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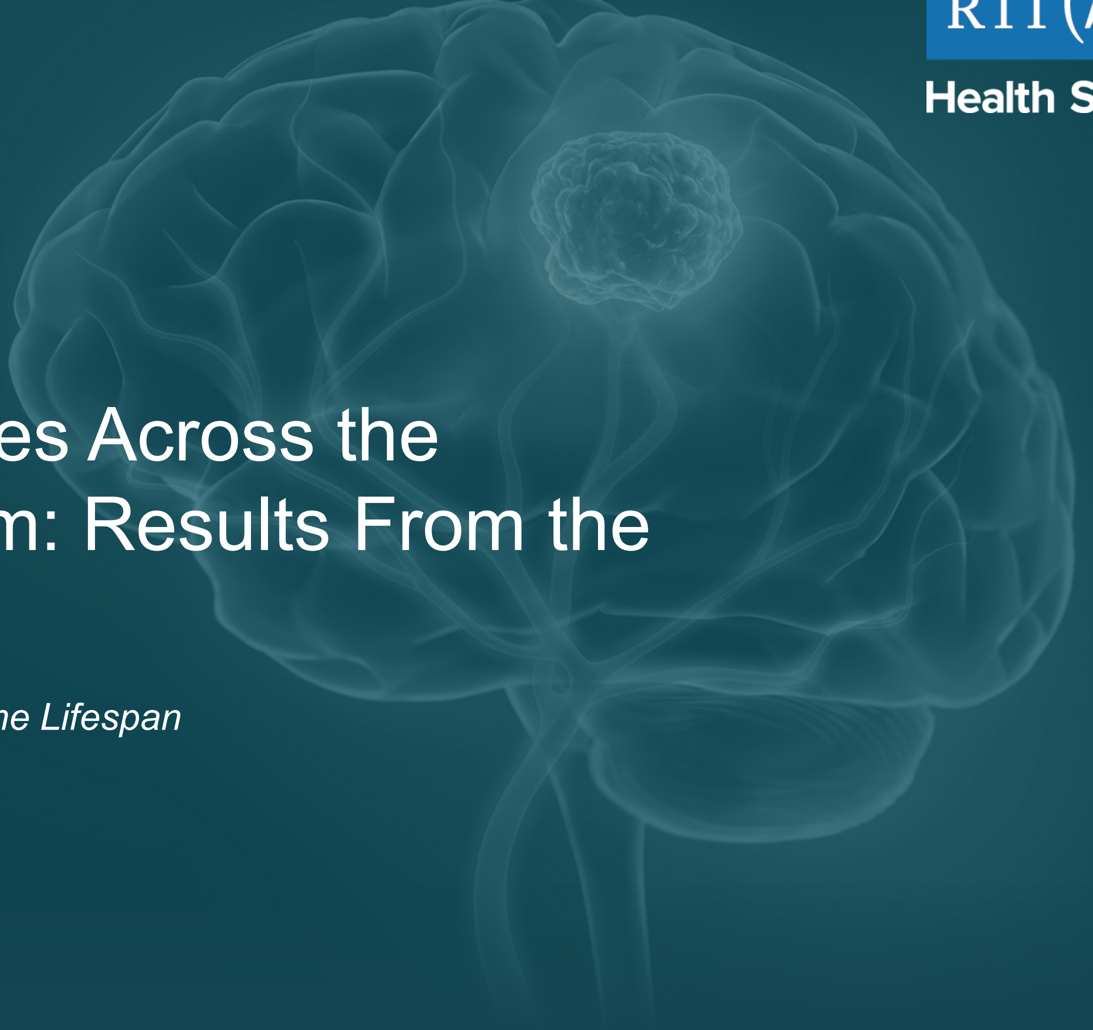

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Quality of Life and Utility Values Across the Alzheimer’s Disease Spectrum: Results From the What Matters Most™ Survey

