

# The Importance of Care Partner Input in Alzheimer's Disease (AD) Drug Development

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## Background

In Alzheimer's Disease (AD), the role of the care partner is essential due to their gradually increasing role over the course of disease progression. Family and friends of those living with AD take on unique roles, including providing care and representing the wishes of their loved ones in later stages of disease.

Many current trials require care partners (CPs) to report on patient symptoms later in the disease. Studies have also suggested that the role of the CP-patient dyad may be linked to reliable outcomes in drug development. However, there are concerns around reliability of information and reporting bias.

The Alzheimer's Disease Patient and Caregiver Engagement (AD PACE) What Matters Most (WMM) study is a two-part study designed to better understand and assess treatment-related needs (i.e. what matters) as well as treatment preferences and priorities (i.e. what matters most) among individuals with or at risk for AD and their caregivers. In-depth understanding of the impact of AD on specific treatment needs of people with and at risk for AD and their CPs across the continuum of the disease is needed to inform:

1. the development of AD therapies and care services;
2. the need for new tools and measures that assess outcomes that are confirmed as most meaningful to individuals with AD and CPs;
3. the regulatory review of new therapies to treat AD;
4. health technology assessments and reimbursement decisions for new therapies and services to treat and manage AD; and
5. a growing understanding of the unique experience of CPs of people with AD.

The AD PACE program has begun to explore the appropriate role a CP can serve when reporting on experiences of someone living with AD and their response to a treatment (experimental or approved).

## Methods

**SAMPLE:** The AD PACE WMM Studies included participants throughout AD through both qualitative and quantitative methods.

**Group 1:** Individuals with unimpaired cognition who have evidence of AD pathology

**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 CPs (Qualitative Study); CPs of individuals with a diagnosis of moderate AD (Quantitative Study)

**Group 5:** CPs of individuals with a diagnosis of severe AD

In the Qualitative Study, CPs in Groups 4 and 5 reported on symptoms they observed in their care recipients, their own worries and impacts to their lives, and the treatment outcomes they desired. CP interviews obtained the CP's voice in how AD impacts them (not the patient), including, CP worries, and desired treatment outcomes for their care recipients.

Results from the qualitative phase were used to develop patient and CP surveys in which respondents rated the importance of 42 items in the quantitative study. The item content and order were the same in both the patient and CP surveys; however, the wording of each item varied slightly to reflect differences in the perspectives of the respondents (see Figure 1). Instructions for the CP survey and in each question made it clear that the respondent was to answer questions relating to their perspective and not the perspective of the patient.

Figure 1: Extract from CP Survey- WMM Qualitative Study

	1 Not at all important (1)	2 A little important (2)	3 Moderately important (3)	4 Very important (4)	5 Extremely important (5)
Possible Symptoms and Behaviors of Alzheimer's Disease or Dementia We will now show you a list of symptoms and behaviors that may be related to Alzheimer's disease or dementia. For each symptom or behavior listed, tell us how important it is <b>TO YOU</b> that your care recipient (the person you are caring for)...					
Remembers names of people they just met?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Remembers things on a list or a reminder?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Remembers what someone just told them?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Remembers why they walked into a room?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Remembers where they placed things?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Remembers appointments?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

## Methods (Cont.)

**ANALYSIS:** Descriptive analyses were conducted for each background and demographic question in the survey. For continuous and ordinal variables, the number of available observations, mean, standard deviation, minimum, and maximum were calculated. For categorical variables, the number of available observations and frequency and percentage in each response category were calculated. Descriptive analyses were performed for each respondent group and demographic subgroup (defined by gender, race/ethnicity, and education).

Ratings data were analyzed separately for each respondent group. First, the frequency with which each rating was selected for each item was tabulated. Then the mean, median, standard deviation, minimum, and maximum of the rating for each item were calculated. Descriptive and ratings data were managed and analyzed using STATA 14 (Stata Corp, College Station, TX).

The distribution of mean ratings (minimum, maximum, median, and interquartile range) over all items was calculated for each respondent group.

