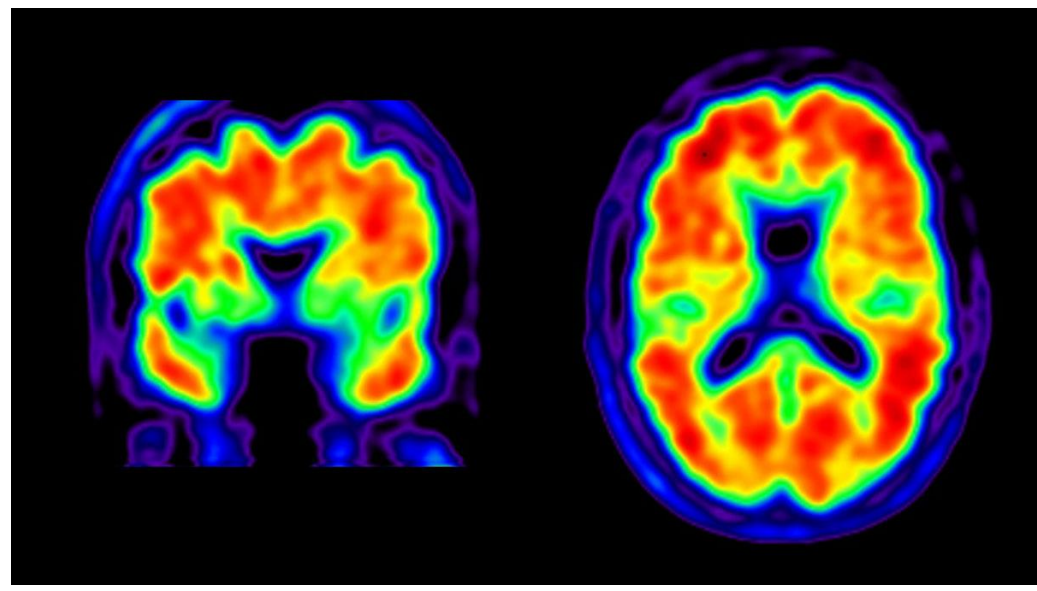


A Delphi Consensus Study on Cognitive Decline in Preclinical Alzheimer’s

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Introduction

Problem: Objective cognitive decline in Stage 2 of the Alzheimer’s continuum is not well defined



Stage 1: Cognitively normal
Stage 2: ?
Stage 3: Mild cognitive impairment

Research questions:

- What is the most appropriate term to describe objectively identified cognitive decline that does not rise to impairment?
- How can “objective subtle cognitive decline” be operationalized for clinical trials?

Method

Delphi consensus study:

Survey Round 1:

-Read Thomas & Edmonds (2025) systematic review
-16 terms reviewed
-11 operational approaches reviewed

Survey Round 2:

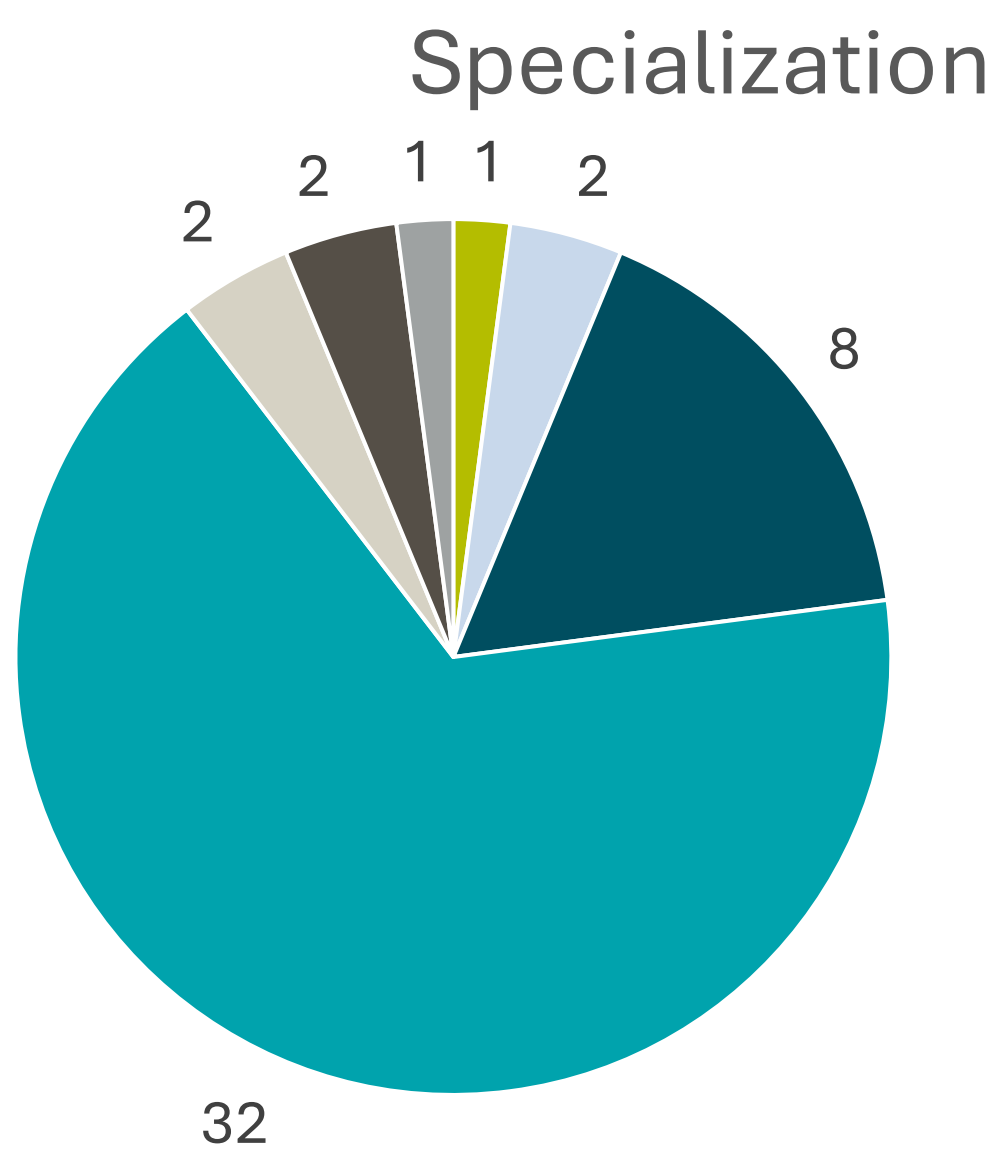
-Review summaries of Round 1 responses
-4 terms reviewed
-10 operational approaches reviewed

Survey Round 3:

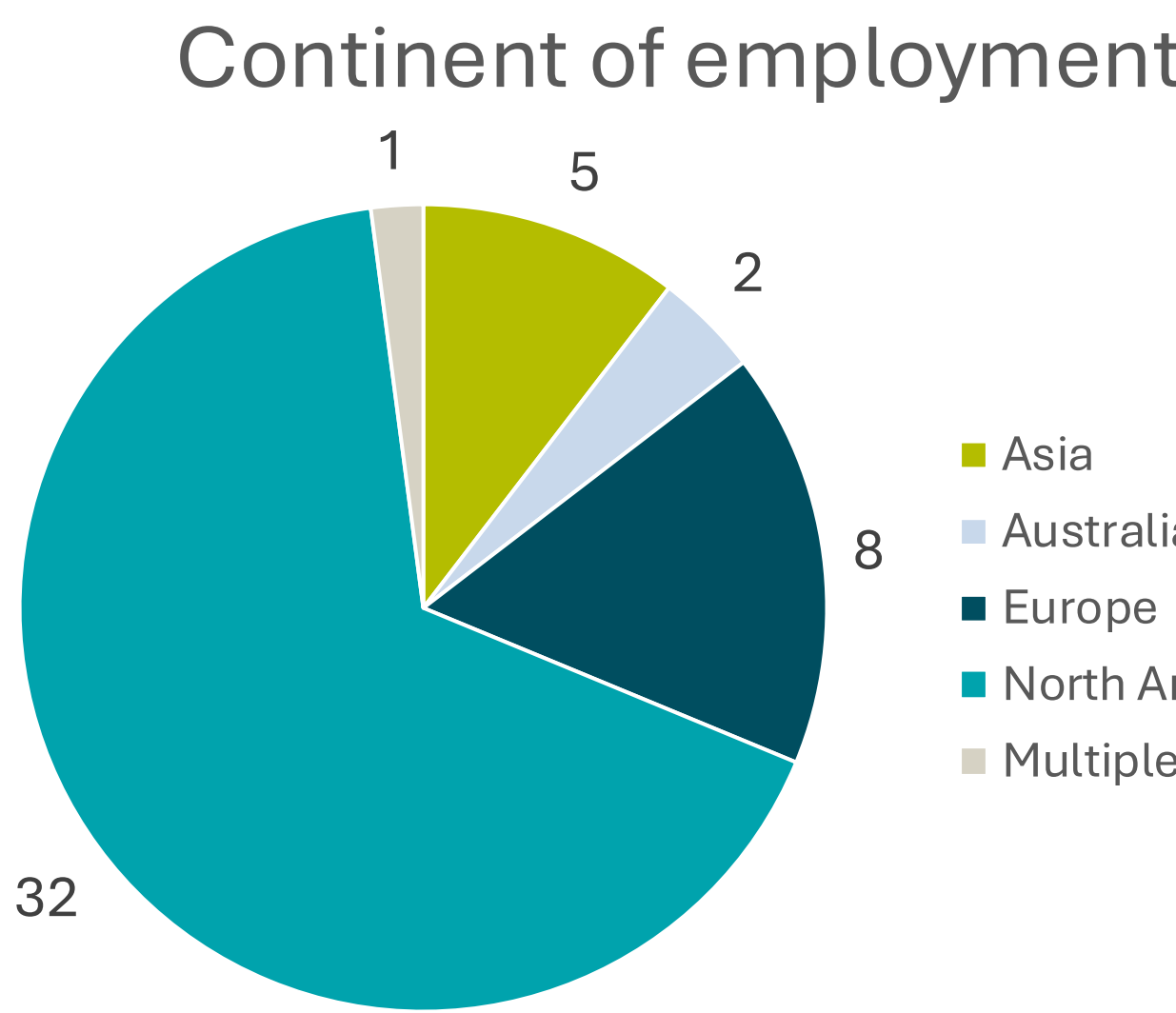
-Review summaries of Round 2 responses
-3 terms reviewed
-Abbreviations for each term reviewed
-9 operational approaches reviewed

Expert panelist invitations:

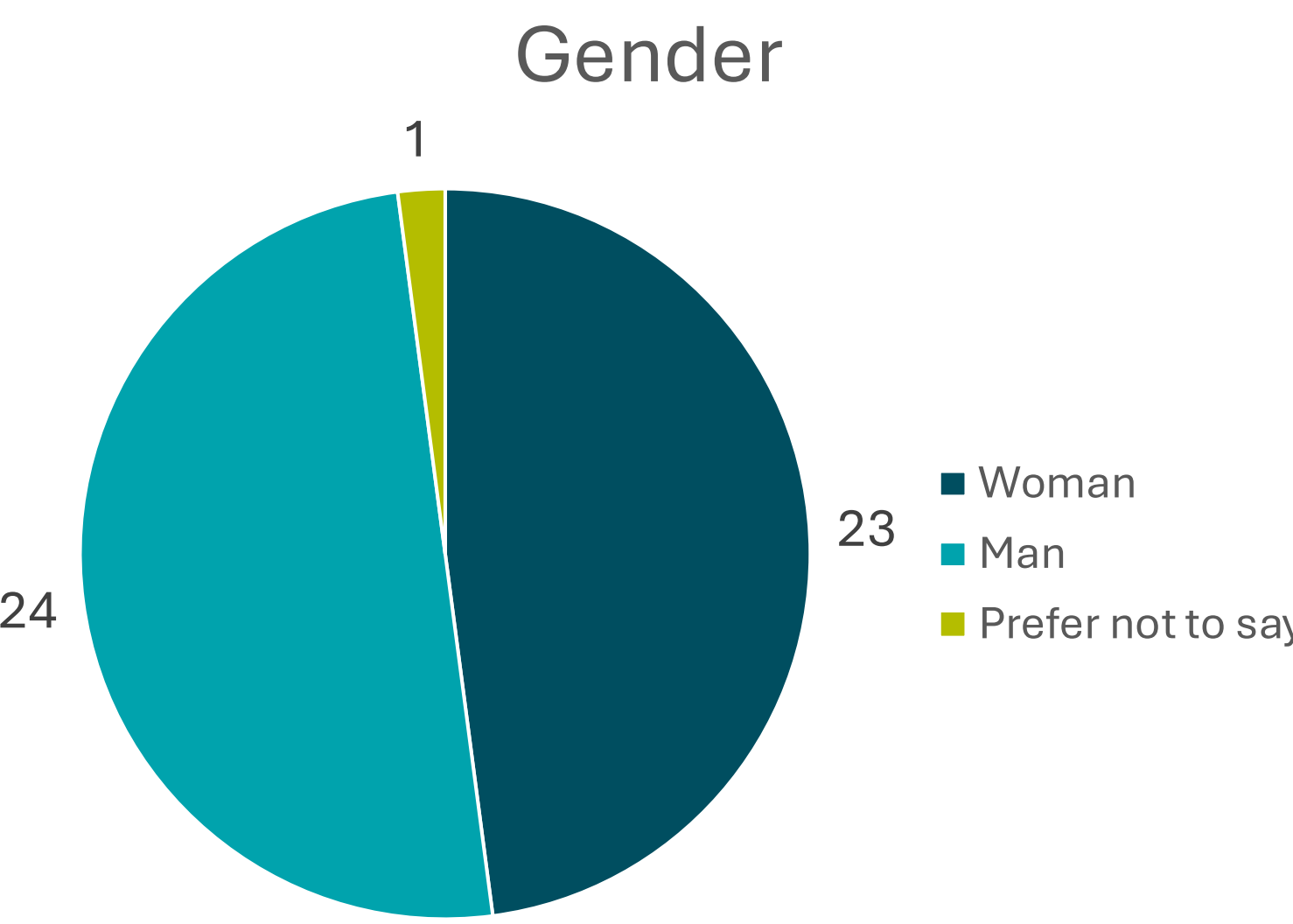
Number invited = 102
Number accepted = 61 (59.8%)
Responded to each round = 52 (85.3%)



Geropsychology
Neuroradiology
Neurology
Neuropsychology
Neuroscience
Psychiatry
Statistics



Round 1 Variable	M (SD)	Range
Age	51.48 (12.64)	27-74
Years experience: AD	20.81 (9.87)	4-40
AD = Alzheimer’s disease		

