Neurol Ther (2023) 12:505–527
https://doi.org/10.1007/s40120-023-00445-0

ORIGINAL RESEARCH

Assessing What Matters to People Affected by Alzheimer's Disease: A Quantitative Analysis

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Received: November 20, 2022 / Accepted: January 23, 2023 / Published online: February 10, 2023

ABSTRACT

Introduction: In this phase of the ongoing What Matters Most study series, designed to evaluate concepts that are meaningful to people affected by Alzheimer's disease (AD), we quantified the importance of symptoms, impacts, and outcomes of AD to people at risk for or with AD and care partners of people with AD.
Methods: We administered a web-based survey to individuals at risk for or with AD (Group 1: unimpaired cognition with evidence of AD pathology; Group 2: AD risk factors and subjective cognitive complaints/mild cognitive impairment; Group 3: mild AD) and to care partners of individuals with moderate AD (Group 4) or severe AD (Group 5). Respondents rated the importance of 42 symptoms, impacts, and outcomes on a scale ranging from 1 ("not at all important") to 5 ("extremely important").

John Winfield—Deceased (2022).

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40120-023-00445-0.

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Results: Among the 274 respondents (70.4% female; 63.1% white), over half of patient respondents rated all 42 items as "very important" or "extremely important," while care partners rated fewer items as "very important" or "extremely important." Among the three patient groups, the minimum (maximum) mean importance rating for any item was 3.4 (4.6), indicating that all items were at least moderately to very important. Among care partners of people with moderate or severe AD, the minimum (maximum) mean importance rating was 2.1 (4.4), indicating that most items were rated as at least moderately important. Overall, taking medications correctly, not feeling down or depressed, and staying safe had the highest importance ratings among both patients and care partners, regardless of AD phase.

Conclusion: Concepts of importance to individuals affected by AD go beyond the common understanding of "cognition" or "function" alone, reflecting a desire to maintain independence, overall physical and mental health, emotional well-being, and safety. Preservation of these attributes may be key to understanding whether interventions deliver clinically meaningful outcomes.

Keywords: Alzheimer's disease; Caregiver; Patient; Preference; Clinical meaningfulness; Outcomes; Value

Key Summary Points

Why carry out this study?

A better understanding of the priorities and disease experience of individuals at risk for or living with AD and their care partners is critical for assessing the clinical meaningfulness of treatments along the continuum of AD

Results may be used to identify or build clinical outcome assessments that capture important aspects of living with AD, such as impacts on psychological and emotional well-being

These findings support the robustness of qualitative data collection in early phases of WMM studies and lay the groundwork for future research to capture rankings

What did the study ask?

This study evaluated the importance of a set of 42 concepts identified in prior research, including treatment-related needs, symptoms, impacts, and outcomes, to individuals at risk for or living with AD and the care partners of individuals living with AD

What was learned from the study?

A broad range of AD-related symptoms and impacts are important to individuals with or at risk for AD. The most important symptoms and impacts extend beyond memory and gross functional abilities to include emotional impacts and impacts on an individual's ability to maintain their independence, health, and safety

Care partners and individuals living with disease may rate the importance of the symptoms and impacts of AD differently and for different reasons. For patients, as an example, the desire to maintain independence appeared to be driven by a desire not to be a burden to their family or care partners. For caregivers, the same concept may have a different underlying driver, such as the desire to maintain the patient at home. Assessing these impacts and the underlying source of their importance to patients and to care partners may aid in understanding the clinical meaningfulness of current and emerging treatment options from both the perspective of the patient and of the care partner

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An incidental finding was striking: a majority (57.4%) of individuals in Group 1 (unimpaired cognition with evidence of AD pathology) reported having a problem with their memory or thinking despite being assessed by a physician as having unimpaired cognition. This may bolster the rationale for early intervention in this presymptomatic population

Findings from this quantitative assessment are fully supportive of qualitative WMM phase 1 study results

INTRODUCTION

Alzheimer's disease (AD) pathology is often evident among individuals without overt signs or symptoms of dementia, suggesting that AD is best conceptualized as a continuum across both preclinical and clinical stages [1, 2]. Current evidence suggests that the most commonly used clinical outcome assessments may not capture important aspects of living with AD, regardless of stage, such as impacts on psychological and emotional well-being [3]. Therefore, greater insight into the experiences of individuals at risk for or living with AD and their care partners is critical for informing the development of clinically meaningful treatments at different stages of AD.

The What Matters Most (WMM) series is an ongoing initiative designed to evaluate concepts that are important to people affected by AD in a rapidly evolving treatment landscape. Specifically, this initiative aims to better understand and assess treatment-related needs, symptoms, impacts, and outcomes of individuals at risk for or living with AD and the care partners of individuals living with AD. In phase 1 of WMM, we conducted qualitative research with individuals at risk for or living with mild AD and care partners of individuals with more advanced AD to identify a comprehensive set of 42 AD symptoms, impacts, and treatment-related outcomes that are meaningful to individuals across the AD continuum [4]. In phase 2, reported here, individuals at risk for or living with mild AD and the care partners of individuals with moderate to severe AD assessed the importance of the concepts identified in phase 1 to confirm and provide further support for the robustness of phase 1 findings. Based on the WMM phase 2 findings, a subsequent study was conducted to evaluate the extent to which the concepts that are of greatest importance to people with or at risk for AD and their care partners are reflected in the clinical outcome assessments most commonly used in AD clinical trials (DiBenedetti et al., companion manuscript).

METHODS

Study Population

Individuals across different stages of AD were recruited through clinicians and AD organizations (Tables 1 and 2). Individuals were eligible for the study if they were at least 18 years old and able to read, write, and understand English. Those who met these criteria were, with clinician input, sorted into 1 of 5 respondent groups, including three groups of individuals at risk for or living with AD and two groups of care partners of individuals living with moderate or severe AD. Group 1 included individuals with clinician-assessed unimpaired cognition with evidence of AD pathology (i.e., a positive amyloid positron emission tomography scan, cerebrospinal fluid test) or individuals who were at risk for AD (based on a genetic test for apolipoproteins E4 and E7 or other genetic test, such as presenilin 1). Group 2 included individuals with mild cognitive impairment with evidence of AD pathology or who were at risk for AD as described for Group 1. Group 3 included individuals with a diagnosis of mild AD. Groups 4 and 5 contained care partners of individuals with a diagnosis of moderate (Group 4) and severe (Group 5) AD. We limited the respondents in Group 4 and Group 5 to care partners because observations from the qualitative interviews clearly indicated that people with moderate or severe AD would not be able to complete a survey.

Table 1 Demographic characteristics of patient respondents in groups 1–3

Demographic characteristic	Group 1 (*n* = 54)	Group 2 (*n* = 51)	Group 3 (*n* = 50)
Current age, years			
Mean (SD)	63.7 (11.6)	67.8 (11.1)	65.3 (12.9)
Range	30–87	44–91	32–92
Assignment to group, *n* (%)			
Clinical assignment	52 (96.3)	45 (88.2)	49 (98.0)
Self-report	2 (3.7)	6 (11.8)	1 (2.0)
Gender, *n* (%)			
Male	18 (33.3)	18 (35.3)	15 (30.0)
Female	36 (66.7)	33 (64.7)	35 (70.0)
Current marital status, *n* (%)			
Single	9 (16.7)	12 (23.5)	9 (18.0)
Married/living with partner	24 (44.4)	21 (41.2)	27 (54.0)
Divorced or separated	10 (18.5)	5 (9.8)	9 (18.0)
Widowed	7 (13.0)	10 (19.6)	4 (8.0)
Other	2 (3.7)	3 (5.9)	1 (2.0)
Prefer not to answer	2 (3.7)	0 (0.0)	0 (0.0)
Current living situation, *n* (%)[a]			
Alone, in own home or apartment	13 (24.07)	12 (23.5)	7 (14.0)
With spouse/partner	27 (50.0)	23 (45.1)	27 (54.0)
With children	9 (16.7)	13 (25.5)	16 (32.0)
With another relative (not spouse/partner or child)	6 (11.1)	3 (5.9)	9 (18.0)
Other	6 (11.1)	2 (3.9)	1 (2.0)
Comorbidities, *n* (%)[a]			
Type 1 diabetes	4 (7.4)	3 (5.9)	4 (8.0)
Type 2 diabetes	8 (14.8)	14 (27.5)	17 (34.0)
Thyroid disease	5 (9.3)	5 (9.8)	5 (10.0)
High blood pressure (hypertension)	20 (37.0)	31 (60.8)	30 (60.0)
High cholesterol	14 (25.9)	19 (37.3)	17 (34.0)
Other heart conditions	5 (9.3)	6 (11.8)	3 (6.0)
Sleep apnea	6 (11.1)	6 (11.8)	4 (8.0)
COPD	6 (11.1)	4 (7.8)	3 (6.0)
Osteoporosis	2 (3.7)	2 (3.9)	2 (4.0)

