

Associations Between Cognitive Status Transitions And Prior Concentrations Of Cerebrospinal Fluid Biomarkers

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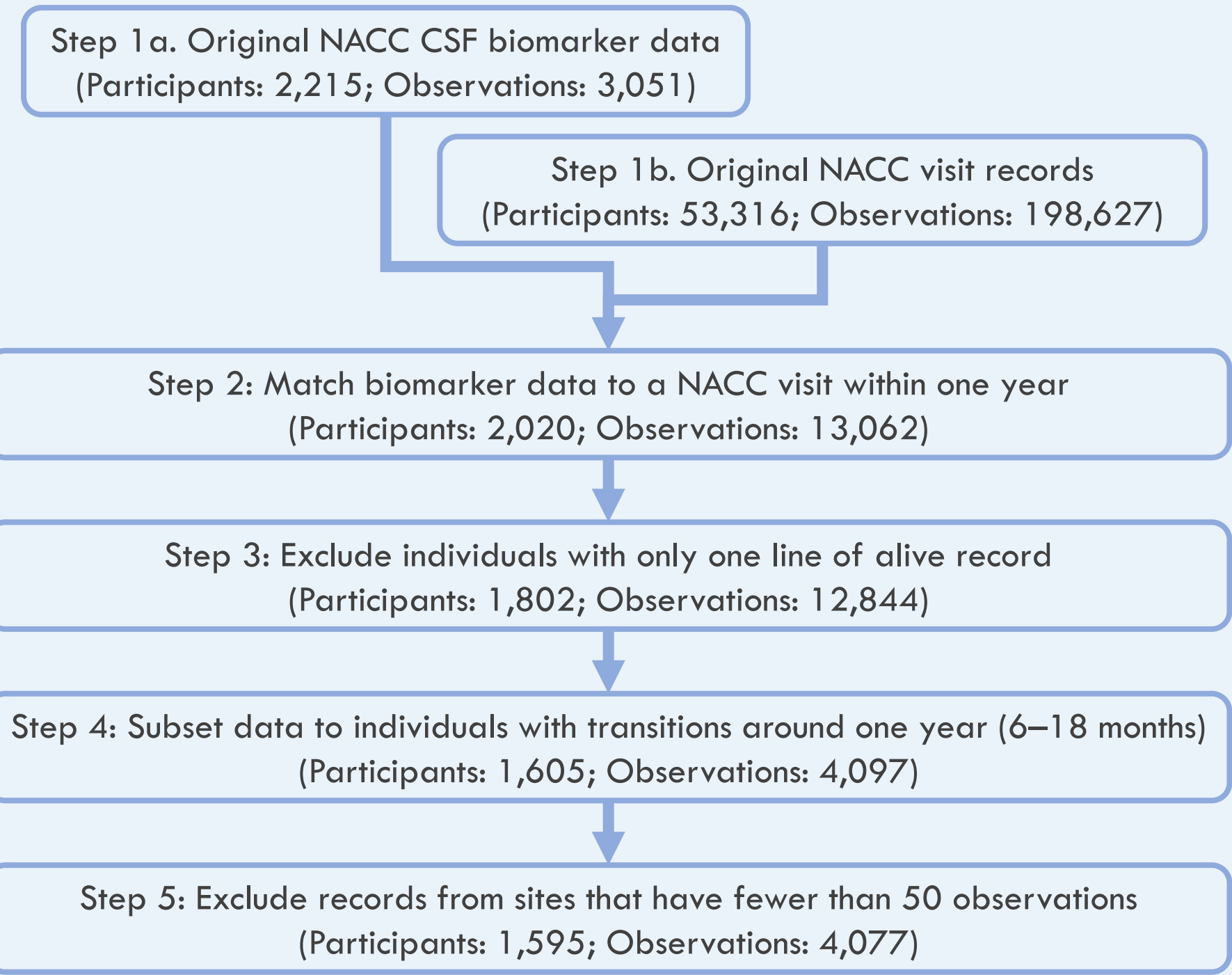
Introduction

- Cerebrospinal fluid (CSF) biomarkers for Alzheimer's disease and related dementias (ADRD), including amyloid- β ($A\beta_{42}$), phosphorylated tau (P-tau₁₈₁), and total tau (T-tau), are known to differ by cognitive status, but their power for predicting future transitions is less established.
- In multi-center studies, assay variability and demographic heterogeneity may confound true associations.

