depend on lists or reminders	Participants indicated that this was repetitive and less accurately reflects participant experience compared with "Forgetting things on a list (e.g., grocery list, list of things to do)"	"Needing to depend on lists or reminders" was removed, and "Forgetting things on a list (e.g., grocery list, list of things to do)" was changed to "Remember things on a list or a reminder."
"Feeling frustrated" and "Being impatient/irritable"	Participants recommended combining the items "Feeling frustrated" and "Being impatient/irritable" and including "agitation." Participants also recommended removing "impatience" because irritability, frustration, and agitation were more important to them.	"Feeling frustrated" and "Being impatient/irritable" were removed and replaced with "Not being irritable, frustrated, or agitated."
"Being self-confident"	Participants noted that "Being self-confident" did not reflect an outcome that was important to them. Participants noted that "self-worth" or "having a sense of purpose" was what mattered most to them.	"Being self-confident" was removed and replaced with "Feel like you have a sense of purpose (self-worth)."
"Remember to turn off running water or appliances"	Participants noted that the item "Remember to turn off running water or appliances" was related to safety.	"Remember to turn off running water or appliances (e.g., the sink, the stove/oven, coffee pot, iron)" was removed, and the item that read, "Be able to stay safe (e.g., not wandering, starting a fire, flooding the house, being taken advantage of)" was revised to read, "Are able to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)."
N/A	Participants noted that driving was an important function for them because it reflected the ability to be independent.	"Drive" was added.

Results:

The final set of 42 items used in the WMM Quantitative Study (Phase 2) are presented in Table 3.

TABLE 3: Items Included in the Final Survey Instrument (Patient Version)

1.	Remember names of people you just met
2.	Remember things on a list or a reminder
3.	Remember what someone just told you
4.	Remember why you walked into a room
5.	Remember where you placed things
6.	Remember appointments
7.	Not repeat yourself frequently
8.	Remember words or names of familiar objects
9.	Remember names of people you have known for a long time
10.	Recognize people you have known for a long time
11.	Know the date and time
12.	Not get lost in familiar places
13.	Not put things in obviously wrong places (e.g., a shoe in the refrigerator)
14.	Take your medications correctly
15.	Manage money or pay bills correctly
16.	Not lose your train of thought in conversations
17.	Understand what other people are saying in conversations
18.	Understand what you are reading
19.	Can follow a TV show or movie
20.	Not have difficulty with work
21.	Can complete basic household chores (e.g., preparing a meal, laundry, cleaning, caring for a pet)
22.	Learn new information, tasks, or procedures
23.	Can follow instructions or steps to do something
24.	Can use household objects (e.g., TV remote, can opener)
25.	Plan or schedule appointments
26.	Plan or organize activities (e.g., social events, trip)
27.	Socialize with family or friends
28.	Keep an interest in doing things you enjoy
29.	Not have difficulty doing your hobbies or leisure activities
30.	Not feel down or depressed
31.	Not feel anxious, worried, stressed
32.	Feel like you have a sense of purpose (self-worth)
33.	Not be irritable, frustrated, or agitated
34.	Not have angry outbursts
35.	Not be suspicious, or not trust family, friends, or care partner/caregiver
36.	Drive
37.	Are able to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)
38.	Wash, dress, or groom yourself
39.	Use the bathroom on your own
40.	Are able to live on your own
41.	Are able to be left alone (unsupervised)
42.	Not feel as if you are a burden to others

Conclusion:

Recent work in this area has primarily focused on identifying concepts that are relevant to people with early signs of cognitive impairment or mild AD. The concepts identified in Phase 1 of the WMM Study will be leveraged to further refine concepts important to those living with or at risk of AD and their care partners, across the entire continuum of AD. Additional research may support use of existing AD-specific instruments or the need to develop or modify questionnaires that are both sensitive and specific to concepts that matter most in this population. This research further provides global concepts of interest with the potential to develop a standardized set to support the clinical research community's understanding of the performance of current and future clinical outcome assessments. This research may also inform the understanding of differences and adaptations across discrete sub populations as defined by geography, race, ethnicity, social economic status, access to healthcare, or otherwise.

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About AD PACE: UsAgainstAlzheimer's AD PACE initiative, is a pre-competitive collaboration that brings together nonprofit entities, people living with or at risk for AD, AD care partners, academic leaders, healthcare and biopharmaceutical industry, and government advisors to identify and quantify treatment-related needs, preferences, and priorities among individuals representing different stages of the AD continuum and their care partners to inform drug development, regulatory and reimbursement decision-making.

If you are interested in partnering with AD PACE, please contact Allison.Martin@FaegreBD.com

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