Table 1 continued

Demographic characteristic	Group 1 (*n* = 54)	Group 2 (*n* = 51)	Group 3 (*n* = 50)
Osteoarthritis	7 (13.0)	4 (7.8)	4 (8.0)
Rheumatoid arthritis	4 (7.4)	3 (5.9)	3 (6.0)
Glaucoma	2 (3.7)	3 (5.9)	1 (2.0)
Depression	6 (11.1)	14 (27.5)	7 (14.0)
Anxiety	7 (13.0)	16 (31.4)	10 (20.0)
None of the above	7 (13.0)	4 (7.8)	7 (14.0)
Race/ethnicity, *n* (%)[a]			
White/Caucasian	33 (61.1)	32 (62.8)	35 (70.0)
Black/African American	10 (18.5)	10 (19.6)	8 (16.0)
Asian	1 (1.9)	2 (3.9)	3 (6.0)
Hispanic or Latino	8 (14.8)	4 (7.8)	4 (8.0)
Other	0 (0.0)	1 (2.0)	1 (2.0)
Prefer not to answer	2 (3.7)	2 (3.9)	1 (2.0)
Current employment, *n* (%)[a]			
Employed full time	15 (27.8)	7 (13.7)	11 (22.0)
Employed part time	7 (13.0)	9 (17.7)	2 (4.0)
Retired	23 (42.6)	31 (60.8)	30 (60.0)
Disabled	6 (11.1)	4 (7.8)	4 (8.0)
Unemployed	4 (7.4)	2 (3.9)	3 (6.0)
Highest level of education, *n* (%)			
Less than high school	3 (5.6)	1 (2.0)	1 (2.0)
High school diploma or equivalent (GED)	13 (24.1)	9 (17.6)	10 (20.0)
Associates degree/technical school	8 (14.8)	5 (9.8)	6 (12.0)
Some college	8 (14.8)	13 (25.5)	12 (24.0)
College degree	19 (35.2)	16 (31.4)	17 (34.0)
Some graduate school but no degree	1 (1.9)	1 (2.0)	0 (0.0)
Graduate of professional degree	2 (3.7)	6 (11.8)	4 (8.0)
Total household income before tax and other deductions in 2018, *n* (%)			
Less than US$25,000	8 (14.8)	10 (19.6)	7 (14.3)
$25,000 to $49,999	14 (25.9)	11 (21.6)	14 (28.6)
$50,000 to $74,999	14 (25.9)	13 (25.5)	11 (22.4)
$75,000 to $99,999	8 (14.8)	6 (11.8)	9 (18.4)

Table 1 continued

Demographic characteristic	Group 1 ($n = 54$)	Group 2 ($n = 51$)	Group 3 ($n = 50$)
\$100,000 to \$149,999	3 (5.6)	2 (3.9)	2 (4.1)
\$150,000 to \$199,999	1 (1.9)	2 (3.9)	0 (0.0)
\$200,000 or more	0 (0.0)	0 (0.0)	2 (4.1)
Do not know or not sure	2 (3.7)	2 (3.9)	3 (6.1)
Prefer not to answer	4 (7.4)	5 (9.8)	1 (2.0)

COPD chronic obstructive pulmonary disease; *SD* standard deviation

Group 1 contained individuals with unimpaired cognition (as assessed by a physician) who had evidence of AD pathology (i.e., a positive amyloid positron emission tomography scan, cerebrospinal fluid test) or individuals who were at risk for AD (based on a genetic test for apolipoproteins E4 and E7 or other genetic test such as presenilin 1). Group 2 consisted of individuals with mild cognitive impairment or subjective cognitive complaints who had evidence of AD pathology or who were at risk for AD as described for Group 1. Group 3 consisted of individuals with a diagnosis of mild AD

[a] Respondents could select more than one response, so total responses may add up to more than 100%

Eligible individuals were recruited through three channels: a specialty recruiting firm with a database of clinical sites throughout the United States (Global Market Research Group), a senior-living nonprofit organization (Integrace Institute), and an AD patient advocacy organization (UsAgainstAlzheimer's). All patients recruited by Global Market Research Group were assigned to 1 of the 5 groups by the patient's own clinician or a clinician who had access to the patient's medical records.

This study was conducted in accordance with the standards of the Helsinki Declaration. RTI International's institutional review board determined that this study met the criteria for exemption from full review on 30 April 2019 (RTI International's Institutional Review Board Identification No. STUDY00020627). All respondents were informed of the study objectives, and all provided online informed consent to participate in the survey and have their responses published in summary form.

Survey Instruments

Concept Reduction and Item Creation

We developed the 42 WMM survey items through the literature, previously reported qualitative research [4], and item reduction. Some 50 unique concepts, including AD symptoms, impacts, and treatment-related outcomes, were identified through 60 in-person interviews conducted in phase 1 of the WMM study [4, 5]. Additional concepts of interest were identified in the literature, specifically 56 unique concepts from a conceptual model of patient-relevant concepts in mild AD [3], 26 unique concepts from a composite measure of patient-relevant changes in early AD [6], and 17 unique concepts from an instrument that measures progression from normal aging to dementia [7]. This process resulted in an initial list of 83 potential concepts of interest, which were streamlined and further refined to a pool of 45 concepts that were sufficiently distinct and retained for pretest interviews conducted among a convenience sample of patients and care partners. Following the pretest interviews, the item pool was further refined to the 42 items included on the two survey instruments (the Patient Survey for Groups 1–3 and the Care Partner Survey for Groups 4–5) [5]. Example items from the patient survey included, for instance, "How important it is to you that you take medications correctly?"; "How important it is to you that you are able to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)?"; and "How important it is to you that you not feel down or

Table 2 Demographic characteristics of care partner respondents and care recipients in groups 4 and 5

Demographic characteristic	Group 4 (*n* = 65)		Group 5 (*n* = 54)	
	Care partner	Care recipient	Care partner	Care recipient
Current age, years				
Mean (SD)	58.5 (14.9)	79.6 (9.1)	56.4 (14.1)	80.5 (8.7)
Range	25–99	51–99	23–87	53–97
Missing	0		2	0
Gender, *n* (%)				
Male	11 (16.9)	22 (33.8)	17 (31.5)	20 (37.0)
Female	54 (83.1)	42 (64.6)	35 (64.8)	32 (59.3)
Prefer not to say	0 (0.0)	0 (0)	0 (0.0)	1 (1.9)
Missing	0 (0.0)	1 (1.5)	2 (3.7)	1 (1.9)
Current marital status, *n* (%)				
Single	9 (13.8)	2 (3.1)	7 (13.0)	3 (5.6)
Married	42 (64.6)	31 (47.7)	34 (63.0)	19 (35.2)
Living with partner	5 (7.7)	0 (0)	2 (3.7)	2 (3.7)
Divorced or separated	6 (9.2)	4 (6.2)	7 (13.0)	5 (9.3)
Widowed	3 (4.6)	27 (41.5)	2 (3.7)	24 (44.4)
Prefer not to answer	0 (0.0)	0 (0)	1 (1.9)	0 (0.0)
Missing	0 (0.0)	1 (1.5)	1 (1.9)	1 (1.9)
Current living situation, *n* (%)[a]				
Alone, in own home or apartment	6 (9.2)	9 (13.8)	12 (22.2)	4 (7.4)
With spouse/partner	44 (67.7)	29 (44.6)	31 (57.4)	14 (25.9)
With children	13 (20.0)	10 (15.4)	16 (29.6)	17 (31.5)
With another relative (not spouse/partner or child)	6 (9.2)	4 (6.2)	4 (7.4)	8 (14.8)
In an assisted living community	1 (1.5)	10 (15.4)	0 (0.0)	6 (11.1)
In a nursing home or rehabilitation community	0 (0.0)	3 (4.6)	1 (1.9)	7 (13.0)
Other	5 (7.7)	2 (3.1)	3 (5.5)	2 (3.7)
Missing	0 (0.0)	1 (1.5)	2 (3.7)	0 (0.0)
Race/ethnicity, *n* (%)[a]				
White/Caucasian	47 (72.3)	45 (69.2)	26 (48.1)	29 (53.7)
Black/African American	13 (20.0)	13 (20)	17 (31.5)	15 (27.8)
Asian	0 (0.0)	0 (0)	4 (7.4)	2 (3.7)
Hispanic or Latino	3 (4.6)	4 (6.2)	6 (11.1)	5 (9.3)
Other	3 (4.6)	3 (4.6)	1 (1.9)	1 (1.9)

