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PERSPECTIVE

Meaningful to whom? Minimal clinically important differences and the priorities of individuals living with dementia for everyday function

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Abstract

Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD) have a significant impact on an individual's functional cognitive abilities, highlighting the need to prioritize measures of function in evaluating minimally clinically important difference (MCID) thresholds in AD/ADRD research. Input directly from individuals living with AD/ADRD on measures of function are lacking in MCID discussions, including what it means to live with AD/ADRD and what type and degree of improvements are most meaningful across the disease continuum. Most measures for assessing function in AD/ADRD trials are largely focused on basic and instrumental activities of daily living (BADL, IADL), which lack aspects of everyday function that matter most to individuals living with AD/ADRD. Expanding outcome evaluation to other dimensions of everyday function and diversifying measurement approaches is essential for optimizing inclusion of personally meaningful aspects of everyday function prioritized by individuals living with AD/ADRD and improving detection of potentially more sensitive changes in functioning. This perspective outlines four directions to expand and integrate what matters most to individuals living with AD/ADRD into trial outcome evaluation, including (1) consideration of how what matters most to individuals living with AD/ADRD may change across the disease continuum from mild to advanced dementia, (2) identification and evaluation of goals around strengths-based domains such as social participation rather than solely emphasizing deficits and losses, (3) utilization of goal-attainment scaling to more specifically match individually-specific functional goals, and (4) strengthening the inclusion and use of self-report and performance-based measures of function and triangulating these measures with informant-report measures.

KEYWORDS
dementia, detection, disease continuum, everyday function, minimally clinically important difference

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Highlights

- Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD) have a significant impact on an individual' functional cognitive abilities, of which changes in these abilities are measured through detection of minimally clinically important difference (MCID) thresholds to determine the effectiveness of AD/ADRD clinical trials.
- Widely used measures for assessing MCID thresholds in AD/ADRD trials focus on basic and instrumental activities of daily living, presenting opportunities to expand measurement of MCID to account for other dimensions of everyday function that are prioritized by individuals living with AD/ADRD.
- To expand outcome evaluation and improve integration of aspects of functioning that matter most to people living with AD/ADRD, we identify opportunities to incorporate more diverse strategies via goal-attainment scaling, self-report, and performance-based measures as appropriate. We also highlight the importance of incorporating strengths-based domains such as social participation, moving beyond deficit-focused assessment of functioning.

The significant impact Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD) have on an individual's functional cognitive abilities underly the high costs, burden, and societal impact of these conditions—highlighting the need to prioritize measures of function in evaluating clinically meaningful outcomes in AD/ADRD research, particularly for longitudinal cognitive aging studies and AD/ADRD clinical trials.[1,2] Clinically meaningful outcomes are often considered through the detection of minimal clinically important difference (MCID) thresholds, traditionally defined as the smallest unit of change in an outcome measure that is clinically meaningful for patients.[3] The concept of MCID thresholds began as a way to overcome the shortcomings of relying on statistically significant differences to evaluate clinical trial outcomes, as a change in an outcome measure may be statistically significant yet not make a meaningful difference in the health or quality of life of the patient.[4,5] MCIDs in AD-focused research have largely focused on cognitive measures, omitting other salient aspects of daily functioning that may be more aligned to patient and caregiver priorities including emotional well-being and quality of life.

As there is currently no consensus on MCID thresholds for outcomes in AD/ADRD trials, there remains active debate around what is clinically meaningful for people living with AD/ADRD.[6–8] Disease progression in AD/ADRD is highly heterogenous, making it challenging to create a universal MCID threshold for AD/ADRD trials.[7] Despite the importance of personal relevance to the designation of what is clinically meaningful—discussions on MCID thresholds have rarely included direct input from individuals living with AD/ADRD, who have diverse perspectives on what living with AD/ADRD means and what type and degree of improvements are most meaningful.[4] There remains an important opportunity to better integrate the priorities of individuals living with AD/ADRD into MCIDs that are relevant to their everyday function.

