

# Longitudinal remote speech biomarkers enable early detection of Alzheimer’s Disease pathology-related cognitive change in individuals with Subjective Cognitive Decline

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## BACKGROUND

- Early detection of cognitive decline related to preclinical Alzheimer’s disease (AD) remains challenging [1, 2].
- Traditional cognitive assessments require in-person visits, are costly and time-consuming, and show limited sensitivity to preclinical AD-related cognitive changes [1, 2].
- In this context, The Speech Biomarker for Cognition (SB-C) is a remote, low-burden speech-based tool, based on a phone call, and designed to monitor cognitive change in naturalistic settings [3].

## AIM

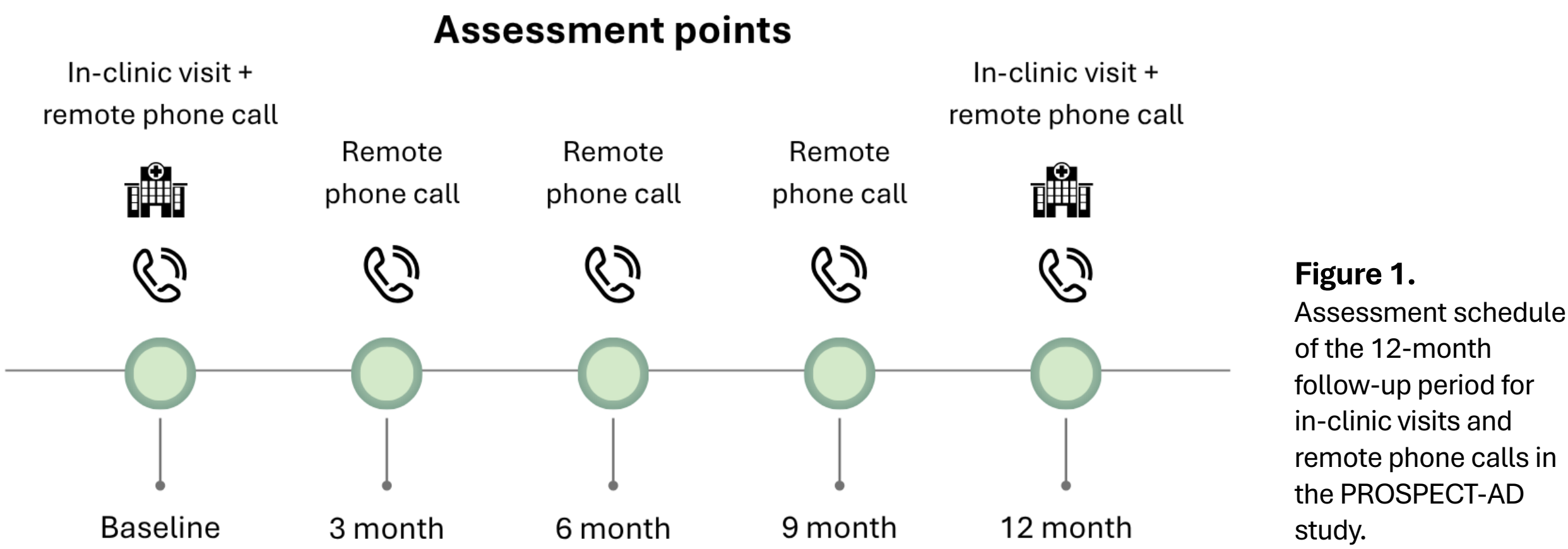
To examine whether the remote SB-C tool is sensitive to AD-related cognitive change in individuals with Subjective Cognitive Decline, alongside the modified Preclinical Alzheimer Cognitive Composite (mPACC).