Session: Measuring Health-Related Quality of Life Across the Lifespan

Supported by: UsAgainstAlzheimer’s

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The power of **knowledge.**
The value of **understanding.**

Disclosures

- WLH and coauthors (CR, KH, GD, LM) are full-time employees of RTI Health Solutions.
  - Not-for-profit research organization retained by UsAgainstAlzheimer’s to conduct the research that is the subject of this presentation and to provide publication support in the form of writing, styling, and submission. Their compensation is unconnected to the studies on which they work.
- WLH is affiliated with research with Karolinska Institutet.
  - Receives no compensation from this affiliation. Karolinska Institutet was not involved in this study.
- RP is an employee of UsAgainstAlzheimer’s.

AD PACE = Alzheimer’s Disease Patient and Caregiver Engagement; CDC = Centers for Disease Control and Prevention; FDA = Food and Drug Administration; NIH = National Institutes of Health.

Thank you, collaborators!

Research Partners:

AD PACE

AD PACE Steering Committee and Working Groups including members of FDA, CDC, and NIH

Clinical and qualitative research site partners

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To all the persons living with Alzheimer’s disease, care partners, and families, without whom the research is not possible, we are so grateful for your time, energy, and candor. We hope this work honors your truth.

Introduction and Overview

1 Background: WMM Research Program

2 Study-Specific Background and Objective

3 Methods

4 HRQOL Analysis

5 Conclusions, Context, and Future Directions

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HRQOL= health-related quality of life; WMM = What Matters Most™

What Matters Most in Alzheimer’s Disease

- AD is a prevalent, devastating, progressive disease affecting not only those at risk or with a diagnosis but also their care partners, family members and loved ones, and society as a whole.
- A greater understanding of the experiences, needs, and priorities of PLWAD and their care partners across the continuum of the disease is central to defining clinically meaningful treatment outcomes.
- The WMM research program is a series of studies seeking to identify and measure treatment-related needs, preferences, and priorities of PLWAD and their care partners across the full spectrum of AD and among a diverse and inclusive participant population.

AD = Alzheimer’s Disease; PLWAD = people living with AD.

WMM is sponsored by the AD PACE initiative of UsAgainstAlzheimer’s.

WMM Phased Research and AD Severity Groups

	Phase 1 Studies	**Phase 2 Studies**	***Key Publications***
Qualitative *“What Matters”*	• 60 PLWAD/care partners (12/Group)[1] • Identified 42 outcomes that matter to individuals across the continuum of AD and their care partners (WMM concepts)	• 64 PLWAD/care partners (8-16/Group)[2,3] • Confirmed prior research and identified 50 concepts that matter to respondents • Stronger, diverse perspectives (~50% people of color)	1. DiBenedetti et al., 2020. Alz Res Ther; 12:90 2. Romano et al., 2023. AAIC 3. Romano et al., 2023. CTAD
Quantitative *“How Much it Matters”*	• 274 PLWAD/care partners (50-65/Group)[4] • Rated 42 concepts of interest • Top 10 rated concepts of interest across all Groups mostly concerned emotional well-being	• Large & diverse sample: 600 PLWAD/care partners (~120 individuals & ≥ 50% people of color/Group)[5, 6] • WMM concept priority ranking, impacts; health economic analyses; construct validity • Subgroup analyses, differences by race and ethnicity	4. Hauber et al., 2023. Neurol Ther; 12:505-27 5. Romano et al., 2024. AAIC 6. Romano et al., 2025. AAIC
COA Technical Assessment *“Measuring What Matters”*	• Mapped 20 widely used COAs to the 42 WMM concepts of interest[7] • A number of concepts of importance to PLWAD Groups were represented in a limited number of COAs	• Updated COA mapping based on ranked priorities to follow ongoing research[5, 6]	7. DiBenedetti et al., 2023. Neurol Ther; 12:571-95 ◦ ***Work ongoing***

Additional Publication

Paulsen et al., 2025. Alzheimer’s Dement; 11:e70095

Increasing sample representation; importance rating to priority ranking; from concept to COA