Widely used measures for assessing function in AD/ADRD trials have been relatively limited and largely focused on basic and instrumental activities of daily living (BADL, IADL, respectively).[6] While highly useful for interpreting the level of independence in everyday functioning, commonly used BADL/IADL instruments arguably represent a narrow set of dimensions salient to function broadly and lack aspects of everyday function that are prioritized by individuals living with AD/ADRD.[6,9] Everyday function is multidimensional, spanning physical, emotional, psychological, and social domains reflecting independence *and* capacity for engagement and social participation.[10] As a result of the significant progress in the inclusion of perspectives and lived experiences from individuals living with AD/ADRD in research, findings from recent qualitative studies demonstrate that there are common priorities reflective of everyday functioning, including (1) finding meaning and enjoyment in activities, (2) having autonomy/independence, (3) connecting with self and identity, (4) connecting with others and having a sense of belonging, and (5) managing and adapting to changes over time.[11–13] Across these domains, participants frequently emphasize values of enjoyment, fulfillment, connection, belonging, autonomy, and identity.[11,13] The meaningfulness of changes in ability to participate in these activities may lie within the value ascribed to them, rather than within the activity itself—suggesting individualized outcome assessment may be a useful strategy to facilitate detection of MCID in everyday function.

In addition to integrating the individualized values of people living with AD/ADRD into MCID detection, dementia-specific measures such as the quality of life in AD (QOL-AD) and EuroQuol 5-dimension (EQ-5D) can further complement functional assessments and shed light on dimensions that are not well addressed in standard BADL/IADL measures.[14,15] Respectively, these measures address quality-of-life and self-reported health asking questions such as "How do you feel about your physical health?" and "How do you feel about yourself?" As with the BADL/IADL measures, it is still important to consider the meaningfulness people living with AD/ADRD attribute to these measures, as their importance may change across individuals and as the disease progresses.

Across multiple studies, individuals with AD/ADRD have highlighted the importance of valuing adaptations/accommodations by reflecting a strengths-based perspective rather than emphasizing deficits and losses.[16–19] Occupational therapists have developed performance-based assessments designed to identify residual strengths that form the basis of interventions for the individual or care partner directed at maximizing functional independence.[20,21] These interventions, when coupled with engagement in the activities most meaningful to the individual with AD/ADRD, have been associated with maintenance of self-care skills and reductions in behavioral symptoms. Individuals living with AD/ADRD identify strengths-based priorities relating to retaining identity and life satisfaction through meaningful activities and emphasize the critical roles of community engagement in realizing this value.[22–24] Attention to how individual preferences and cultural values shape goals around strengths-based domains such as social participation will be essential to ensuring measures are sufficiently holistic and appropriate across diverse socio-cultural backgrounds.

Along with integrating strengths-based approaches to measuring MCID in everyday function, a broad continuum of values and priorities meaningful to the lived experience of AD/ADRD must be considered for outcome measures. A useful framework for expanding current foci is the Geriatric 5Ms framework, which addresses mind, mobility, medications, multi-complexity, and "matters most"—which is designed to directly address and facilitate attention toward the heterogeneity of what individuals determine is most meaningful.[25] This is particularly important considering the well-documented variability in the rate of functional decline with BADL/IADL-based assessments given the heterogenous and individualized nature of progression in AD/ADRD.[26,27] These trajectories demonstrate that decline in BADL/IADL function progressively accelerates across subsequent disease stages, illustrating differences between MCID in the earliest and more advanced stages of disease.[28] Variable trajectories may also shape specific/individual MCID. For example, an individual experiencing slower cognitive decline may experience greater opportunities for social participation than an individual experiencing rapid decline. As a result, the stage at which they prioritize social or psychological dimensions of everyday functioning, and the degree of improvement that may be experienced as clinically meaningful, is likely individualized and distinct from what may constitute a MCID for someone with more advanced disease. Although beyond the scope of this article, it is important to note that preclinical stages of AD/ADRD can also be heterogenous and individualized, creating differences in what is considered to be MCID in everyday functioning as it relates to individuals' priorities and values. The process of narrowing an array of goals to a select few, such as prioritization of social or psychological dimensions of everyday functioning, is well-described by the Baltes' metamodel of selective optimization with compensation (SOC).[29] This model has been used to study adaptive aging and can be applied to describe clinical meaningfulness of optimized performance in social participation through compensatory strategies to maintain social and psychological function across the disease continuum.[29]

Goal attainment scaling is another approach that can be used to facilitate detection of MCID in everyday function, an intervention method that can be used to monitor incremental progress towards larger goals over time rooted in one's strengths.[30] This approach could be particularly valuable for measuring strengths-based domains, such as social participation, where optimal outcomes can be specified in target goals and measured, and where even small improvements could have a substantial perceived/experiential impact on everyday life, particularly in advanced disease.[18] Even in the setting of substantial decline in BADLs/IADLs, individuals may still be able to enjoy and actively contribute to community-based activities with their family and peers, which is meaningful to them and important to their sense of identity and belonging.[13] While these domains (feeling valued, maintaining identity, sense of belonging) are not well reflected in BADL/IADL-based assessments, they may provide valuable insight into MCID in everyday function and can potentially be measured via goal scaling, presenting opportunities to improve the sensitivity of outcome evaluation in AD/ADRD trials.

