

Comparing longitudinal trajectories of Storyteller and CDR-SB: Initial data from ADNI4

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- Storyteller showed significant differences in cognitive trajectories between CU and MCI, present already at 6 month follow-up. This was not observed for the CDR-SB at one-year follow-up.
- Storyteller change at six-months predicted CDR-SB change at one-to-two year follow-up, particularly in participants with Mild Cognitive Impairment.

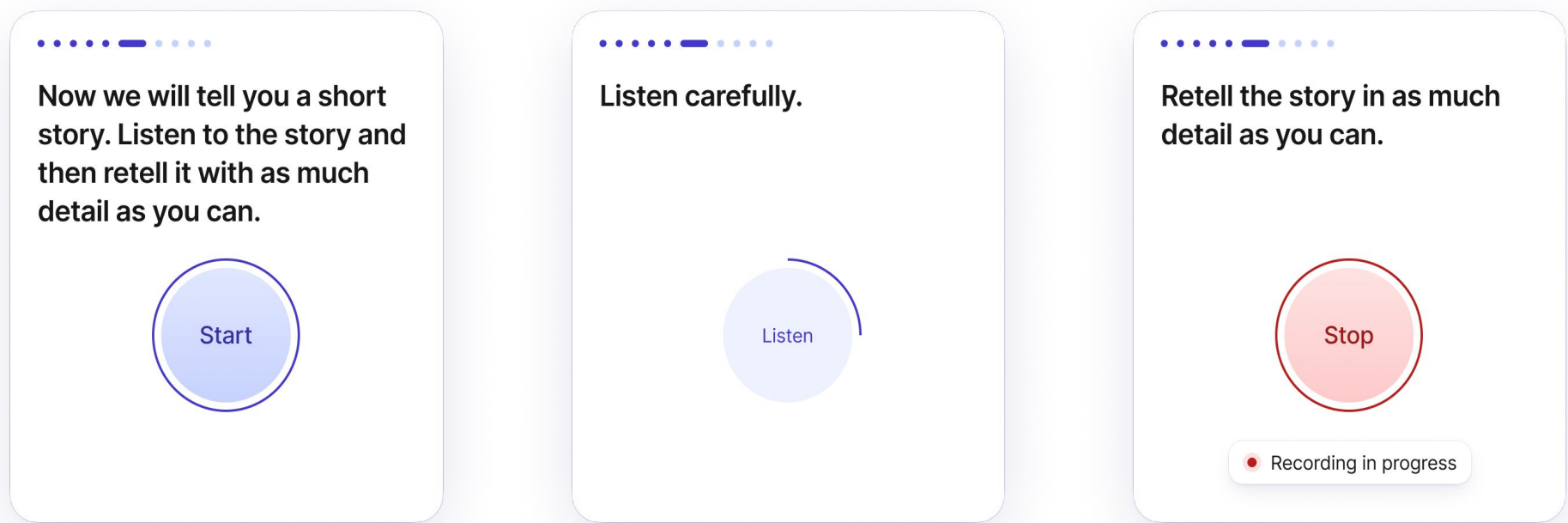
Background

- Accurate measures of cognitive change are critical for detecting treatment effects in clinical trials for Alzheimer’s disease (AD).
- The Clinical Dementia Rating (CDR) is a common primary endpoint in AD trials. It is time consuming, requires expertly trained staff to administer and interviews with both a study partner as well as the patient.
- Storyteller, a brief, self-administered, remote story-recall task, enables low-burden repeat assessments in ADNI4.
- We compared its longitudinal trajectories to the Clinical Dementia Rating sum-of-boxes (CDR-SB) between Mild Cognitive Impairment (MCI) and Cognitively Unimpaired (CU) participants.

Methods

Storyteller

- Storyteller is a self-administered and automatically scored, speech-based assessment evaluating memory function via story recall tasks and automated speech analysis.
- Participants access Storyteller via a link as a secure web application that runs on all standard devices and browsers.



- One of the scores produced by Storyteller, **G-match**, is a measure of proportional recall previously shown to classify Mild Cognitive Impairment (MCI) and Cognitively Unimpaired (CU), and correlate with traditional endpoints such as CDR-SB and PACC5.