## METHODS

- 93 SCD participants from the PROSPECT-AD study were included [3].
- Speech samples were automatically collected remotely every 3 months over 1 year using structured cognitive tasks by phone (semantic verbal fluency and verbal memory).
- Speech was processed using an AI-driven pipeline (ki:elements) [3], generating the SB-C scores for overall cognition and specific domains (memory, executive function, processing speed).
- Paper-and-pencil mPACC (z-scored) assessments were administered at baseline and after one year in-clinic.
- Biomarker groups were defined using validated cut-offs for CSF Aβ42/40 ratio (for amyloid), p-tau181 (for tau), and an AD profile measure (Aβ42/p-tau181) [4].
- Linear mixed models were used to examine whether the rate of change in SB-C scores differed by biomarker group, with biomarker as the main predictor and cognition as the outcome. Models included biomarker status × time interaction, and are adjusted for age, sex, and education. Tau models were adjusted for Aβ status. Alternate task versions for speech samples were administered at different timepoints and included as a covariate where applicable.

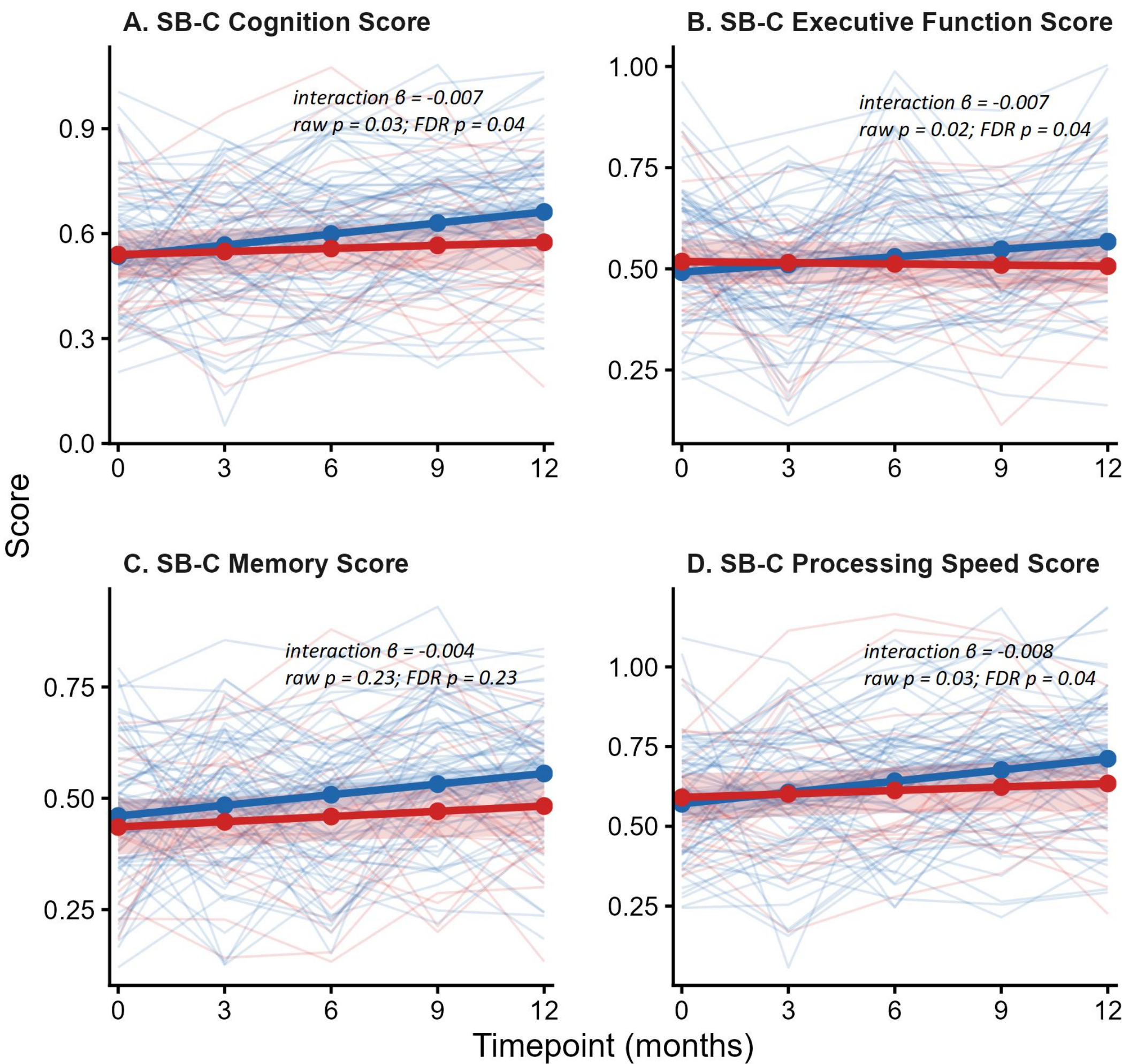
| Characteristic               | N  | N = 93 <sup>1</sup> |
|------------------------------|----|---------------------|
| Age (years), mean (SD)       | 93 | 65.72 (6.66)        |
| Sex (female), n (%)          | 93 | 57 (61%)            |
| Education (years), mean (SD) | 93 | 15.78 (3.59)        |
| CSF Aβ positive, n (%)       | 93 | 20 (22%)            |
| CSF tau positive, n (%)      | 93 | 8 (8.6%)            |
| CSF AD profile, n (%)        | 93 | 11 (12%)            |