Group 1: Individuals with unimpaired cognition per self-report who have evidence of AD pathology (similar to stage 1 in FDA Draft Guidance [2024][1])

Group 2: Individuals with MCI and evidence of AD pathology (similar to stage 2, stage 3, and early stage 4 in FDA Draft Guidance)

Group 3: Individuals with a diagnosis of mild AD (similar to stages 3-4 in FDA Draft Guidance)

Group 4: Care partners of individuals with a diagnosis of moderate AD (stage 5 in FDA Draft Guidance)

Group 5: Care partners of individuals with severe AD (stage 6 in FDA Draft Guidance)

AAIC = Alzheimer's Association International Conference; COA = clinical outcome assessment; CTAD = Clinical Trials on Alzheimer's Disease; MCI = mild cognitive impairment.

[1] US FDA. (2024).

WMM Phase 2 Quantitative Survey and Objectives

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- As part of the current phase of WMM research, a quantitative survey was strategically developed and administered among a large, diverse cohort of PLWAD and care partners across the full AD severity spectrum, aiming to:
  - Examine how cohorts prioritize among WMM concepts and conceptual model domains.
  - Assess the impacts of the lived experience of WMM concepts on daily life.
  - Evaluate selected psychometric properties of the conceptual model domains to inform a roadmap from WMM concept to COA.
  - **Conduct HRQOL analyses to inform future health economic evaluations for new AD treatments.**

- Prior HRQOL research in AD has investigated impacts across MCI and dementia severity levels, differences between self- and proxy-reported ratings, and impacts on care partners.
  - To date, limited studies have assessed HRQOL and utility values across the full spectrum of AD.[1]

HRQOL Analysis Objective:

To address an important data gap, estimates of HRQOL and health utility were assessed for PLWAD across the full spectrum of disease in AD.

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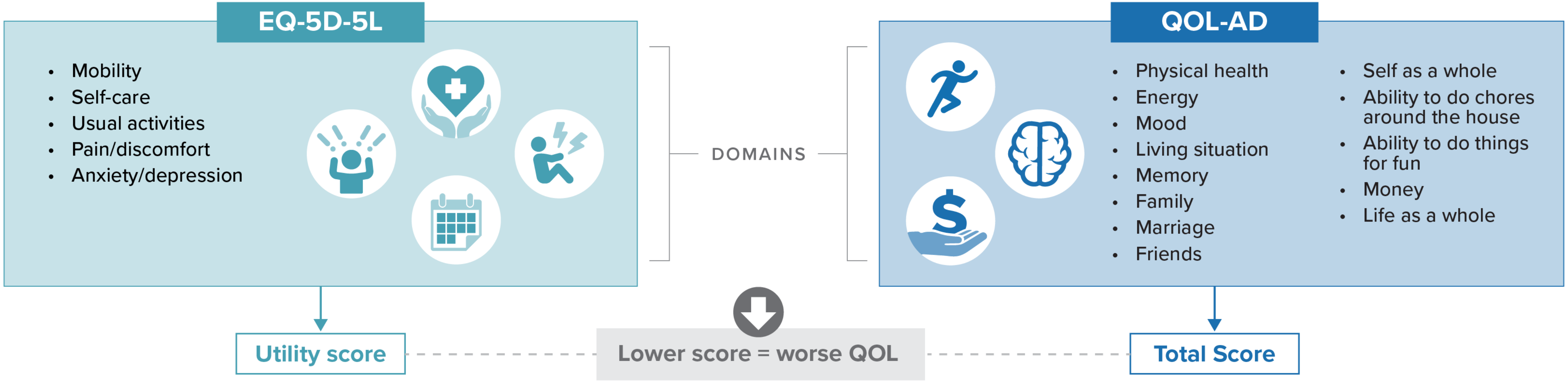
[1] Lin et al. (2025).