Table 2 continued

Demographic characteristic	**Group 4 (*n* = 65)**		**Group 5 (*n* = 54)**	
	Care partner	**Care recipient**	**Care partner**	**Care recipient**
Prefer not to answer	0 (0.0)	0 (0)	1 (1.9)	1 (1.9)
Missing	0 (0.0)	1 (1.5)	1 (1.9)	1 (1.9)
Current employment, *n* (%)[a]				
Employed full time	24 (36.9)	1 (1.5)	20 (37.0)	1 (1.9)
Employed part time	10 (15.4)	0 (0)	14 (25.9)	0 (0.0)
Student (part time or full time)	0 (0.0)	0 (0)	0 (0.0)	0 (0.0)
Retired	30 (46.2)	58 (89.2)	16 (29.6)	40 (74.1)
Disabled	1 (1.5)	3 (4.6)	3 (5.6)	10 (18.5)
Unemployed	2 (3.1)	3 (4.6)	1 (1.9)	4 (7.4)
Missing	0 (0.0)	1 (1.5)	1 (1.9)	0 (0.0)
Highest level of education, *n* (%)				
Less than high school	0 (0.0)	4 (6.2)	1 (1.9)	12 (22.2)
High school diploma or equivalent (GED)	6 (9.2)	18 (27.7)	9 (16.7)	17 (31.5)
Associates degree/technical school	4 (6.2)	5 (7.7)	6 (11.1)	5 (9.3)
Some college	18 (27.7)	11 (16.9)	15 (27.8)	8 (14.8)
College degree	21 (32.3)	15 (23.1)	15 (27.8)	7 (13.0)
Some graduate school but no degree	1 (1.5)	2 (3.1)	1 (1.9)	0 (0.0)
Graduate of professional degree	15 (23.1)	9 (13.8)	6 (11.1)	4 (7.4)
Missing	0 (0.0)	1 (1.5)	1 (1.9)	1 (1.9)
Total household income before tax and other deductions in 2018, *n* (%)				
Less than $25,000	2 (3.1)	8 (12.3)	9 (16.7)	18 (33.3)
$25,000 to $49,999	12 (18.5)	13 (20)	5 (9.3)	10 (18.5)
$50,000 to $74,999	13 (20.0)	14 (21.5)	12 (22.2)	6 (11.1)
$75,000 to $99,999	14 (21.5)	9 (13.8)	9 (16.7)	4 (7.4)
$100,000 to $149,999	11 (16.9)	2 (3.1)	7 (13.0)	0 (0.0)
$150,000 to $199,999	2 (3.1)	0 (0.0)	3 (5.6)	0 (0.0)
$200,000 or more	3 (4.6)	1 (1.5)	1 (1.9)	1 (1.9)
Do not know or not sure	2 (3.1)	11 (16.9)	0 (0.0)	6 (11.1)
Prefer not to answer	5 (7.7)	6 (9.2)	7 (13.0)	8 (14.8)
Missing	1 (1.5)	1 (1.5)	1 (1.9)	1 (1.9)

SD standard deviation

[a] Respondents could select more than one response, so total responses may add up to more than 100%

Table 3 Mean rating for each item by patient respondent group (groups 1–3)

Item	Group 1 (*n* = 54)		Group 2 (*n* = 51)		Group 3 (*n* = 50)		Groups 1–3 (*n* = 155)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1. Remember names of people you just met	3.56	1.00	3.69	0.97	3.70	0.99	3.65	0.99
2. Remember things on a list or a reminder	3.81	1.01	3.98	0.93	3.86	0.88	3.88	0.94
3. Remember what someone just told you	4.02	0.92	4.04	0.89	4.28	0.64	4.11	0.83
4. Remember why you walked into a room	3.96	0.95	3.84	1.03	3.92	0.88	3.91	0.95
5. Remember where you placed things	4.13	0.97	3.98	0.93	4.10	0.84	4.07	0.91
6. Remember appointments	4.28	0.94	4.47	0.76	4.44	0.76	4.39	0.83
7. Not repeat yourself frequently	3.74	1.05	3.59	0.94	3.68	1.11	3.67	1.03
8. Remember words or names of familiar objects	4.24	0.80	4.20	0.69	4.14	0.83	4.19	0.77
9. Remember names of people you have known for a long time	4.35	0.73	4.25	0.77	4.26	0.85	4.29	0.78
10. Recognize people you have known for a long time	4.30	0.86	4.31	0.88	4.18	0.88	4.27	0.87
11. Know the date and time	4.19	0.91	4.06	0.76	3.92	1.01	4.06	0.9
12. Not get lost in familiar places	4.30	0.94	4.18	0.89	4.22	1.00	4.23	0.94
13. Not put things in obviously wrong places (e.g., a shoe in the refrigerator)	4.20	1.07	4.02	1.10	3.98	1.02	4.07	1.06
14. Take your medications correctly	4.48	0.91	4.45	0.97	4.36	0.96	4.43	0.94
15. Manage money or pay bills correctly	4.37	0.96	4.18	1.07	4.30	0.97	4.28	1
16. Not lose your train of thought in conversations	4.09	0.98	4.12	0.93	3.90	0.97	4.04	0.96
17. Understand what other people are saying in conversations	4.13	0.93	4.24	0.91	4.08	0.94	4.15	0.92
18. Understand what you are reading	4.09	0.92	4.25	0.87	4.02	0.98	4.12	0.92
19. Can follow a TV show or movie	3.72	1.15	3.73	1.00	3.60	1.09	3.68	1.08
20. Not have difficulty with work	4.00	1.23	3.71	1.36	3.43	1.57	3.72	1.4
21. Can complete basic household chores (e.g., preparing a meal, laundry, cleaning, caring for a pet)	4.35	0.68	4.14	0.96	4.02	0.91	4.17	0.86
22. Learn new information, tasks, or procedures	4.09	0.76	3.80	0.98	3.84	1.00	3.92	0.92
23. Can follow instructions or steps to do something	4.13	0.83	4.02	0.93	3.98	0.89	4.05	0.88
24. Can use household objects (e.g., TV remote, can opener)	4.33	0.82	3.86	1.08	4.18	0.83	4.13	0.93
25. Plan or schedule appointments	4.37	0.90	4.14	0.98	4.04	0.90	4.19	0.93
26. Plan or organize activities (e.g., social events, trip)	3.96	0.93	3.63	1.20	3.60	1.09	3.74	1.08
27. Socialize with family or friends	4.22	0.96	4.20	0.92	4.14	0.81	4.19	0.9
28. Keep an interest in doing things you enjoy	4.00	1.01	3.96	1.06	4.12	0.75	4.03	0.95
29. Not have difficulty doing your hobbies or leisure activities	3.89	0.95	3.94	1.08	4.00	0.78	3.94	0.94

Table 3 continued

Item	Group 1 (*n* = 54)		Group 2 (*n* = 51)		Group 3 (*n* = 50)		Groups 1–3 (*n* = 155)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
30. Not feel down or depressed	4.48	0.84	4.45	0.81	4.38	0.75	4.44	0.8
31. Not feel anxious, worried, stressed	4.37	0.85	4.31	0.79	4.32	0.77	4.34	0.8
32. Feel like you have a sense of purpose (self-worth)	4.37	0.76	4.39	0.90	4.24	0.82	4.34	0.82
33. Not be irritable, frustrated, or agitated	4.17	0.84	4.22	0.90	4.08	0.99	4.15	0.91
34. Not have angry outbursts	4.33	0.87	4.12	1.05	4.18	1.10	4.21	1.01
35. Not be suspicious, or not trust family, friends, or care partner/caregiver	4.28	0.71	4.29	0.88	4.30	0.93	4.29	0.84
36. Drive	4.06	1.28	3.61	1.52	3.55	1.46	3.75	1.43
37. Are able to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)	4.57	0.74	4.39	0.85	4.39	0.91	4.45	0.83
38. Wash, dress, or groom yourself	4.35	1.01	4.31	0.93	4.24	1.01	4.31	0.98
39. Use the bathroom on your own	4.46	0.93	4.35	1.00	4.42	0.95	4.41	0.95
40. Are able to live on your own	4.40	0.95	4.22	0.99	4.22	1.02	4.28	0.98
41. Are able to be left alone (unsupervised)	4.31	0.99	4.35	0.98	4.34	0.94	4.34	0.96
42. Not feel as if you are a burden to others	4.43	0.81	4.39	0.87	4.34	0.94	4.39	0.87

SD standard deviation

depressed?" Tables 3 and 4 present all 42 items evaluated in the survey instruments.