**Table 1.** Demographics, clinical and biomarker characteristics for the sample of the study.  
<sup>1</sup>Mean (SD) for continuous variables; n (%) for categorical variables.



## RESULTS

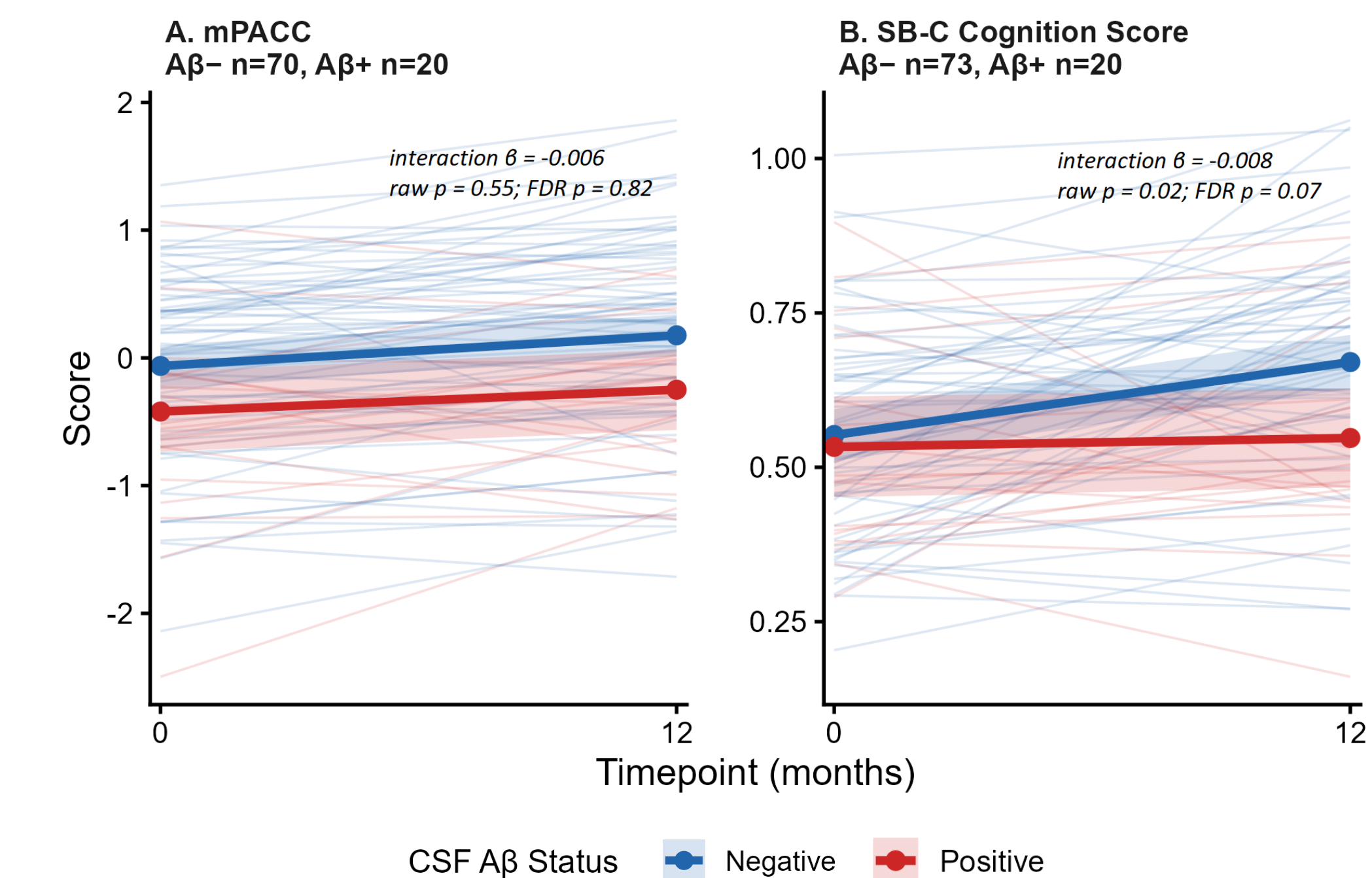
### 1 SB-C captures longitudinal cognitive changes associated with AD-related pathology