HRQOL and Health Utility were Estimated Using the EQ-5D-5L and QOL-AD

- **Quantitative survey participants:** Clinically confirmed PLWAD at risk or with up to mild AD (Groups 1-3) and care partners of individuals with clinically confirmed moderate or severe AD (Groups 4-5) in the US targeting equal participation and ≥ 50% people of color within and across groups.
- **Instruments**: The survey included generic (EQ-5D-5L)[1-3] and AD-specific (QOL-AD)[4] measures.



EQ-5D-5L

- Mobility
- Self-care
- Usual activities
- Pain/discomfort
- Anxiety/depression

DOMAINS

QOL-AD

- Physical health
- Energy
- Mood
- Living situation
- Memory
- Family
- Marriage
- Friends
- Self as a whole
- Ability to do chores around the house
- Ability to do things for fun
- Money
- Life as a whole

Utility score

Lower score = worse QOL

Total Score

- **Analysis**: EQ-5D-5L and QOL-AD scores were analyzed descriptively by group.
  - Regression analysis was used to test the significance of score differences across groups.

QOL = quality of life; QOL-AD = Quality of Life in AD; US = United States.

[1] EuroQol (1990); [2] Rabin et al. (2011); [3] Pickard et al. (2019); [4] Logsdon et al. (2002).

Study Population Characteristics

- A total of 640 participants from the US completed the survey:
  - 375 clinically confirmed PLWAD through mild AD
  - 265 care partners reporting on behalf of clinically confirmed PLWAD with moderate or severe AD
- Overall and within each AD Group, respondents represented diverse race and ethnicity, sex, age, and educational status groups.

PLWAD characteristics (N = 640)[a]	**Group 1 At risk/preclinical (n = 134)**	**Group 2 MCI (n = 120)**	**Group 3 Mild AD (n = 121)**	**Group 4 Moderate AD (n = 133)**	**Group 5 Severe AD (n = 132)**
Group description (survey respondents)	Individuals with unimpaired cognition per self-report with evidence of AD pathology	Individuals with MCI due to AD	Individuals with mild AD dementia	Care partners of individuals with moderate AD dementia	Care partners of individuals with severe AD dementia
Age, mean (SD)	58.5 (13.2)	61.1 (14.0)	65.8 (10.5)	78.0 (8.2)	76.6 (8.8)
Sex assigned at birth, n (%)					
Female	79 (59.0)	66 (55.0)	63 (52.1)	76 (57.1)	71 (53.8)
Male	55 (41.0)	53 (44.2)	58 (47.9)	55 (41.4)	59 (44.7)
Intersex	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)
Race or ethnicity,[b] n (%)					
African American or Black	41 (30.6)	46 (38.3)	48 (39.7)	46 (34.6)	42 (31.8)
Alaska Native, American Indian, or Native American	4 (3.0)	3 (2.5)	2 (1.7)	4 (3.0)	1 (0.8)
Asian or Asian American	6 (4.5)	7 (5.8)	0 (0.0)	4 (3.0)	8 (6.1)
Hispanic, Latina/o, Latine, or Latinx	32 (23.9)	26 (21.7)	27 (22.3)	22 (16.5)	26 (19.7)
Middle Eastern and/or North African	0 (0.0)	1 (0.8)	2 (1.7)	0 (0.0)	1 (0.8)
Native Hawaiian or Pacific Islander	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
White	55 (41.0)	40 (33.3)	48 (39.7)	62 (46.6)	57 (43.2)
A race or ethnicity not listed	1 (0.7)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Highest grade or level of education,[c] n (%)					
High school diploma or equivalent (e.g., GED)	15 (11.2)	12 (10.0)	23 (19.0)	52 (39.1)	48 (36.4)
Associate’s degree/technical school	11 (8.2)	10 (8.3)	9 (7.4)	16 (12.0)	18 (13.6)
Some college	30 (22.4)	28 (23.3)	31 (25.6)	17 (12.8)	30 (22.7)
College degree (e.g., BA, BS)	35 (26.1)	37 (30.8)	36 (29.8)	23 (17.3)	13 (9.8)
Graduate or professional degree (e.g., MS, MD, PhD, JD)	33 (24.6)	27 (22.5)	13 (10.7)	14 (10.5)	8 (6.1)

SD = standard deviation.