Analysis

- 416 ADNI4 participants with baseline clinical diagnosis of MCI (n=120) or CU (n=296) who completed both Storyteller and the Clinical Dementia Rating (CDR) at baseline were included. At analysis, 136 (103 CU; 33 MCI) had completed Storyteller and 47 (7 CU; 40 MCI) had completed CDR at one-year follow-up, 245 (183 CU; 62 MCI) had completed Storyteller at six-month follow-up, and 52 (36 CU; 16 MCI) at 18-month follow-up.
- Separate mixed models for repeated measures examined fixed effects of time, diagnosis, time*diagnosis interaction, age, sex, and education, with random intercepts by participant. Primary outcome was the time*diagnosis interaction.
- In 57 participants with both a six-month Storyteller test and a CDR at annual follow-up (year 1 or 2), we analyzed the relationship between short-term Storyteller decline and longer term decline on the CDR-SB (Spearman correlation).

Results

	Overall	CU	MCI	P-Value
n	416	296	120	
Age (years)	72.0 (8.4)	71.5 (8.3)	73.2 (8.5)	0.064
Sex, n (%)				
Female	247 (59.4)	196 (66.2)	51 (42.5)	<0.001
Male	169 (40.6)	100 (33.8)	69 (57.5)	
Education (years)	16.2 (2.5)	16.3 (2.6)	16.1 (2.4)	0.465
Storyteller (baseline)	60.9 (12.9)	63.7 (12.1)	54.2 (12.5)	<0.001
CDR-SB	0.45 (0.82)	0.06 (0.19)	1.40 (0.98)	<0.001

Table 1. Baseline demographic characteristics grouped by clinical diagnosis. Age (p=0.064) and education level (p=0.465) did not differ significantly between groups, but the MCI group had lower proportion of females (p<0.001), lower Storyteller score at baseline (p<0.001) and higher CDR sum of boxes (CDR-SB) at baseline (p<0.001).

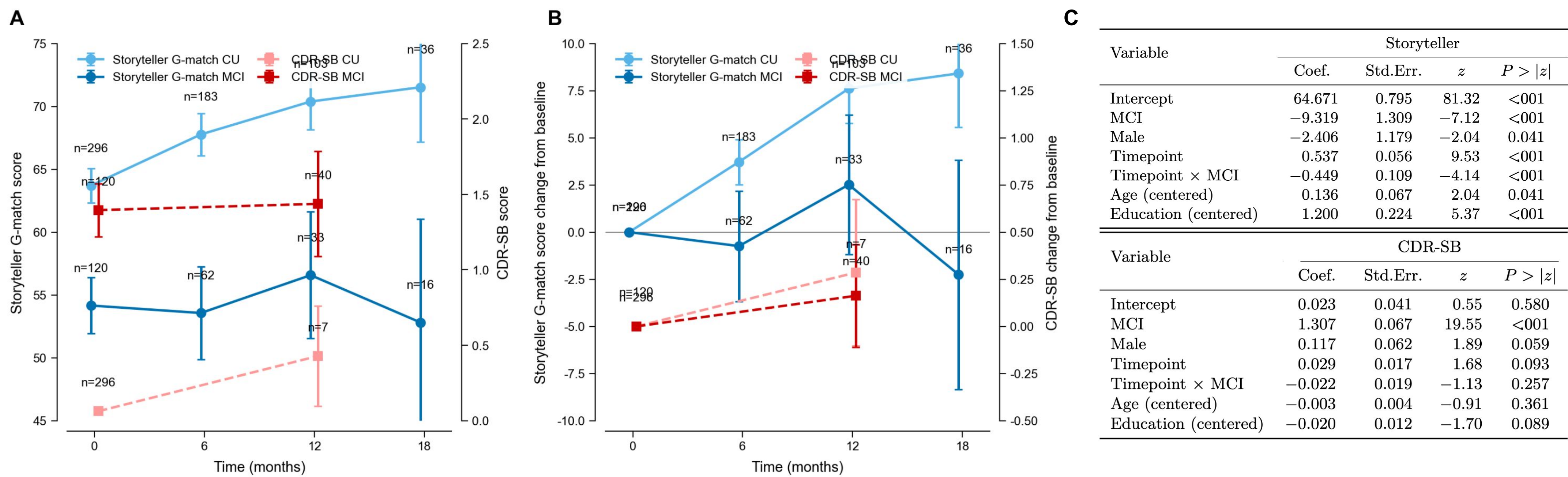


Figure 1. Longitudinal trajectories of Storyteller and CDR-SB grouped by clinical diagnosis, showing absolute scores (A) and change in scores from baseline (B). The CDR was only conducted at yearly follow-ups. Unlike the CDR-SB, Storyteller showed significant differences in cognitive trajectories between CU and MCI; differences in Storyteller trajectories were present already at six months follow-up (C).