## Results

CPs (n=119) were mostly women in their mid-50s with high socioeconomic statuses. The average age of the corresponding care recipients was approximately 80 years, and most were women. **Table 1.**

Table 1: Demographic Characteristics of Care Partner Respondents and Care Recipients (Groups 4 and 5)

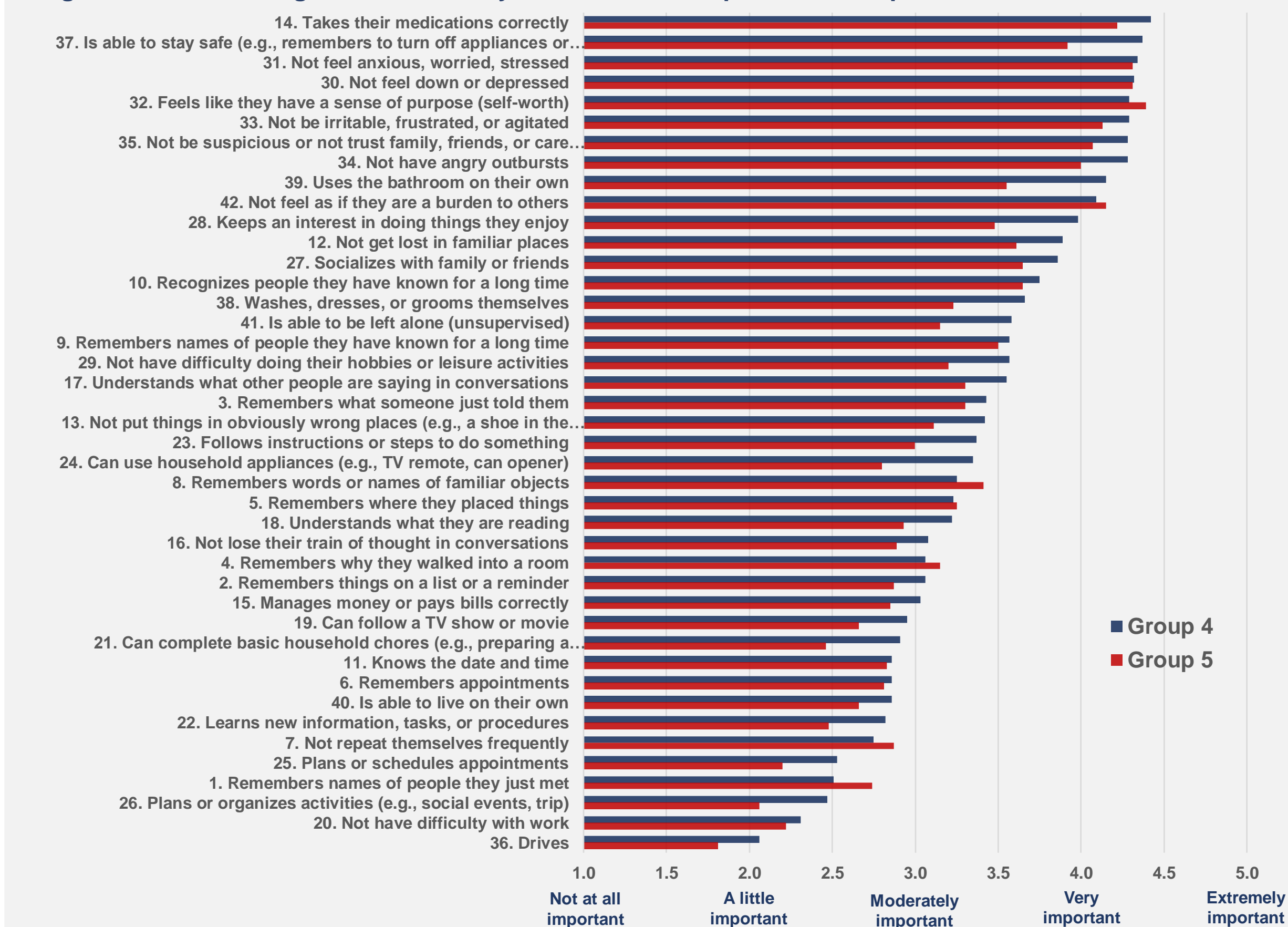
Characteristic	Group 4 (n = 65)		Group 5 (n = 54)	
	Care Partner	Care Recipient	Care Partner	Care Recipient
<b>Mean Age (SD)</b>	58.5 (14.9)	79.6 (9.1)	56.4 (14.1)	80.5 (8.7)
<b>Gender, n<sup>a</sup> (%)</b>				
Male	11 (16.9)	22 (33.8)	17 (31.5)	20 (37.0)
Female	54 (83.1)	42 (64.6)	35 (64.8)	32 (59.3)
<b>Race/ethnicity, n<sup>b</sup> (%)</b>				
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)
<b>Highest level of education, n<sup>c</sup> (%)</b>				
Less than high school	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 or professional degree	15 (23.1)	9 (13.8)	6 (11.1)	4 (7.4)
<b>Total household income before tax and other deductions in 2018, n<sup>d</sup> (%)</b>				
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 \$99,999	27 (41.5)	23 (35.3)	21 (38.9)	10 (18.5)
\$100,000 or more	16 (24.6)	3 (4.6)	11 (20.5)	1 (1.9)
Do not know or not sure/ Prefer not to answer	7 (10.8)	17 (26.1)	7 (13.0)	14 (25.9)
<b>Care recipient relationship to care partner, n<sup>e</sup> (%)</b>				
Spouse/partner	19 (29.2)	-	11 (20.4)	-
Parent	33 (50.8)	-	24 (44.4)	-
Another family member	9 (13.8)	-	14 (25.9)	-
A friend	3 (4.6)	-	4 (7.4)	-
<b>Total time each week providing direct care for the care recipient (hours) <sup>f</sup></b>				
Mean (SD)	40.3 (37.2)	-	46.9 (41.6)	-

