Quantifying What Matters Most to Patients and Care Partners in Alzheimer's Disease

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Background & Objectives

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. Phase 1, of this two-phase study involved in-depth interviews with 5 groups comprising 60 individuals and care partners to elicit all notable disease-related symptoms and impacts on the lives of individuals with or at risk for AD and their care partners (Vradenburg et al., 2019). Phase 2 of the study, reported here, quantitatively estimated the importance of each of the symptoms, impacts or outcomes identified in phase 1 to people with or at risk for AD and care partners of people with moderate and severe AD.

The primary objectives of phase 2 of the WMM study was to quantify the importance of symptoms, impacts, and outcomes of AD and dementia identified in phase 1 to those with or at risk of AD and separately to care partners of people with moderate and severe AD.

Methods

The survey instrument was developed by first applying a process of concept reduction and item creation to the results from phase 1 of this study. The elicitation format was then determined following a review of potential methods for quantifying preferences and priorities. Finally, the draft survey instrument was pretested with convenience samples of people with or at risk for AD and care partners of people with moderate and severe AD before being programmed for data collection.

The survey was administered to people in five mutually exclusive respondent groups -- Group 1 (non-clinically impaired individuals with AD risk or AD pathology), Group 2 (individuals with mild cognitive impairment and AD pathology), Group 3 (individuals with mild AD), Group 4 (care partners of individuals with moderate AD), and Group 5 (care partners of individuals with severe AD).

Respondents were recruited through multiple recruitment channels: Global Market Research Group (GMRG), the Integrace Institute, and UsAgainstAlzheimer's (UsA2).

Two versions of the survey instruments were developed using the same set of items and the same elicitation format – one for people with or at risk for AD (referred to as the patient version of the survey and administered to respondents in respondent groups 1 through 3) and one for care partners of people with moderate and severe AD (referred to as the care partner version of the survey and administered to respondents in respondent groups 4 and 5). The 42 items in the patient version and care partner version of the survey are listed in **Figures 1 and 2**. Each respondent was asked to rate the importance of each item using a verbal rating scale ranging from 1 ("Not at all important") to 5 ("Extremely important").

Respondents in respondent groups 1, 2, and 3 (i.e., patients) were asked to indicate how important it was ***to them that they*** had the ability associated with each item or were able to avoid the specific symptom or impact captured by each item. Respondents in respondent groups 4 and 5 (i.e., care partners) were asked to indicate how important it was ***to them (i.e., the care partner) that the person for whom they were providing care (i.e., the care recipient)*** had the ability associated with each item or was able to avoid the specific symptom or impact captured by each item. The item content and order were the same in both the patient and care partner versions of the survey; however, the wording of each item varied slightly to reflect differences in the perspectives of the respondents.

Results

A total of 274 respondents completed the survey fielded between June 17, 2019 through September 20, 2019. Most respondents (n = 221) were recruited by GMRG and assigned to a respondent group by physicians from four memory clinics in the United States (US) (located in Chicago, IL; St. Louis, MO; Los Angeles, CA; and St. Paul, MN). Additional respondents (n = 53) were recruited through clinic referral and public outreach by the Integrace Institute, by minority outreach by UsA2, and recruitment through the A-LIST and were assigned to a participant group by the screener at the Integrace Institute based on the information reported by the potential participant.

Respondents with or at risk of AD in groups 1 through 3 were aged in their mid-60s. In contrast, the patients for whom the care partners in groups 4 and 5 provided care were much older (mean age 80 years). In addition, the care partners in groups 4 and 5 were, on average 57.5 years old.

Among patients with or at risk for AD (including care recipients of care partners in group 4 and group 5), the majority were married or widowed. The majority of care partners were married (but not necessarily to the patient). Approximately 41% of people at risk for AD in group 1 were employed either full or part time. However, the proportion of people with or at risk for AD who were employed decreased steadily as the severity of AD increased (from group 1 through group 5). The majority of care partners were employed either full time or part time.

The number of respondents in each respondent group and the number of respondents in each pre-specified demographic subgroup (gender, race/ethnicity, education) are presented **in Table 1**.

Table 1: Number of Respondents by Respondent Group and Demographic Subgroup

Group	Total	Gender Subgroups n, (%)			Race/Ethnicity Subgroups n, (%)		Education Subgroups n, (%)	
		Male	Female	Missing	White	Nonwhite	High School or Less	More Than High School
Group 1	54	18 (33.3)	36 (66.7)	0 (0.0)	33 (61.1)	21 (38.9)	16 (29.6)	38 (70.4)
Group 2	51	18 (35.3)	33 (64.7)	0 (0.0)	32 (62.7)	19 (37.3)	10 (19.6)	41 (80.4)
Group 3	50	15 (30.0)	35 (70.0)	0 (0.0)	35 (70.0)	15 (30.0)	11 (22.0)	39 (78.0)
Group 4	65	11 (16.9)	54 (83.1)	0 (0.0)	47 (72.3)	18 (27.7)	6 (9.2)	59 (90.8)
Group 5	54	17 (31.5)	35 (64.8)	2[a] (3.7)	26 (48.1)	28 (51.9)	10 (18.5)	44 (81.5)
Total	274	79 (28.8)	193 (70.4)	2 (0.7)	173 (63.1)	101 (36.9)	53 (19.3)	221 (80.7)

[a] One respondent did not provide a response to the question about gender and one respondent answered, "Prefer not to say."