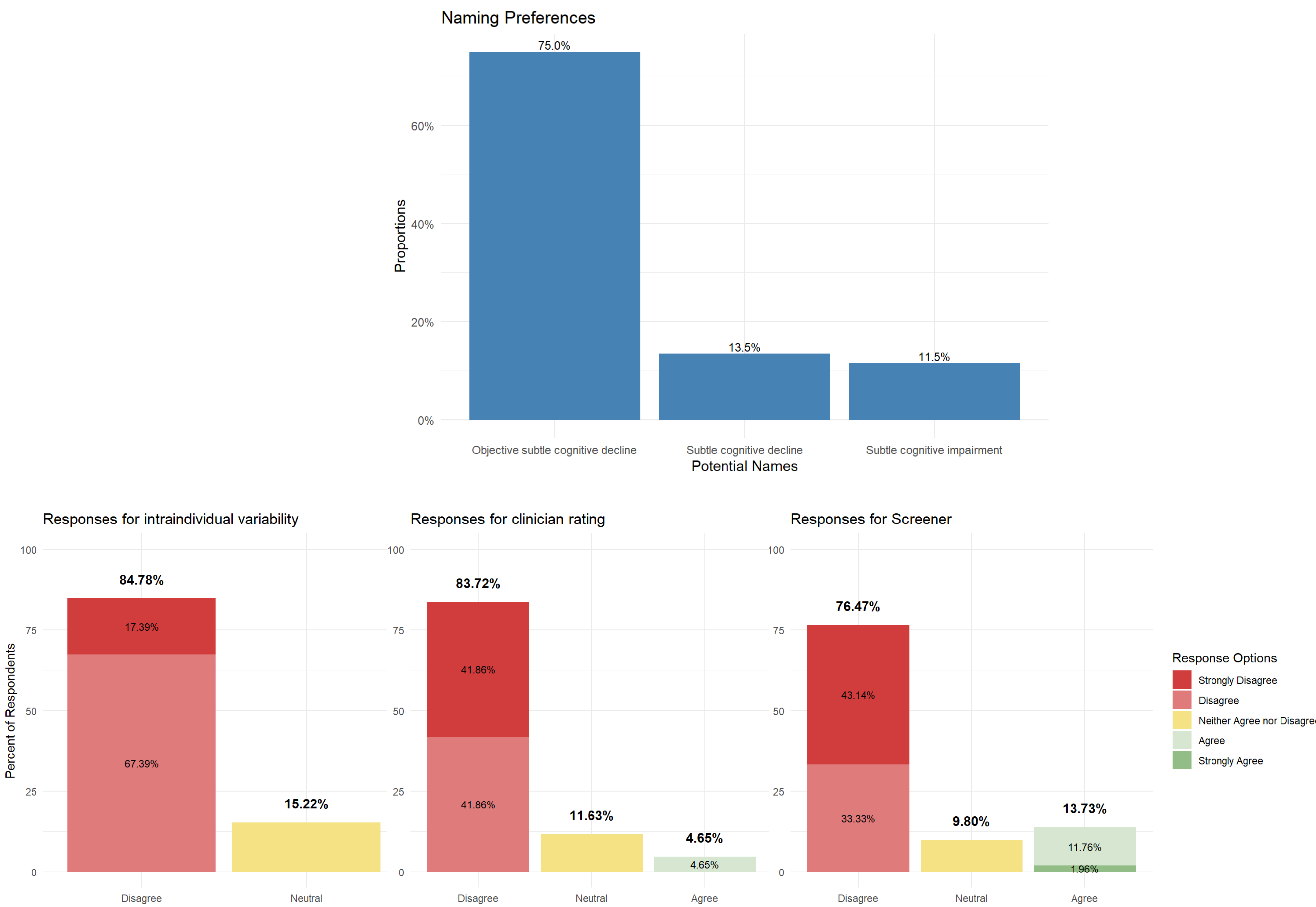


Gender

Woman
Man
Prefer not to say

Results

Consensus Recommendations:



Preliminary Guidance:

The pattern of low scores approach has the best balance between practicality and rigor.

“This method can be applied seamlessly while offering better reliability”

Serial assessment methods using reliable change approaches are the most scientifically rigorous.

“Despite the practical issues, it is a psychometrically sound and empirically supported approach.”

Combining multiple approaches for Obj-SCD could be superior to using one approach to define the construct.

“The combination of different potential indicators...rather than any single one...will lead to greater stability/accuracy.”

Future Directions

- Head-to-head comparisons of operational approaches
- Integration of objective subtle cognitive decline with other Stage 2 symptoms (e.g., subjective cognitive decline)
- Investigations of how operational approaches impact clinical trial sample characteristics