<sup>a</sup> Five missing responses or preferred not to say; <sup>b</sup> Four missing responses or preferred not to answer; <sup>c</sup> Three missing responses; <sup>d</sup> Four missing responses; <sup>e</sup> Two missing responses; <sup>f</sup> Four missing responses.

In general, CPs rated items related to the emotional well-being of the care recipient (e.g., having a sense of self-worth; not feeling down, depressed, anxious, worried, stressed; not feeling like a burden to others) highly. When taken as a whole, mean CP ratings for what is important to them were equal to or lower than mean patient ratings, especially for items with lowest importance ratings (driving, not having difficulty with work, planning and organizing activities). **Figure 2.**

## Results (Continued)

Figure 2: Mean Rating for Each Item by Care Partner Respondent Group



Patients (Groups 1-3) responded with higher minimum mean ratings (range 3.43 and 3.59) and maximum mean rating (range 4.44 and 4.57) for any item (data not shown). Rating of any item for CPs (Groups 4 and 5) demonstrated a broader distribution (1.81 and 2.06 minimum range; 4.42 and 4.39 maximum range) with some items are less important than other items. While mean ratings among CPs showed greater distribution, Patients and CPs priorities were aligned with the most highly rated items (**Table 2**).

Table 2: Ten Highest-Rated Items by Respondent Group (Patients and Care Partners)