Elicitation Format

We asked respondents to rate the importance of each survey item using a verbal rating scale ranging from 1 ("not at all important") to 5 ("extremely important"). Patient respondents in Groups 1, 2, and 3 indicated how important the concept reflected in each item was to them. Care partner respondents in Groups 4 and 5 indicated how important it was to the care partner that the care recipient was able to avoid the specific symptom or impact or maintain the specific ability or function captured by that item.

Surveys' Content

The survey instrument for Groups 1–3 varied slightly from the survey instrument for Groups 4 and 5. The survey administered to patients in Groups 1–3 had 4 sections: introductory text, background questions about respondents' experiences with memory and thinking problems and comorbidities, questions to elicit item importance ratings, and sociodemographic questions (age, gender, marital status, living situation, race or ethnicity, highest level of education, employment status, and income). The introductory text included a statement to anyone who may have been assisting the patient respondent in completing the survey: "*A note to those who are helping someone complete this survey: Thank you for helping this person complete*

Table 4 Mean rating for each item by care partner respondent group (groups 4–5)

Item	Group 4 (n = 65)		Group 5 (n = 54)		Groups 4 and 5 (n = 119)	
	Mean	SD	Mean	SD	Mean	SD
1. Remembers names of people they just met	2.51	1.26	2.74	1.43	2.61	1.34
2. Remembers things on a list or a reminder	3.06	1.12	2.87	1.37	2.97	1.24
3. Remembers what someone just told them	3.43	0.95	3.3	1.26	3.37	1.1
4. Remembers why they walked into a room	3.06	1.1	3.15	1.38	3.1	1.23
5. Remembers where they placed things	3.23	1.18	3.25	1.4	3.24	1.28
6. Remembers appointments	2.86	1.3	2.81	1.46	2.84	1.36
7. Not repeat themselves frequently	2.75	1.15	2.87	1.18	2.81	1.16
8. Remembers words or names of familiar objects	3.25	1.09	3.41	1.17	3.32	1.13
9. Remembers names of people they have known for a long time	3.57	1.03	3.5	1.21	3.54	1.11
10. Recognize people they have known for a long time	3.75	1.03	3.65	1.15	3.71	1.08
11. Knows the date and time	2.86	1.31	2.83	1.54	2.85	1.41
12. Not get lost in familiar places	3.89	1.11	3.61	1.35	3.76	1.23
13. Not put things in obviously wrong places (e.g., a shoe in the refrigerator)	3.42	1.21	3.11	1.25	3.28	1.23
14. Takes their medications correctly	4.42	0.93	4.22	1.08	4.33	1
15. Manages money or pay bills correctly	3.03	1.61	2.85	1.43	2.95	1.53
16. Not lose their train of thought in conversations	3.08	1.04	2.89	1.27	2.99	1.15
17. Understands what other people are saying in conversations	3.55	1.02	3.3	1.16	3.44	1.09
18. Understands what they are reading	3.22	1.23	2.93	1.32	3.08	1.27
19. Can follow a TV show or movie	2.95	1.15	2.66	1.33	2.82	1.24
20. Not have difficulty with work	2.31	1.32	2.22	1.34	2.27	1.32
21. Can complete basic household chores (e.g., preparing a meal, laundry, cleaning, caring for a pet)	2.91	1.23	2.46	1.37	2.71	1.31
22. Learns new information, tasks, or procedures	2.82	1.17	2.48	1.44	2.66	1.3
23. Follows instructions or steps to do something	3.37	1.07	3	1.3	3.2	1.19
24. Can use household objects (e.g., TV remote, can opener)	3.35	1.27	2.8	1.35	3.1	1.33
25. Plans or schedules appointments	2.53	1.39	2.2	1.42	2.38	1.41
26. Plans or organizes activities (e.g., social events, trip)	2.47	1.38	2.06	1.31	2.28	1.36
27. Socializes with family or friends	3.86	1.04	3.65	1.08	3.76	1.06
28. Keeps an interest in doing things they enjoy	3.98	0.99	3.48	1.26	3.76	1.14
29. Not have difficulty doing their hobbies or leisure activities	3.57	1.3	3.2	1.35	3.4	1.33

Table 4 continued

Item	Group 4 (n = 65)		Group 5 (n = 54)		Groups 4 and 5 (n = 119)	
	Mean	SD	Mean	SD	Mean	SD
30. Not feel down or depressed	4.32	0.79	4.31	0.97	4.32	0.87
31. Not feel anxious, worried, stressed	4.34	0.8	4.31	0.93	4.33	0.85
32. Feels like they have a sense of purpose (self-worth)	4.29	0.8	4.39	0.86	4.34	0.83
33. Not be irritable, frustrated, or agitated	4.29	0.82	4.13	1.05	4.22	0.93
34. Not have angry outbursts	4.28	0.96	4	1.2	4.15	1.08
35. Not be suspicious, or not trust family, friends, or care partner/caregiver	4.28	1.01	4.07	1.23	4.18	1.11
36. Drives	2.06	1.31	1.81	1.4	1.95	1.35
37. Is able to stay safe (e.g., remembers to turn off appliances or running water, does not wander, is not taken advantage of)	4.37	0.94	3.92	1.44	4.17	1.21
38. Washes, dresses, or grooms themselves	3.66	1.25	3.23	1.23	3.47	1.26
39. Uses the bathroom on their own	4.15	1.15	3.55	1.29	3.88	1.25
40. Is able to live on their own	2.86	1.51	2.66	1.53	2.77	1.52
41. Is able to be left alone (unsupervised)	3.58	1.4	3.15	1.52	3.39	1.47
42. Not feel as if they are a burden to others	4.09	0.95	4.15	1.15	4.12	1.04

SD standard deviation

this online survey. The person's responses are very important to us and your help is appreciated. However, please do not provide the answers for the person completing this survey. It is important that we get this information directly from the person so that we can understand what matters to them."

The survey administered to care partners in Groups 4 and 5 had 4 sections: background questions about respondents' relationship to their care recipient, questions to elicit ratings of item importance to care partner respondents, questions regarding the demographic characteristics of the care partner, and questions regarding the demographic characteristics of the care recipient.

Survey Administration

We administered the surveys as a Qualtrics web-based data-collection and management application, and hosted it on the secure Qualtrics survey data-collection platform. A unique link to the online survey was provided to each qualified participant. All respondents were informed of the study objectives, and all provided online informed consent to participate in the survey and have their responses published in summary form. For respondents in Groups 1–3, the informed consent form contained teach-back questions to ensure that each respondent understood the key elements of the consent form. Each respondent received a US$25 e-gift card to compensate them for their time and participation.

Only deidentified survey data were available to the study team, who had no access to any information identifying patients or care partners.

Analysis

We conducted descriptive analyses for each background and demographic question in the surveys, both overall and by respondent and demographic groups. We conducted descriptive analyses of the importance rating data for each respondent group and calculated the distribution of mean ratings for all items within each respondent group. We then sorted all items within each respondent group by mean rating in descending order. For items with the same mean rating, the item with the smaller standard deviation (SD) was assumed to have the higher rating. The mean ratings were qualitatively compared among the 5 respondent groups, and we identified the 10 items with the highest mean rating and the 10 items with the lowest mean rating for each group. Mean items within each respondent group were compared using an unpaired (2-sample) t test to calculate P values for the difference between the item with the highest mean rating and each other item.

RESULTS

Respondent Demographic Characteristics

The 274 respondents who completed their respective survey were evenly distributed across respondent groups, with 54 in Group 1, 51 in Group 2, 50 in Group 3, 65 in Group 4, and 54 in Group 5. Overall, most respondents were female (70.4%), were white (63.1%), and had more than a high school education (80.7%). Across groups, respondents were diverse with respect to race and ethnicity (Tables 1 and 2). Respondents at risk for or living with mild AD were, on average, in their mid-60s; those in Group 1 had a mean (SD) age of 64 (12) years; in Group 2, 68 (11) years; and in Group 3, 65 (13) years. In contrast, care recipients in Groups 4 and 5 were much older [mean (SD), 80 (9) and 81 (9) years, respectively]. Care partners in Groups 4 and 5 were younger [59 (15) and 56 (14) years, respectively] than both their care recipients and the patient respondents in Groups 1–3. Most patient respondents were married or widowed in Groups 1 (57.4%), 2 (60.8%), and 3 (62.0%), and most care recipients were married or widowed in Groups 4 (89.2%) and 5 (79.6%). Nearly two-thirds of care partners in Groups 4 (64.6%) and 5 (63.0%) were married. Over one-third (40.8%) of patient respondents in Group 1 were employed full or part-time, but the proportion of respondents employed full or part-time decreased among those in Groups 2 (31.4%) and 3 (26.0%) and among care recipients in Groups 4 (1.5%) and 5 (1.9%). Over half of care partners in Groups 4 (52.3%) and 5 (62.9%) were employed full or part-time. A greater proportion of patient respondents in Groups 2 and 3 reported having type 2 diabetes, high blood pressure, high cholesterol, depression, and anxiety than patient respondents in Group 1.

