

Enrolling participants in preclinical AD trials in a non-primary language

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Background

Preclinical Alzheimer's disease (AD) trials rely on cognitive screening to determine participant eligibility. These criteria assume fluency in the testing language, primarily English at US sites. However, individuals tested in a non-primary language may score below impairment thresholds despite being cognitively unimpaired. This effect may lead to misclassification and exclusion, where participants are incorrectly deemed ineligible based on language-related testing rather than true cognitive impairment.

Such exclusions may reduce sample diversity, limit generalizability of findings, and slow recruitment and trial efficiency. Understanding how testing language influences preclinical AD trial eligibility is critical to designing more inclusive and effective trials.

Objectives

- To evaluate whether testing in a non-primary language is associated with decreased likelihood of meeting cognitive eligibility criteria among cognitively unimpaired individuals
- To compare eligibility rates across cognitive measures by testing language group
- To quantify the association between primary language status and odds of trial ineligibility after adjusting for demographic factors

Study Sample

We analyzed clinical and cognitive data from participants in the UCI ADRC UDSv3 with a consensus diagnosis of cognitively unimpaired. Primary language status was determined using the Language Profile Survey.

- N = 153 participants
- English as a primary language: n = 109 (71.2%)
- English as a non-primary language: n = 44 (28.8%)

Methods

Participants were classified as trial eligible or ineligible based on commonly used preclinical AD screening measures, or similar tools, and cutoff scores:

- Clinical Dementia Rating (CDR): Eligible score = 0
- Mini-Mental State Examination (MMSE): Eligible score ≥ 27
- Craft Story Recall- Delayed Paraphrase (CSR-D): Eligible score ≥ 6

Statistical analyses include descriptive comparisons of eligibility by language group, chi-square test for unadjusted group differences, and logistic regression models estimating odds of ineligibility adjusted for age, sex, and education.

Results

Figure 1: % Eligibility by Language Status (Unadjusted)