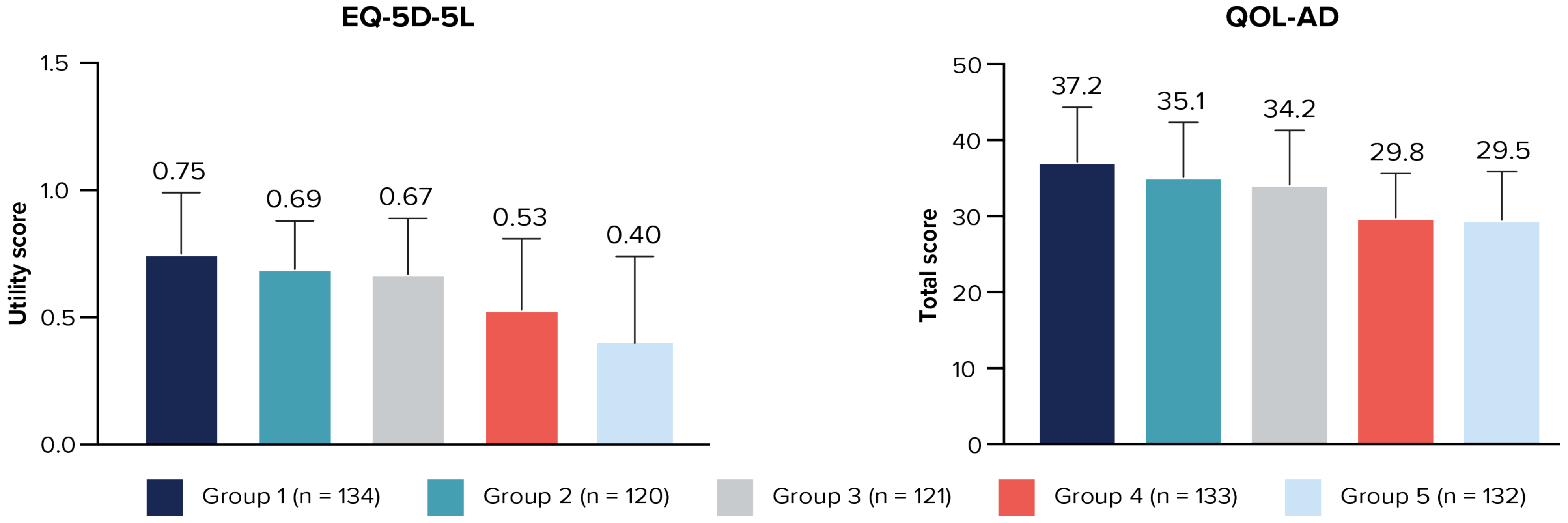
Note: “Missing” or “prefer not to answer” not reported; responses may not add to 100%.

[a] Groups 4 and 5: PLWAD characteristics as reported by care partners.

[b] Respondents could select all that apply; responses may exceed 100%.

[c] Responses reported by ≥ 5% of at least 1 group are shown.

EQ-5D-5L utility scores and QOL-AD total scores indicate that HRQOL impacts increase with severity across groups