Respondent Background Characteristics

A majority of individuals at risk for or with AD were concerned about having a problem with their memory or thinking: 57.4% in Group 1 (despite being assessed by a physician as having unimpaired cognition), 88.2% in Group 2, and 90.0% in Group 3. Of those who reported concern about their memory or thinking, almost all respondents in Group 1 (87.1%), Group 2 (95.6%), and Group 3 (95.6%) discussed their concern with a doctor, an expected finding given clinician involvement in inviting potentially interested patients and care partners to participate in the survey. Respondents in all three groups, including those in Group 1, reported experiencing cognitive symptoms in the last month. Most respondents in Group 1 (68.5%), Group 2 (72.5%), and Group 3 (80.0%) reported forgetting events, tasks, and/or plans and misplacing things in the past month (Table S1, Supplementary Material). Most care partners reported that their care recipients had received a diagnosis of AD (55.4% in Group 4 and 75.9% in Group 5) and/or dementia (56.9%

in Group 4 and 55.6% in Group 5) (Table S2, Supplementary Material).

Importance Ratings

Importance ratings of items reflecting AD symptoms, impacts, and outcomes were similar among patient respondents in Groups 1–3. All items were rated as "very important" or "extremely important" by at least 50% of respondents in Groups 1–3, and most items were rated as "very important" or "extremely important" by at least 80% of respondents in each of these groups. Only five items were rated as "a little important" or "not important at all" by more than 10% of respondents in each patient group: (1) remembering names of people you just met, (2) not repeating yourself frequently, (3) following a TV show or movie, (4) not having difficulty at work, and (5) driving (Fig. 1).

Importance ratings also were similar among respondents in the two care partner groups, but care partner respondents rated fewer items as "very important" or "extremely important" than did patient respondents. Fewer than half of the items were rated as "very important" or "extremely important" by at least 50% of respondents in Groups 4 and 5. For most items, average care partner importance ratings were also lower than ratings provided by people with or at risk for AD (Groups 1–3). At least 50% of respondents in both care partner groups rated the following four items as "not at all important" or "a little important": whether their care recipient (1) remembers names of people they just met, (2) does not have difficulty with work, (3) plans or organizes activities, and (4) drives (Fig. 2).

Overall, 14 items were rated as "very important" or "extremely important" by at least half of respondents in all five groups. The following three items were rated as "extremely important" by at least half of the respondents in all five groups: (1) taking medications correctly, (2) being able to stay safe, and (3) not feeling down or depressed.

Items Sorted by Importance Rating

While the mean ratings for each item within each respondent group were high overall, there were statistically significant differences between the highest- and lowest-rated items. The minimum mean rating for any single item for Groups 1–3 ranged from 3.43 to 3.59, indicating at least moderate importance, and the maximum mean rating for any single item ranged from 4.44 to 4.57. In contrast, the minimum mean rating for any single item for Groups 4 and 5 was 2.06 and 1.81, respectively. The maximum mean rating for any single item in Groups 4 and 5 was 4.42 and 4.39, respectively (Fig. 3).

For each patient group, we created a list of 10 items rated by the patients as having the highest importance; across Groups 1–3, 15 items had the highest mean importance rating (Table 3). Similarly, we compiled a second list of 10 items rated as having the highest importance for each care partner group; 11 items had the highest mean importance rating (Table 4). There was significant overlap in items the groups considered important. The items with the highest mean importance rating from both patient and care partner groups were (1) taking medications correctly; (2) not feeling down or depressed; (3) staying safe; (4) using the bathroom; (5) not feeling like a burden to others; (6) not feeling anxious or worried; (7) feeling a sense of purpose; (8) recognizing people known for a long time; and (9) not being suspicious or not trusting of family, friends, or care partners.

DISCUSSION

This phase in the WMM series confirmed and quantified the symptoms, impacts, and outcomes of AD that had been identified as important in qualitative research with people at risk for or living with AD and care partners of people with moderate to severe AD. Most of the 42 concepts evaluated in the WMM surveys mattered to patient respondents at risk for or with AD, with more than half rating all 42 items as "very important" or "extremely important." In contrast, fewer than half of the 42 items were

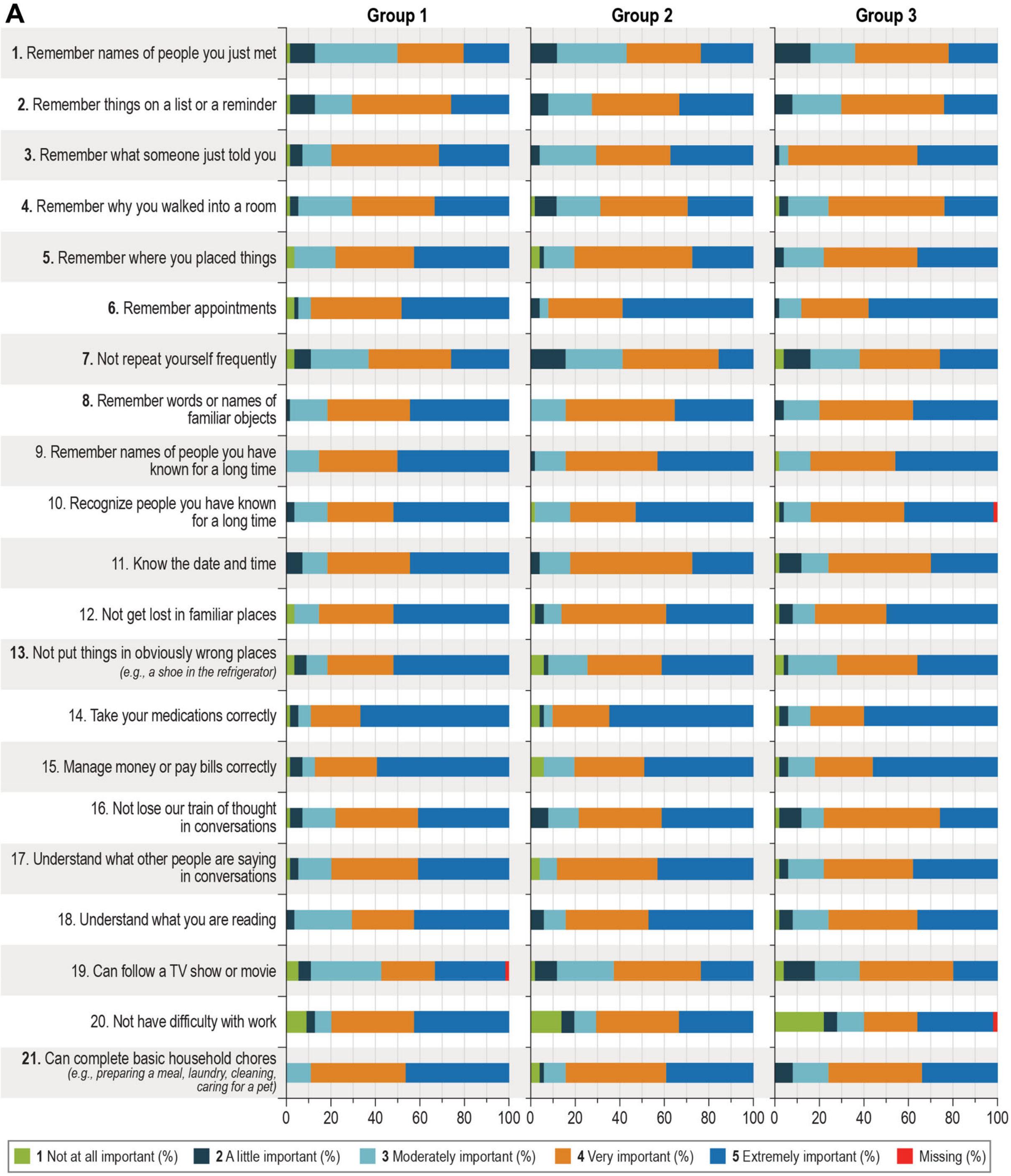
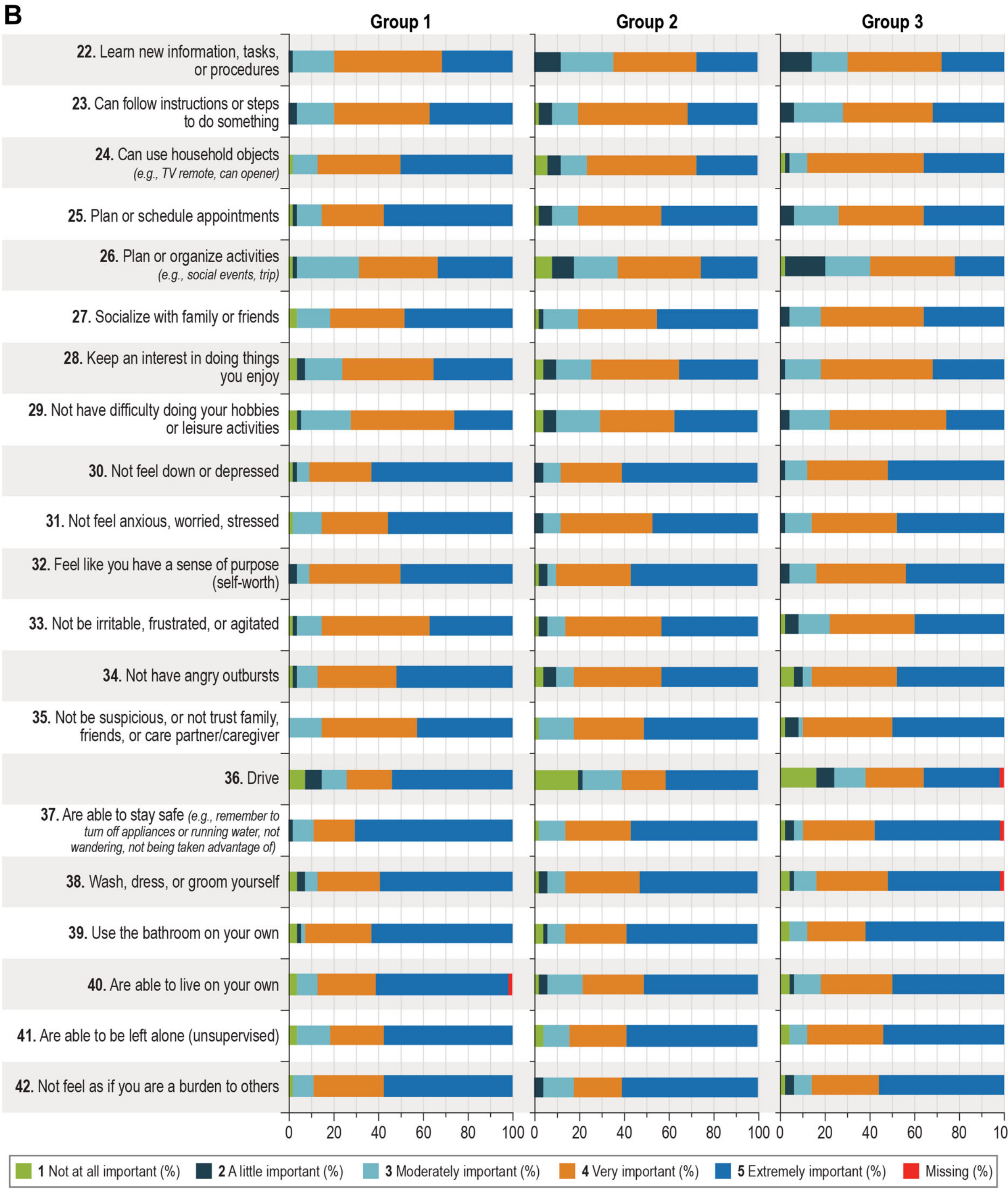