- Aβ+ participants showed significantly less improvement over 12 months on SB-C Cognition (Fig. 2A), Executive Function (Fig. 2B), and Processing Speed (Fig. 2D).
- Tau+ participants showed marginal similar effects in SB-C Cognition Score ( $\beta = -0.01$ ,  $p = 0.04$ ,  $pFDR = 0.08$ ) and Executive Function Score ( $\beta = -0.01$ ,  $p = 0.02$ ,  $pFDR = 0.08$ ).
- AD profile positivity was nominally associated with steeper decline in SB-C Executive Function Score ( $\beta = -0.008$ ,  $p = 0.04$ ,  $pFDR = 0.17$ ).
- No significant biomarker × time interactions were observed for mPACC by CSF Aβ status ( $\beta = -0.006$ ,  $p = 0.55$ ,  $pFDR = 0.82$ ) (Fig. 3A), tau status ( $\beta = -0.0002$ ,  $p = 0.98$ ) or CSF AD profile ( $\beta = -0.013$ ,  $p = 0.26$ ).

**Figure 2.** Lines represent model-estimated marginal means derived from linear mixed models for each SB-C domains by CSF Aβ status, adjusted for age, sex, and education. Shaded bands indicate 95% confidence intervals. Thin lines represent individual participant trajectories. Alternate task versions were administered between timepoints (verbal fluency alternated between animals and supermarket items; three parallel word lists were used for memory), and included as a covariate for SB-C Cognition and Executive Function Score models, where task version had a significant influence on scores.

### 2 Aβ-related effects remain with a two-timepoint SB-C design



- SB-C Cognition Score restricted to baseline and follow-up timepoints (mirroring mPACC design), remained sensitive to Aβ-related change ( $\beta = -0.008$ ,  $p = 0.02$ ,  $pFDR = 0.07$ ) (Fig. 3B).

## CONCLUSIONS

- **Remote** SB-C measures demonstrate greater **sensitivity** than mPACC in **detecting subtle cognitive changes** associated with AD-pathology in individuals with SCD.
- **Remote, low-burden** cognitive assessments may serve as a useful **triage tool** for **selecting at-risk individuals** for clinical trials or future treatments, as well as for **cognitive monitoring**.

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**Figure 3.** Lines represent model-estimated marginal means derived from linear mixed models for mPACC and SB-C Cognition Score including only two timepoints (baseline and follow-up) by CSF Aβ status, adjusted for age, sex, and education. Shaded bands indicate 95% confidence intervals. Thin lines represent individual participant trajectories.