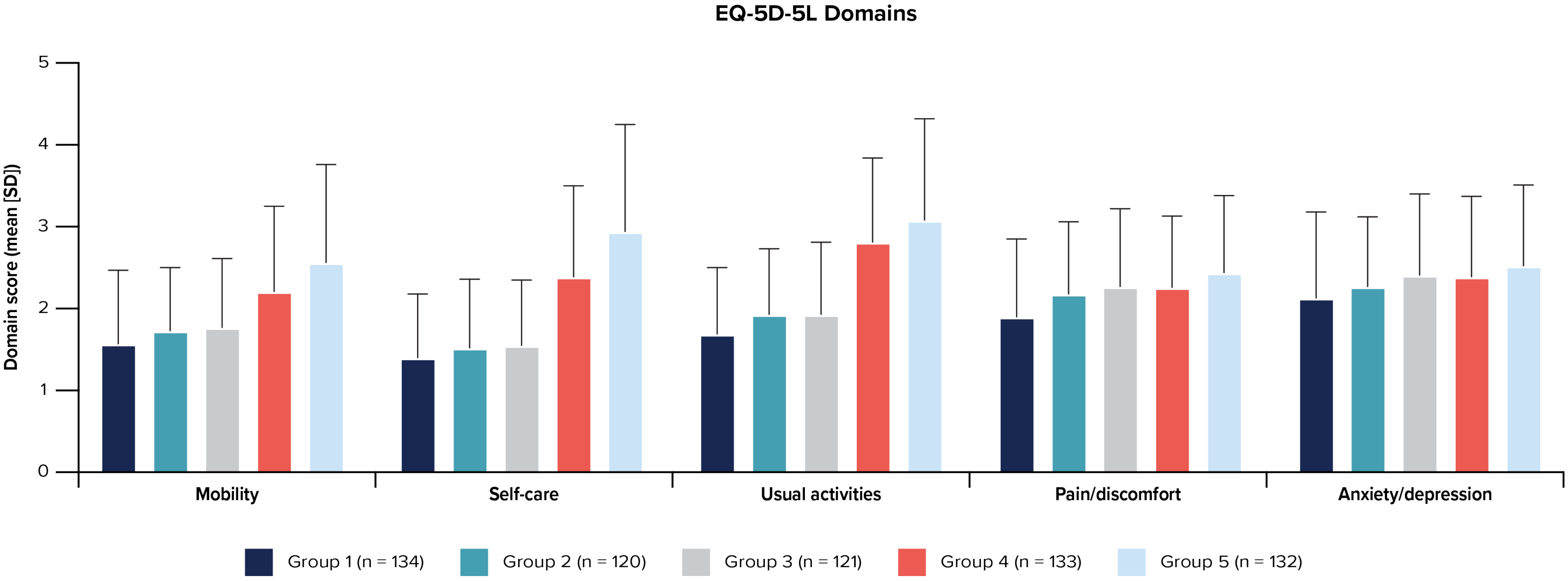


EQ-5D-5L and QOL-AD scores for those at risk, with MCI, and with mild AD were **significantly higher** (**reflecting better HRQOL**; *P* < 0.001) than for those with moderate and severe AD.

EQ-5D-5L utility scores estimated from domains using the US value set (Pickard et al., 2019) with lower scores representing worse quality of life (range, -0.573 to 1). Regression analyses controlled for age, sex, and race.

QOL-AD total scores derived from sum of 13 domain item scores (range, 13-52) with lower scores representing worse HRQOL.

EQ-5D-5L domain scores indicate greater impacts with increasing disease severity for each domain



EQ-5D-5L domains scored with 5 ordinal response categories (1 = no problems; 5 = extreme problems), with higher scores representing greater severity.

QOL-AD domain scores similarly indicate increasing impact with increasing disease severity for each domain