Fig. 1 Proportion of respondents choosing each rating for each item by patient respondent Groups 1–3

rated as “very important” or “extremely important” by at least half of the care partners of people with moderate to severe AD. All respondent groups consistently rated taking medications correctly, being able to stay safe, and not feeling down or depressed as the most important items. These items represent a wide range of domains that shape both patients’ and



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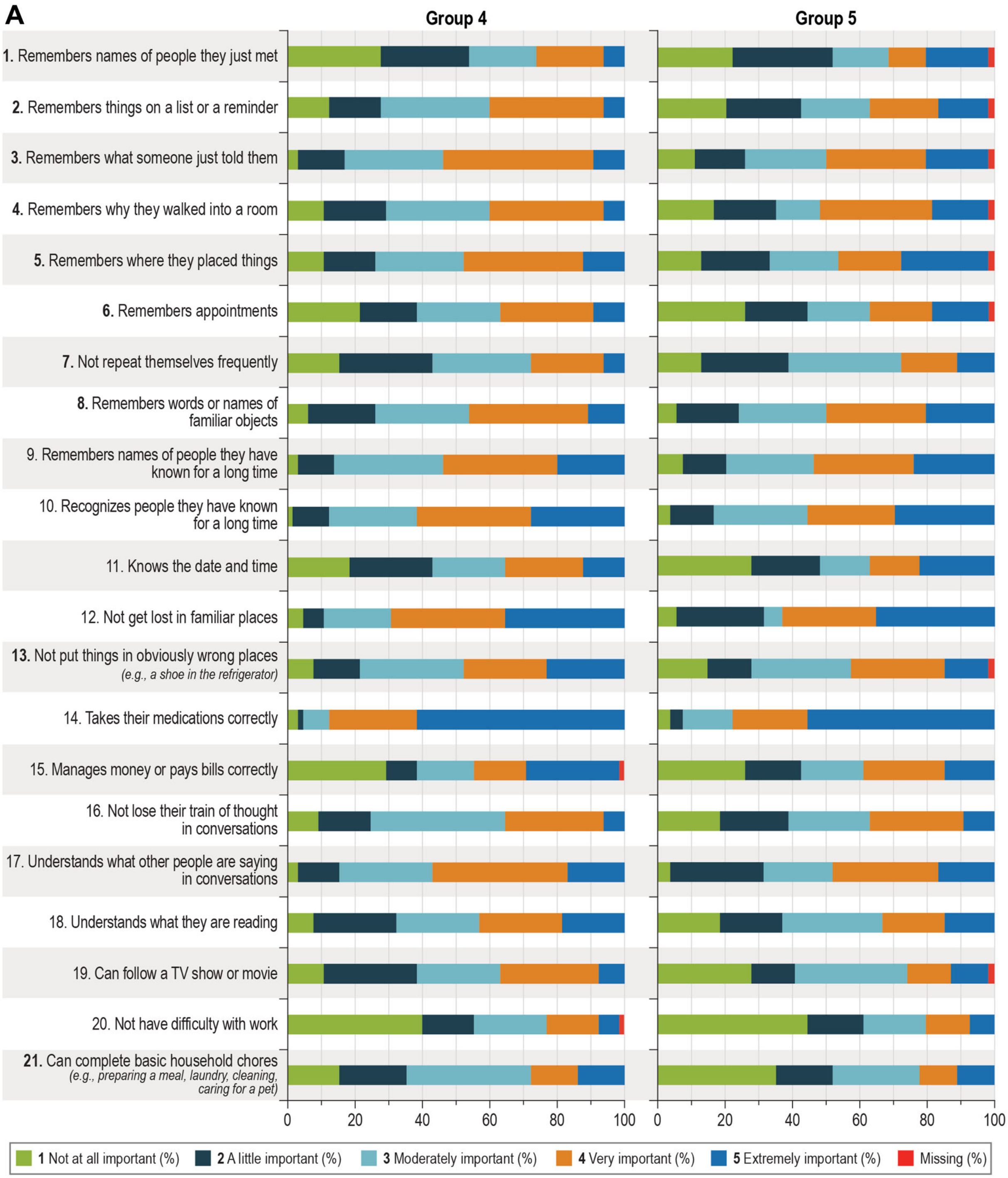

Fig. 2 Proportion of respondents choosing each rating for each item by care partner respondent Groups 4–5

care partners' experiences of AD, reflecting a desire to maintain patients' health, emotional well-being, and safety. Findings from this phase of the WMM work confirm the strength of the phase 1 qualitative findings [4], with consistent importance ratings in this heterogeneous condition.