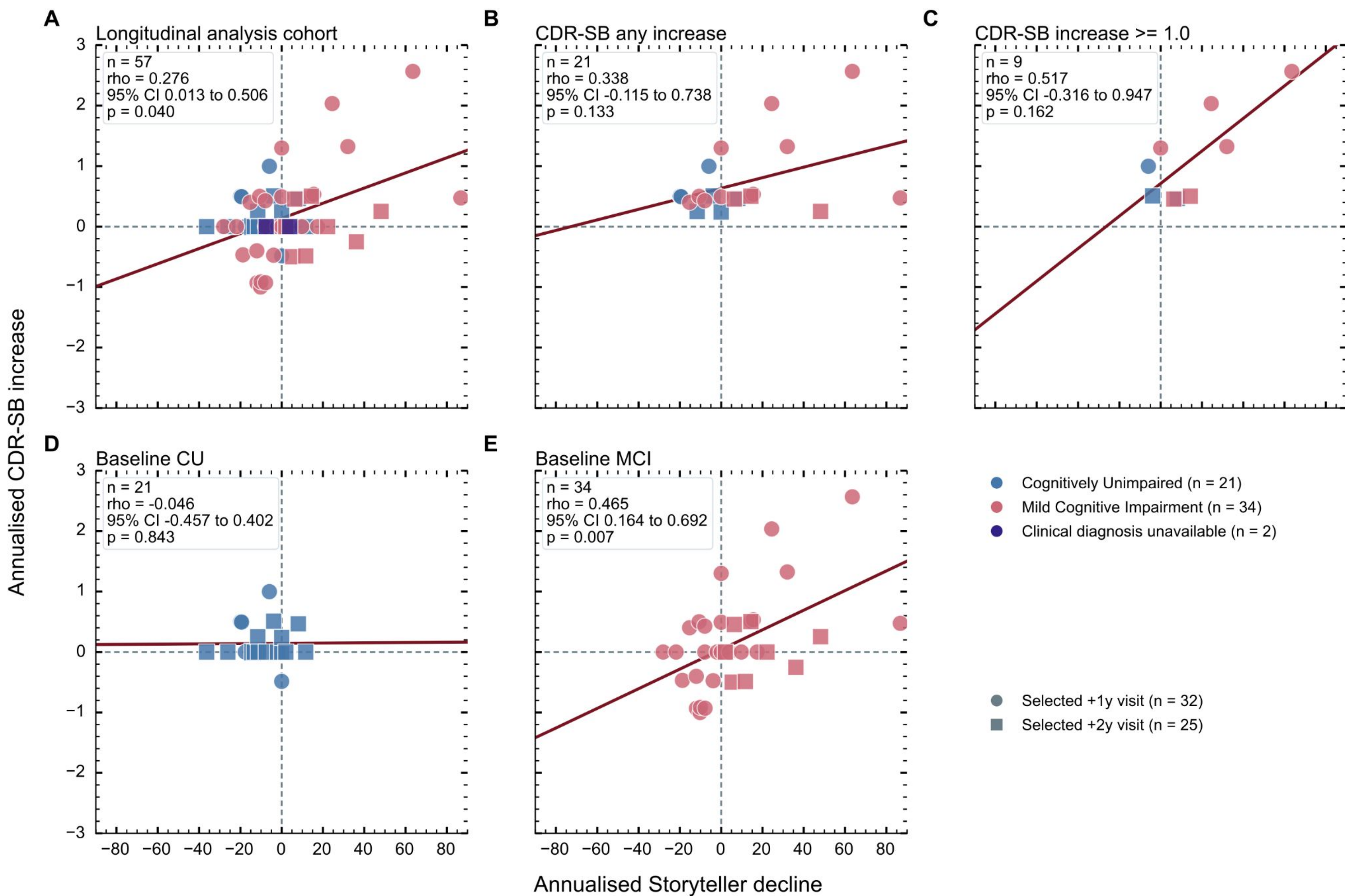


Figure 2. Annualised 6-month Storyteller decline versus annualized 1-2 year CDR-SB increase. 6-month Storyteller change predicted longer term CDR-SB change (A), with stronger association in participants that declined on the CDR-SB (B, C); this was observed in the MCI group but not the CU group (D, E).

References

Morris 1993, Neurology; Skirrow et al 2022 JMIR Aging; Fristed et al 2022 Brain Communications; Fristed et al 2022 A&D DADM; Weiner et al 2022 Alzheimer’s and Dementia; Skirrow et al 2024 Alzheimer’s and Dementia; Miller et al 2024 Alzheimer’s and Dementia.