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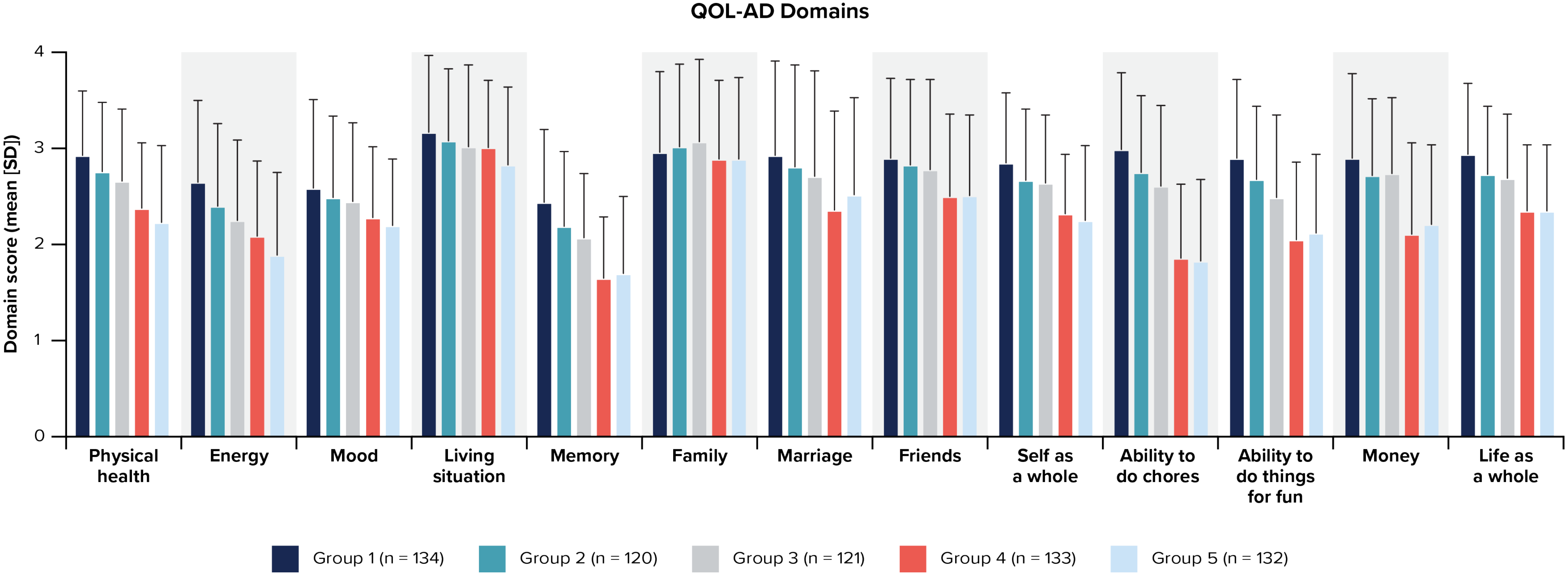
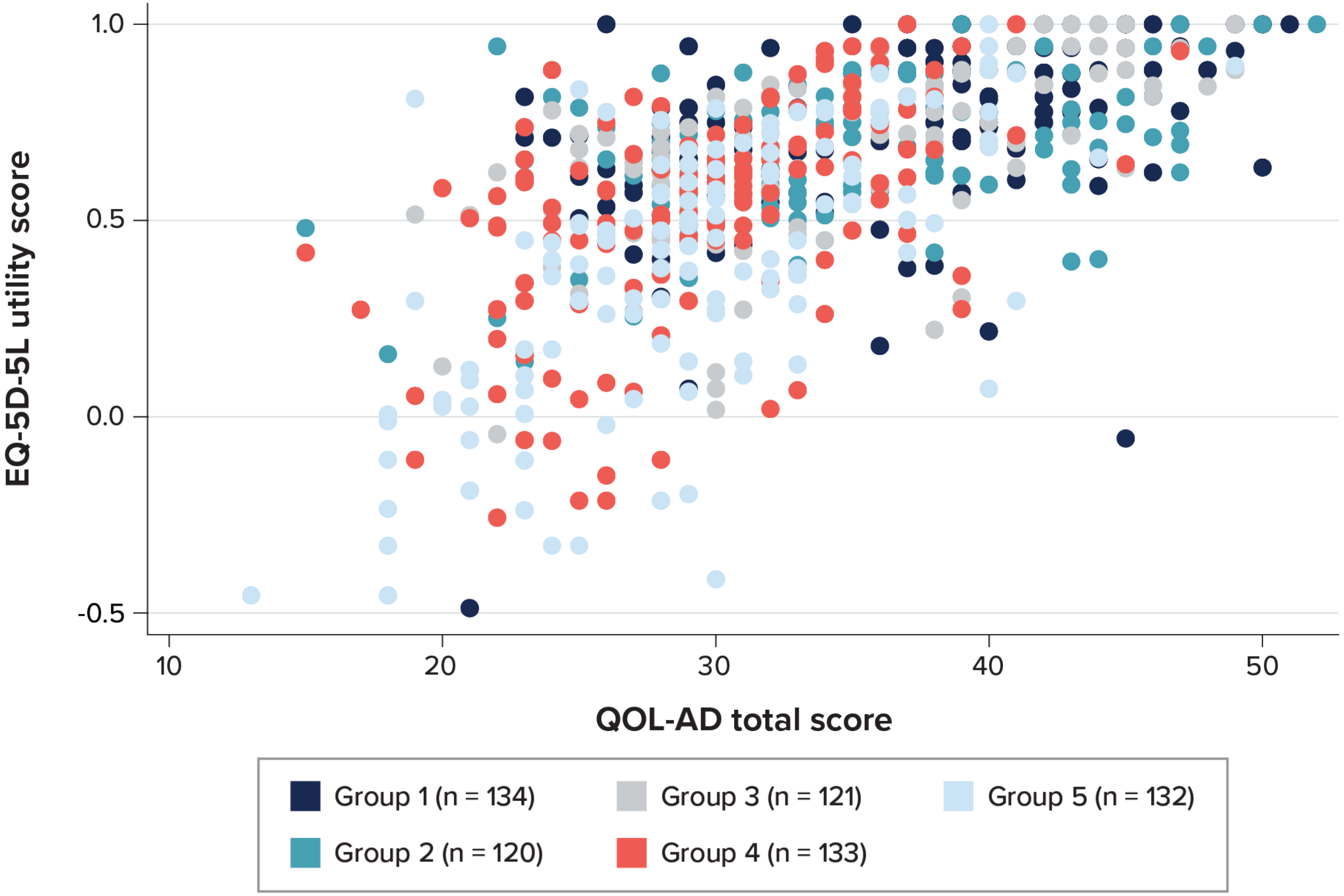