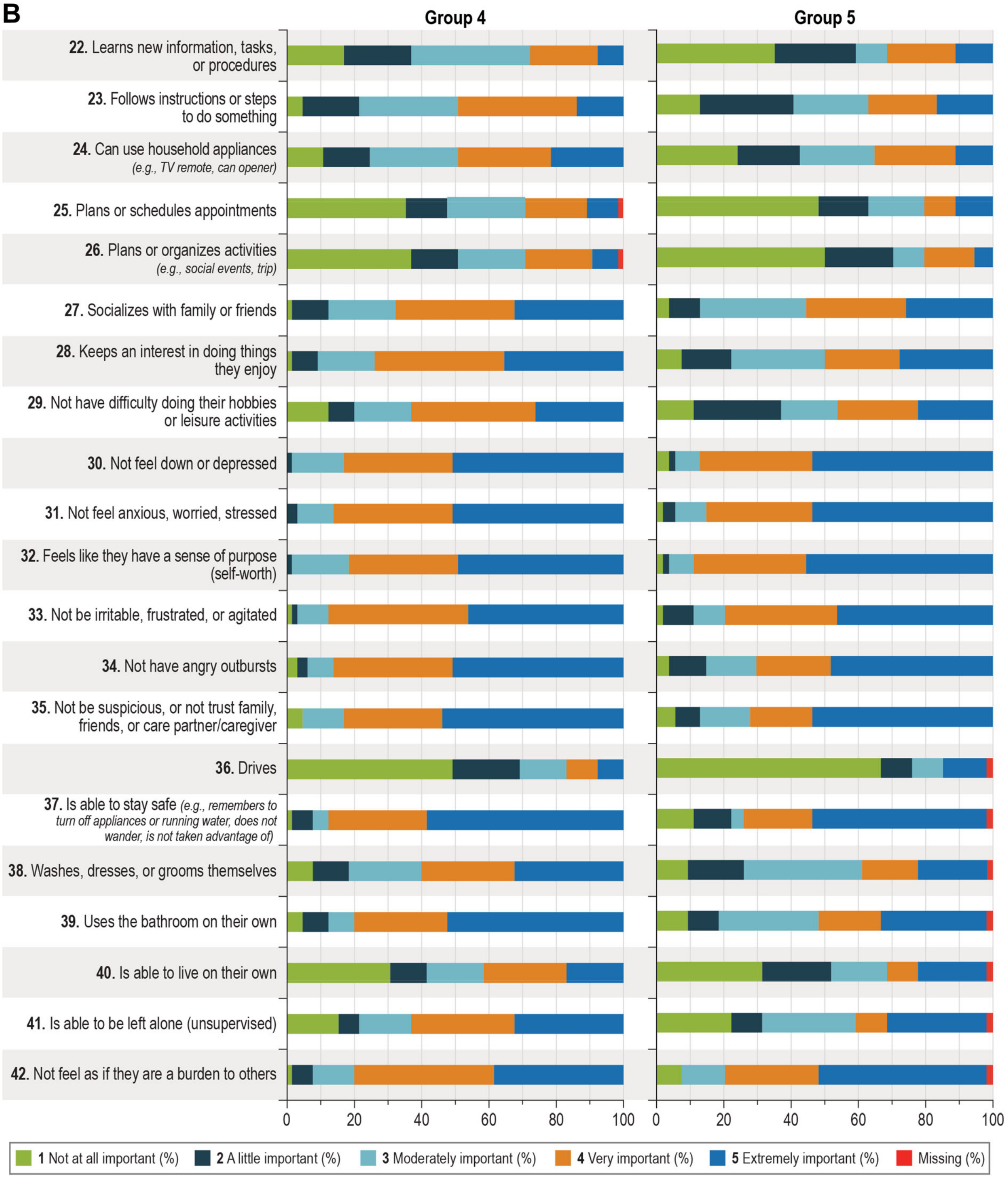

Fig. 2 continued

While the concepts of greatest importance were consistent across all respondent groups, for most items, average care partner importance ratings were lower than ratings provided by people with or at risk for AD. In particular, whether the care recipient was able to work, was able to engage in planning and organizing activities, remembered names of people they

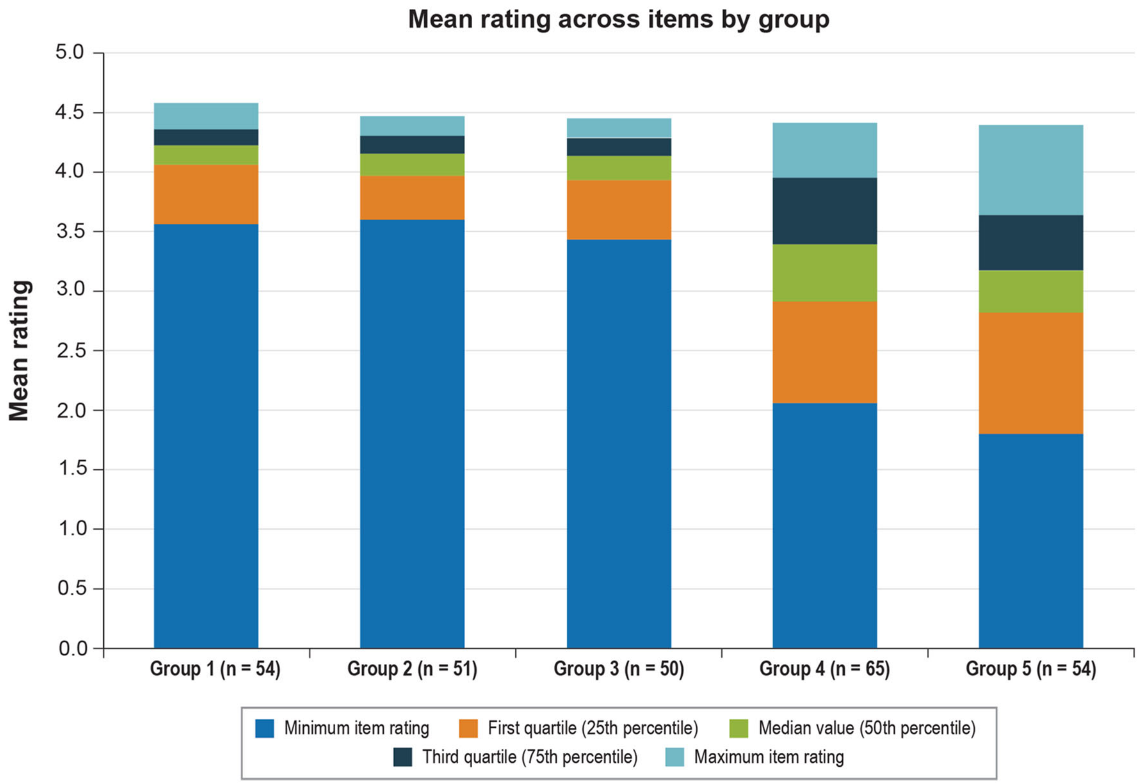

Fig. 3 Distribution of mean ratings over all items of the WMM survey for each respondent group. *WMM* what matters most study

just met, and was able to drive were among the items with the lowest importance rating for care partners and were less important than they were to patient respondents. This finding highlights that care partners and individuals living with AD may prioritize the symptoms and impacts of AD differently, and for different reasons. While patients' focus on maintaining independence may be driven by a desire not to be a burden to their care partners and family, the same concept may have a different underlying driver for care partners, such as the desire to maintain the patient at home. Assessing these impacts and the underlying source of their importance to patients and to care partners may aid in understanding the clinical meaningfulness of current and emerging treatment options from the perspectives of both the patient and the care partner.

Important WMM survey items included symptoms and impacts across a wide range of domains beyond memory, which aligns with prior research [8–10]. For instance, a recent study examining the relevance of a conceptual model of symptoms and impacts of AD found that emotional and psychological impacts were among the most relevant concepts for patients with mild to moderate AD [3]. Hartry et al. [3] also found that individuals with AD expressed a desire to maintain their health and safety. Other prior work has shown that individuals with AD value maintaining their independence and daily physical functioning [9, 11–14], quality of life [11], social engagement and ability to communicate [12, 13], and their identity and personality [13], in addition to alleviating symptoms [14]. Research evaluating patients' and care partners' goals for AD treatment has revealed that the domains of functioning, leisure, behavior, and social interaction, in addition to cognition, all represent clinically important therapeutic goals for patients and care partners [10]. Our findings complement this prior work, and further demonstrate that symptoms and impacts meaningful to patients with AD and their care partners extend beyond issues with memory, or indeed clinical definitions of “cognition” or “function.” Assessing the effects of a treatment on a range of symptoms and impacts related to AD, including those more distal from the core cognitive and functional impacts such as emotional well-being, may yield a more comprehensive understanding of the true clinical meaningfulness of the treatment’s effect.