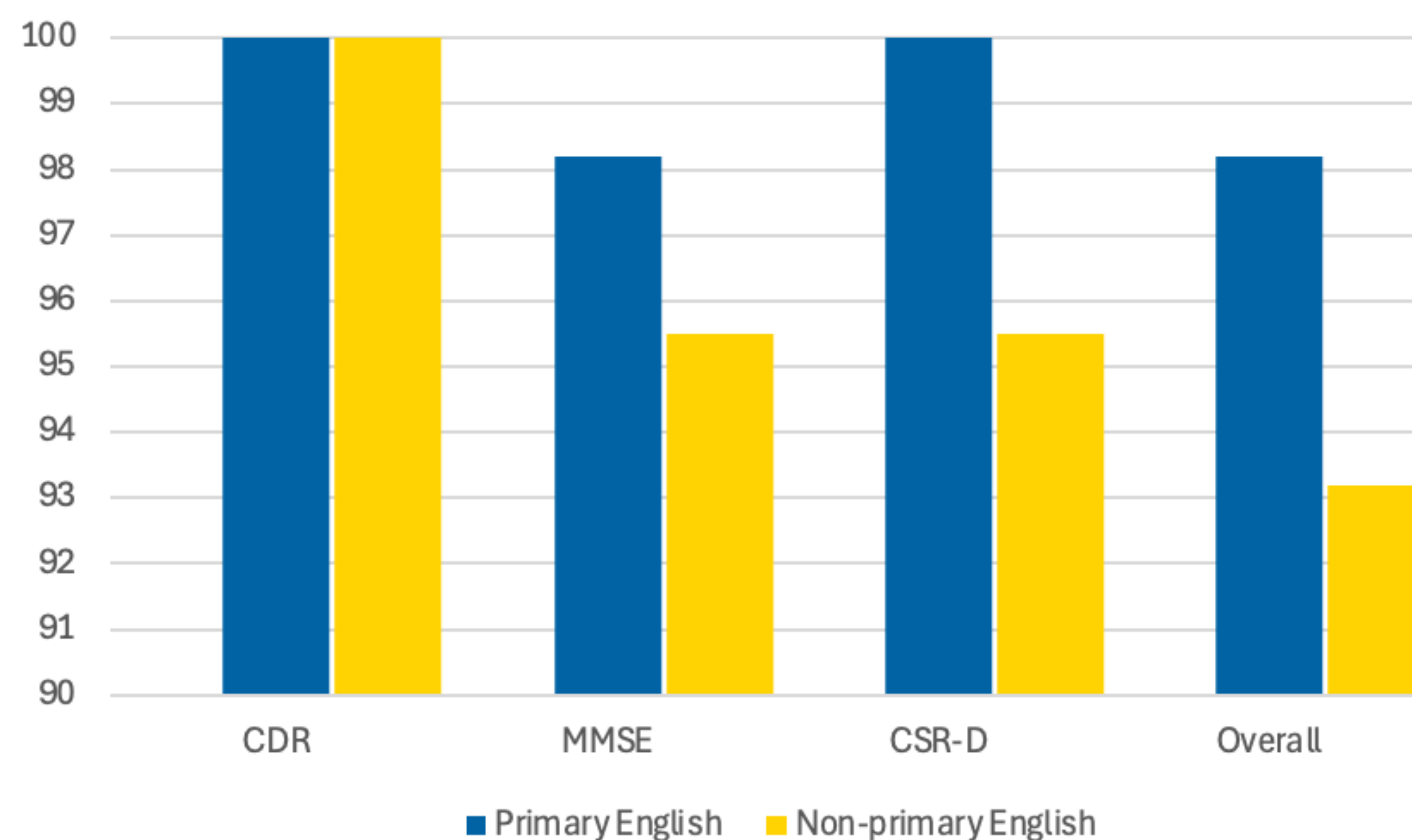


Table 1: Participant Demographics

Cohort characteristics	English as a primary language N= 109	English as a non-primary language N= 44	Total N= 153
Age, mean (SD)	71.4 (6.30)	69.1 (6.40)	70.8 (6.40)
Sex, n (%)			
Female	67 (61.47)	31 (70.45)	98 (64.05)
Race, n (%)			
American Indian or Alaska Native	1 (0.92)	1 (2.27)	2 (1.31)
Asian	9 (8.26)	37 (84.09)	46 (30.07)
Black or African American	2 (1.83)	0 (0.00)	2 (1.31)
Non-Hispanic White	97 (88.99)	6 (13.64)	103 (67.32)
Ethnicity, n (%)			
Hispanic/Latino	11 (10.09)	4 (9.09)	15 (9.80)
Education, n (%)			
High school or less	5 (4.59)	1 (2.27)	6 (3.92)
College or equivalent	49 (44.95)	21 (47.73)	70 (45.75)
Graduate school or equivalent	55 (50.46)	22 (50.00)	77 (50.33)
APOE ε4 status, n (%)			
Non carrier	69 (63.30)	33 (75.00)	102 (66.67)
Heterozygous	30 (27.52)	6 (13.64)	36 (23.53)
Homozygous	7 (6.42)	0 (0.00)	7 (4.58)
Missing genotype	3 (2.75)	5 (11.36)	8 (5.23)

Results (cont.)

Table 2: Adjusted Analysis of Cognitive Screening Ineligibility

Outcome	Predictor	Adjusted OR (95% CI), p-value
MMSE	English as a primary language (ref: English as a non-primary language)	0.45 (0.06-3.37), 0.43
	Age (per year)	0.95 (0.80-1.12), 0.52
MMSE	Education (per year)	0.85 (0.60-1.22), 0.39
CSR-D	English as a primary language (ref: English as a non-primary language)	0.21 (0.00-2.63), 0.22
	Age (per year)	1.00 (0.80-1.22), 0.98
CSR-D	Education (per year)	0.93 (0.62-1.61), 0.75

- Logistic regression modeled cognitive screening ineligibility. Odds ratios <1 indicate lower odds of ineligibility.

Conclusion

- Unadjusted analyses suggested nominally lower eligibility among participants tested in English as a non-primary language overall and for the MMSE and CSR-D.
- In adjusted analyses, however, we did not observe independent associations between non-primary language status and cognitive screening ineligibility.
- The modest sample size and high English proficiency of the non-primary language group are key limitations. These findings may underestimate language-related differences that could be observed in populations with lower English proficiency.
- Future work will extend these analyses to longitudinal clinical and cognitive data to evaluate whether rates of cognitive change over time differ by language status.
- Incorporation of biomarker eligibility will be key to understanding the direct implications to preclinical AD trials.

Acknowledgements

The UCI ADRC is funded by NIA grant P30 AG066519

We would like to thank our ADRC participants for their time and contributions.