QOL-AD domains scored with 4 ordinal response categories (1 = poor; 4 = excellent), with lower scores representing worse HRQOL.

EQ-5D-5L utility score was moderately positively correlated with QOL-AD total score



Population	Correlation coefficient **P* < 0.001
Total sample	0.629*
Group 1	0.492*
Group 2	0.508*
Group 3	0.653*
Group 4	0.544*
Group 5	0.660*

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This study provides evidence across the full AD severity spectrum that HRQOL consistently worsens on generic and AD-specific domains as severity increases

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EQ-5D-5L and QOL-AD scores indicated directionally within each domain that HRQOL impacts increase with severity across groups

- Scores suggesting greater HRQOL impacts were reported by care partners (Groups 4 and 5) than by PLWAD (Groups 1 through 3).
  - Differences were in domains where it may be expected for proxy reporters (care partners) to indicate greater impacts (i.e., Mobility, Self-Care, Usual Activities).
  - A published meta-analysis[1] found that self-rated utility scores were generally higher than proxy-rated utility scores, particularly in more advanced disease stages.
  - Score differences between care partners and PLWAD also reflect increasing disease severity, and as such should be interpreted carefully.
- Overall, the EQ-5D utility scores across groups in the current study are lower than comparable estimates found in other studies,[1-3] particularly in less severe disease stages.
  - Differences from other published analyses[3] may be partly attributable to intentional oversampling of select subgroups in the current study.

Future directions

These results provide evidence of fundamental differences in the lived experience of AD across Groups and can be used in future economic evaluations of new AD treatments.

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[1] Landeiro et al. (2020); [2] Aye et al. (2023); [3] Lin et al. (2025).

Thank You
Questions?

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