Another opportunity to advance measurement of MCID for everyday function is to broaden measurement strategies, including strengthening the inclusion of participant self-report wherever feasible, particularly as study participants with AD/ADRD frequently lack the opportunity to contribute their own input to outcome evaluation.[4] Although many individuals with AD/ADRD can provide valuable data via self-report in early and early/moderate disease stages, a recent review of assessment tools demonstrates that most commonly used measures applied across the disease continuum are informant-based.[28] Thresholds at which a change in BADL/IADL performance is determined to be meaningful are often determined from the perspectives of caregivers of people living with AD/ADRD and clinicians.[31] Individuals with mild cognitive impairment (MCI)/early-stage AD/ADRD have been found to have accurate self-reports of function as compared to complementing informant-reports; however, the discrepancy between self- and informant-reports becomes greater as the disease progresses.[32,33] Advances in the inclusion and engagement of individuals with AD/ADRD in research overwhelmingly demonstrate that it is feasible to elicit their perspective, priorities, and goals of care beyond early disease stages.[34,35] One such strategy is convening a "lived experienced panel" to help guide research progress, including measurement priorities.[36]

Performance-based measures are also under-utilized, and can aid in eliciting MCID by obtaining an objective assessment of an individual "doing" a task or activity in specific contexts without relying on subjective perceptions.[37] Performance-based measures demonstrate a weak to moderate association with traditional neurocognitive assessments and self-reported functional cognition measures,[38,39] indicating that they provide different information and can complement rather than substitute each other.[40] Common performance-based assessments of functional cognition include Actual Reality (AR),[41] the Complex Task Performance Assessment (CTPA),[42] the Executive Functional Performance Test-Enhanced (EFPT-E),[43] Menu Task,[44] and the Weekly Calendar Planning Activity (WCPA).[45] Each of these measures include metacognitive questions, which assess the individual's evaluation of their performance, thus providing opportunities to ascertain the accuracy of self-reported function.[46] Integrating multiple measurement strategies, including self- and informant-reports and performance-based measures across stages, presents valuable opportunities to triangulate data across multiple sources and detect more subtle changes in functioning.[31,47]

We acknowledge that personalizing assessments by clinical stage of AD/ADRD and individual goals is practically challenging. Long-term tracking of personalized outcome measures is resource-intensive and difficult to maintain and requires a high degree of training for clinical trial staff to have a deep understanding of AD/ADRD. Successful personalization of AD/ADRD trial outcomes will require interdisciplinary collaboration between clinicians, researchers, policymakers, and educators to address these methodological challenges.

Existing frameworks such as the Patient-Reported Outcomes Measurement Information System (PROMIS) and International Classification of Functioning, Disability, and Health (ICF) can serve as a starting point for bridging these gaps.[48,49] PROMIS offers a flexible and dynamic approach to measuring health outcomes, including those relevant to people living with AD/ADRD, by including a wide range of patient-reported outcome measures that assess domains such as physical function, cognitive function, pain, fatigue, emotional well-being, and social participation. Importantly, PROMIS measures can be tailored to focus on specific aspects of AD/ADRD that vary across individuals rather than relying on generic measures that may miss key nuances in disease progression.

Expanding AD/ADRD trial outcome evaluation to other dimensions of everyday function and diversifying measurement approaches may offer valuable strategies for optimizing inclusion of meaningful aspects of everyday function prioritized by individuals living with AD/ADRD and improving detection of potentially more sensitive changes in functioning. There remain unmet opportunities to integrate priorities identified by individuals living with AD/ADRD to expand the repertoire of MCID outcomes for trial evaluation. Utilizing a strengths-based approach to measurement may better align with the values of individuals living with AD/ADRD, particularly in more advanced disease stages. It may also be useful to consider the role of behavioral symptoms (i.e., neuropsychiatric symptoms) and their management as these symptoms exert a substantial influence on daily activities which compound as the disease advances.[50] Many measures of functioning emphasize deficits, which serve an important value in understanding change and decline; however, this negates assessment of maintenance of other strengths and abilities that are valued among individuals living with AD/ADRD and may better reflect their lived experience.

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CONFLICT OF INTEREST STATEMENT

None declared. Author disclosures are available in the Supporting information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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