Item number	Item	Patient Groups (1-3)		Care Partner Groups (4-5)	
		10 Highest Rated Items- # of Groups	Item number	Item	10 Highest Rated Items- # of Groups
14	Take your medications correctly	3 of 3	14	Take their medications correctly	2 of 2
30	Not feel down or depressed	3 of 3	30	Not feel down or depressed	2 of 2
37	Are able to stay safe (e.g., remember to turn off appliances or running water, not wandering, not being taken advantage of)	3 of 3	31	Not feel anxious, worried, stressed	2 of 2
39	Use the bathroom on your own	3 of 3	32	Feels like they have a sense of purpose (self-worth)	2 of 2
42	Not feel as if you are a burden to others	3 of 3	33	Not be irritable, frustrated, or agitated	2 of 2
6	Remember appointments	2 of 3	34	Not have angry outbursts	2 of 2
15	Manage or pay bills correctly	2 of 3	35	Not be suspicious, or not trust family, friends, or care partner/caregiver	2 of 2
31	Not feel anxious, worried or stressed	2 of 3	37	Is able to stay safe (e.g., remember to turn off appliances or running water, does not wander, is not taken advantage of)	2 of 2
32	Feel like you have a sense of purpose (self-worth)	2 of 3	42	Not feel as if they are a burden to others	2 of 2
41	Are able to be left alone (unsupervised)	2 of 3	10	Recognizes people they have known for a long time	1 of 2
			39	Uses the bathroom on their own	1 of 2

"Yeah, I get frustrated. I'm very frustrated. I don't take it out on anybody. I certainly would never take it out on my wife. My wife, I love her. But it's frustrating. And I go through the inward thing, which I think the inward frustration leads to depression..."  
**Group 1 Individual**

"He has ideas. In fact, he said that this morning. He was thinking about, he came in and he was, I think he had been crying because he gets emotional sometimes now, a lot more."  
**Group 5 CP**

"I'm more of a homebody than I used to be. I used to be out all the time, shopping, doing... In my home I feel very safe. And I don't like the area where we live, it's too far out. We live way, way north. But I feel comfortable in my house, safer."  
**Group 3 Individual**

"...if he followed directions and stuff, I wouldn't have to worry about like safety things like him leaving or, you know."  
**Group 5 CP**

"[Current symptoms] just makes me very anxious. It makes me think of all the things that I used to be able to do well and I don't do so well now. So that gets me really down. I just don't want to be a burden."  
**Group 2 Individual**

"She could be left alone a little more, and she would be less agitated because she would feel a little freedom, less of a burden... She hates being a burden to her family."  
**Group 5 CP**

## Limitations

- This research asked CPs to rate item importance from their perspective, not as proxies for the patient.
- Comparing mean ratings between CPs and patients may be confounded by severity of disease, as CPs were not surveyed for Groups 1-3 and patients were not surveyed by themselves for Groups 4-5.
- The sample may be lacking diversity in terms of gender and socioeconomic status. The distribution of respondents among urban, suburban, and rural regions is incomplete.
- This study did not require or collect an independent assessment of the patients' or care recipients' cognitive or functional abilities using standardized tests. Therefore, it is not possible to correlate importance ratings with specific clinical characteristics of the patient or care recipient.
- CP ratings were elicited only for those people providing care for people with moderate or severe AD. CPs of people with mild AD or at risk of AD were not included in this study.
- This study was cross-sectional and elicited importance ratings from respondents in different groups across the continuum of AD at a single point in time. Therefore, it is not possible to definitively conclude that any differences between groups are associated directly with the progression of AD.

## Conclusion & Future Directions

Understanding and identifying the multiple ways in which CPs can provide critical input in AD therapeutic development needs further investigation. The WMM study identified emotional well-being as a key priority for CPs for those with moderate or severe AD (Groups 4 and 5). Some participants of Groups 1-3 also identified emotional well-being as a key priority, but expressed it as attached to functional priorities in their life (i.e. the ability to perform or be able to conduct certain activities in their daily life). CPs highlighted emotional well-being of the care recipient as being important to them as a care partner, citing a direct impact on their daily lives as integrated with those of their loved one. Future studies and guidance should examine opportunities for CP input on drug development as CPs provide critical perspectives on the AD patient experience.

### Future Research should explore:

- The role of CPs as proxies, informants/observers throughout AD disease progression
- Opportunities to prioritize symptoms, outcomes, and impact by SES, racial, ethnic, and geographic groups.
- The emotional well-being priorities through the lens of CP-patient dyadic relationships as these relationships have gained significant attention in the field as having impact on health-related outcomes.

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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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