The proportion of respondents choosing each rating for each item is presented graphically for each patient respondent group **in Figure 1** and for each care partner respondent group **in Figure 2**. The distributions of each rating among the patient respondent groups appears similar across the three groups in **Figure 1** with most respondents rating all items as "Very important" or "Extremely important." **All items were rated as "Very important" or "Extremely important" by at least 50% of respondents in each of the patient respondent groups, and most items were rated as "Very important" or "Extremely important" by at least 80% of respondents in each patient respondent group.**

Among care partners, fewer than half of the items were rated as "Very important" or "Extremely important" by at least 50% of respondents in each care partner respondent group which is in stark contrast to patients for whom all items were rated as "Very important" or "Extremely important" by at least 50% of respondents.

In respondent groups 1 through 3, the minimum mean rating for any single item ranged from 3.43 and 3.59, and the maximum mean rating for any single item ranged from 4.44 and 4.57. Among all patient respondent groups, the difference between the mean ratings on the item with the highest mean rating and the item with the lowest mean rating is nominally statistically significant indicating that **there likely is a meaningful difference in importance between the highest and lowest rated items.**

Results (Continued)

Figure 1. Proportion of Respondents Choosing Each Rating for Each Item by Patient Respondent Group

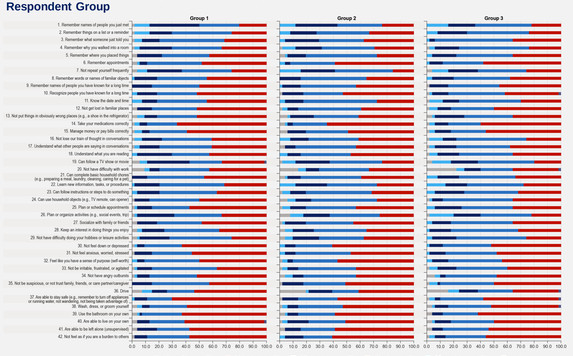
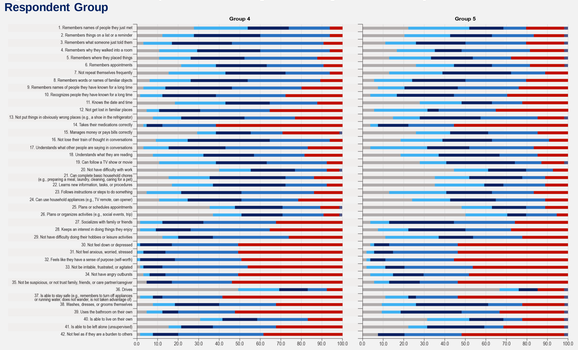


Figure 2. Proportion of Respondents Choosing Each Rating for Each Item by Care Partner Respondent Group

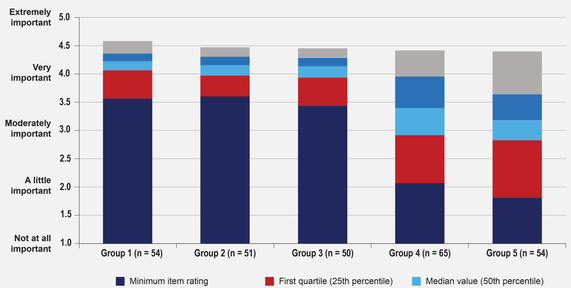


Results (Continued)

Among the care partners in groups 4 and 5, the minimum mean rating of any single item ranged from 1.81 and 2.06. The maximum mean rating for any single item was 4.42 and 4.39 for respondents in groups 4 and 5, respectively. These results suggest that among care partners of individuals with moderate or severe AD, some items are much less important to care partners than other items.

The distribution of ratings over all items for each respondent group is presented **in Figure 3**. These results suggest that **there are similarities among patients (groups 1 through 3) and similarities among care partners of later-stage patients in what they assess as important, but patients and care partners rate items differently.**

Figure 3. Distribution of Mean Ratings Over All Items for Each Respondent Group



Conclusion & Future Directions

For those with or at risk for AD, all items were important. Among care partners of more severe patients, most items were important, and one was unimportant. These results may indicate that the 42 items in the WMM survey capture symptoms and behaviors that are meaningful to patients and care partners and should be considered when evaluating impacts of potential AD treatments.

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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 AD, care partners supporting for those living with AD, 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@faegredrinker.com

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ADPACE A-LIST