It is also noteworthy that respondents in Groups 1–3—ranging from people with unimpaired cognition and evidence of AD pathology to those with a diagnosis of mild AD—reported consistent concerns and desires for therapeutic outcomes. The similarities among Groups 1–3 captured by the WMM surveys suggest that individuals at risk for AD perceive the avoidance of symptoms and impacts of AD in the same way as do patients with mild cognitive impairment or mild AD. This finding provides support for the inclusion of this presymptomatic population in clinical trials for disease-modifying therapies, given the concordance of their perception of treatment benefit with that held by individuals with more advanced disease.

While this phase of the WMM series was not designed to elicit rankings of the 42 concepts of interest from the respondents, the first-of-its-kind findings and importance ratings provide a foundation to begin to understand the concepts and outcomes that are meaningful to people affected by AD across the continuum of disease. The results provide novel insight into the experiences of individuals at risk for or with AD and their care partners, highlight the complexity of what matters to them, and serve as a platform for continued evidence gathering to inform patient-centered evaluations of the clinical meaningfulness of treatment benefits and outcomes across the AD continuum. A subsequent study in the WMM series has explored how the 42 items align with the concepts in commonly used AD clinical outcome assessment measures, thereby elucidating the ability of existing instruments to capture meaningful concepts across AD severity states [15] (DiBenedetti et al., companion manuscript). Future studies in the WMM series are planned to further contextualize WMM findings, to refine the WMM survey to expand its context of use, and to develop a list of prioritized core outcome assessments informed by WMM findings.

Our study has several limitations. While the overall sample consisted of 274 respondents across the continuum of AD and categorized into three groups of patients and two groups of care partners, the number of respondents in each group was relatively small. Further, some clinical details, such as patient respondents’ and care recipients’ genetic-mutation profile, were not collected in this study. The web-based survey design may have limited participation to respondents with internet access, although we did offer respondents a chance to complete the survey in a clinic if they needed help or did not have internet access. Additionally, most respondents were female and had a greater than high school education, and the geographic diversity of respondents (e.g., urban or rural) was unknown. These factors limit the generalizability of our findings. The analyses did not explore whether patients’ and care partners’ survey responses may have been influenced by certain demographic characteristics and living circumstances, such as whether they were employed or lived alone. The potential influences of these factors on respondents’ importance ratings is unknown and will be an interesting topic for future research. There was a clear ceiling effect with the 5-point scale, which makes comparison between items difficult. The cross-sectional study design precludes an assessment of changes in what matters to patients as their disease progresses. Given the differences between the patient and the care partner groups, and the different perspectives they represent, we cannot conduct formal statistical comparisons to further evaluate similarities and differences in importance ratings among individuals across the AD continuum. Finally, individual patients’ and care partners’ priorities for the treatment of AD may include dimensions not reflected in the WMM items (e.g., physical health or aspects of family relations, such as respect, affection, and understanding). The results reported here represent a systematic elicitation of concepts that were confirmed to be important, on average, across the disease spectrum, not the unique perspectives and lived experiences of people living with or affected by AD.

CONCLUSIONS

We developed the 42-item WMM survey to confirm and quantify concepts that matter to individuals at risk for or living with AD and to their care partners across the disease continuum. The WMM items were informed by concepts in the literature and systematically identified from qualitative interviews with people at risk for or with AD and their care partners. We found that nearly all of the 42 items were highly important (mattered) to respondents, ranging from asymptomatic individuals with AD pathology to care partners of people with severe AD. Individuals at risk for or with AD rated more items as important than did care partners, indicating the importance of individual as well as caregiver input. Ratings of importance across the 42 items by individuals who were presymptomatic but with underlying evidence of AD (Group 1) were highly consistent with those rating by individuals with diagnosed cognitive impairment due to AD (Group 2) and with those with mild AD (Group 3). Notably, both patient respondents in Groups 1–3 and care partner respondents in Groups 4 and 5 agreed on the importance of taking medications correctly, not feeling down or depressed, and being able to stay safe. Additionally, a wide range of items, extending beyond cognition and gross functional ability were important to individuals at risk for or with AD and to their care partners, including emotional well-being and a desire to maintain independence, overall physical and mental health, and safety.

ACKNOWLEDGEMENTS

The authors express their gratitude to the patients, care partners, and health care professionals who participated in and assisted with the study.

Funding. This study and the rapid publication fee for this publication were funded by the UsAgainstAlzheimer's AD PACE initiative. AD PACE is a precompetitive collaboration that brings together nonprofit entities, people living with AD, care partners, academic leaders, industry, and government consultants 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 and regulatory and reimbursement decision-making. During the phase of work represented here, AD PACE was funded by the following sponsors: Biogen Inc., Cambridge, MA, USA; Boehringer Ingelheim Ltd., Burlington, ON, Canada; Lundbeck LLC, Deerfield, IL, USA; Otsuka Pharmaceutical Development & Commercialization Inc., Princeton, NJ, USA; Takeda Pharmaceuticals, Cambridge, MA, USA; UsAgainstAlzheimer's, Washington, DC, USA; HomeInstead Inc., Omaha, NE, USA; LEAD Coalition (Leaders Engaged on Alzheimer's Disease), Washington, DC, USA.

Medical Writing/Editorial Assistance. Kimberly Moon of RTI Health Solutions provided overall project management for this study. Joshua Coulter, formerly of RTI Health Solutions, and Colton Leach of RTI Health Solutions provided analytical support for this study. Tyler Barrett, formerly of RTI Health Solutions, and Kate Lothman of RTI Health Solutions provided medical writing services, which were supported by their employer, RTI Health Solutions. John Forbes of RTI Health Solutions and Gail Zona, formerly of RTI Health Solutions, provided editorial services, which were supported by their employer, RTI Health Solutions.

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Prior Presentation. The results presented in this manuscript were presented in part and in preliminary form as: Hauber B, DiBenedetti D, Vradenburg G, Callahan L, Potashman M, Krasa H, Hartry A, Wunderlich G, Hoffman D, Wieberg D, Kremer I. Identifying what matters to people with and at risk for Alzheimer's disease and their care partners: concept elicitation and item development. Poster presented at the 12th Clinical Trials in Alzheimer's Disease (CTAD) Meeting; San Diego, CA; December 6, 2019. Hauber B, Paulsen R, Callahan L, Potashman M, Lee D, Hartry A, Wunderlich G, Hoffman D, Wieberg D, Kremer I, DiBenedetti D. Quantifying what matters most to patients and care partners in Alzheimer's Disease. Poster presented at the 2020 Alzheimer's Association Virtual International Conference (AAIC); July 29, 2020. Majid T, Paulsen R, Callahan L, Potashman M, Lee D, Hartry A, Wunderlich G, Hoffman D, Wieberg D, Kremer I, Hauber B, DiBenedetti D. The importance of care partner input in Alzheimer's Disease (AD) drug development. Poster presented at the 2020 Alzheimer's Association Virtual International Conference (AAIC); July 27, 2020.

Disclosures. Christina Slota, Carla Romano, and Dana B. DiBenedetti are salaried employees of RTI Health Solutions, which received research funding from AD PACE during the conduct of this study. Brett Hauber was a salaried employee of RTI Health Solutions during conduct of this study and is now an employee of Pfizer Inc. Deborah L. Hoffman, Hilary Wilson, Michele Potashman, and Daniel Lee are salaried employees of Takeda Pharmaceuticals, Boehringer Ingelheim, Biogen Inc., and Otsuka Pharmaceutical Development & Commercialization Inc., respectively, but they received no direct compensation related to the development of this manuscript. Ann Hartry was a salaried employee of Lundbeck LLC during conduct of this study and is now a salaried employee of Eli Lilly and Company; she received no direct compensation related to the development of this manuscript. Holly B. Krasa was a salaried employee of Otsuka Pharmaceutical Development and Commercialization Inc. (a funder of AD PACE) during the conduct of this study and is now an employee of Blue Persimmon Group. Allison D. Martin was a salaried employee of Faegre Drinker Consulting during conduct of this study and is now an employee of Sanofi. Leigh F. Callahan, John Winfield, Geraldine A. Taylor, James M. Taylor, Ian N. Kremer, Dan Wieberg, George Vradenburg, Russ Paulsen, Meryl Comer, Debra Lappin, Terry Frangiosa, and Virginia Biggar declare that they have no competing interests.

Compliance with Ethics Guidelines. This study was conducted in accordance with the standards of the Helsinki Declaration. RTI International's institutional review board determined that this study met the criteria for exemption from full review on 30 April 2019 (RTI International's Institutional Review Board Identification No. STUDY00020627). All respondents were informed of the study objectives, and all provided online informed consent to participate in the survey and have their responses published in summary form.

Data Availability. All data generated or analyzed during this study are available from the corresponding author on reasonable request.

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