Data and Methods

- We analyzed longitudinal data from National Alzheimer's Coordinating Center (NACC) case series, including 4,077 observations from 1,595 participants across 8 Alzheimer's Disease Research Centers (ADRCs).
- We only included participants who had a CSF sample taken 6–18 months prior to a cognitive assessment.

Data flowchart

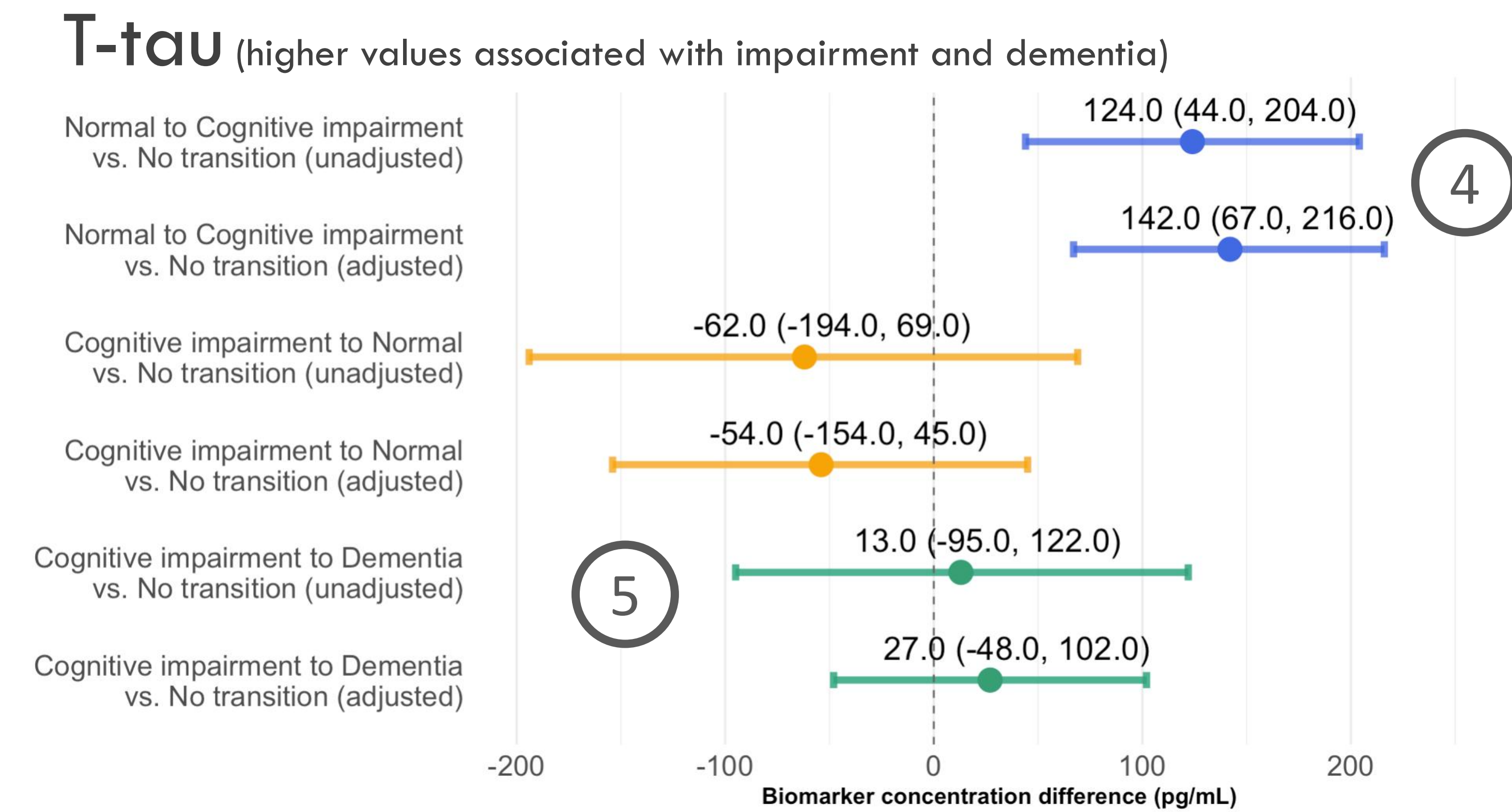
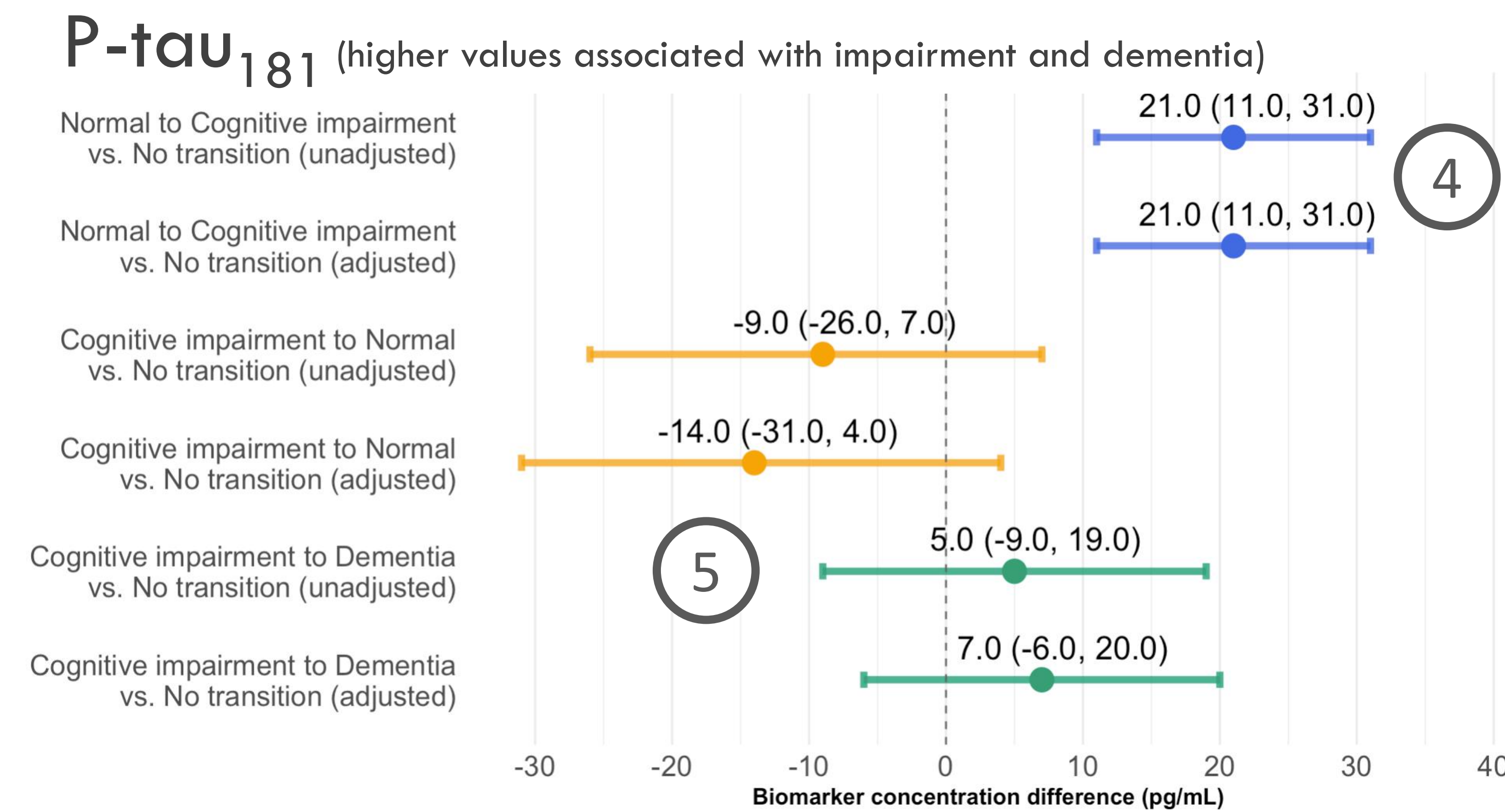
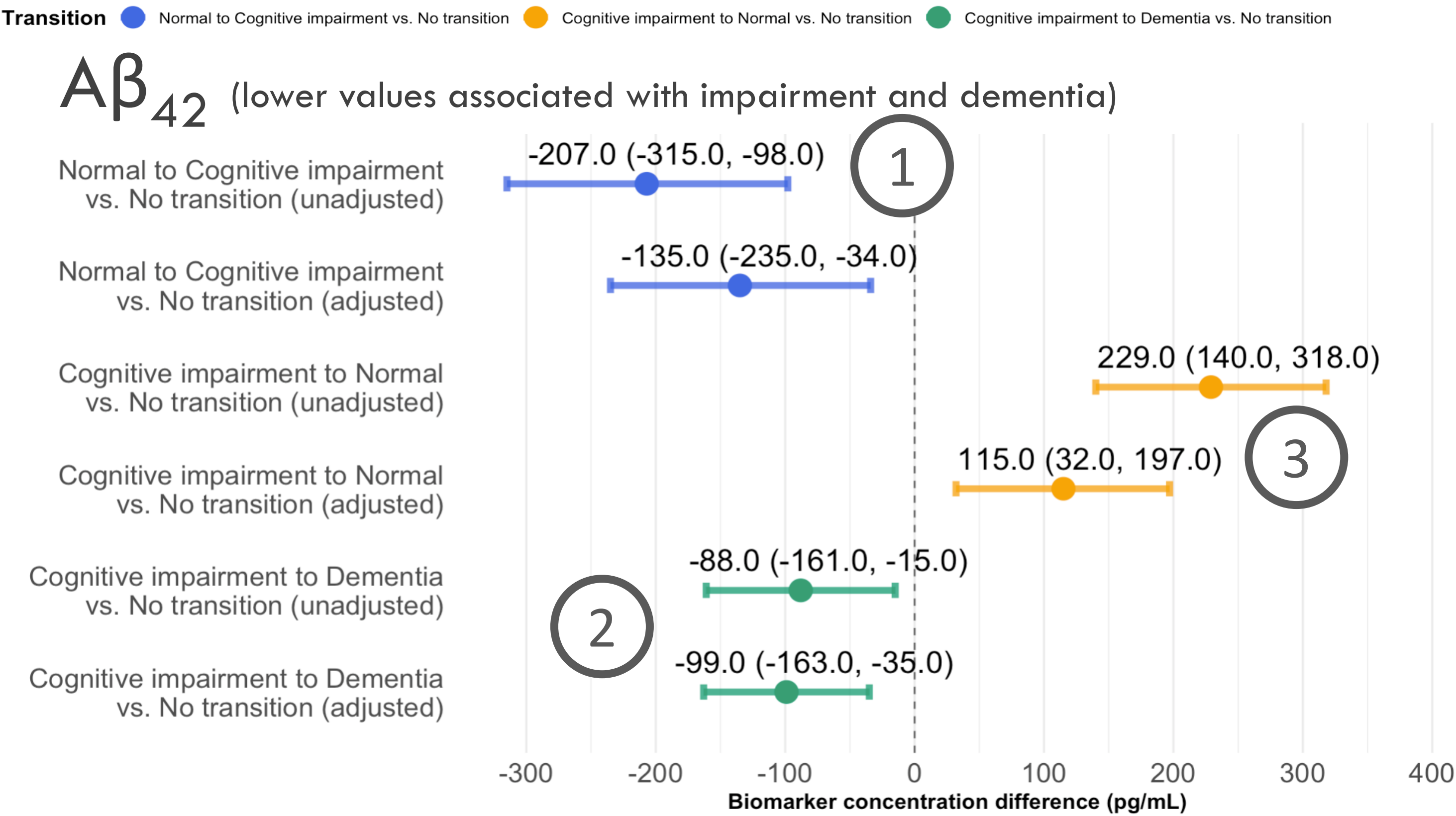


- We investigated three cognitive status transitions:



- Using linear regression, we evaluated associations between transitions in cognitive status with prior-year ADRC biomarker concentrations.
- Models were adjusted for ADRC site, assay type, and potential demographic and medical confounders (any variable that changed the main association by 10% after adjustment).

Associations between cognitive status transitions and prior-year CSF biomarker concentrations



Key Findings

- $A\beta_{42}$ was significantly lower in individuals with normal cognition who later transitioned to impaired cognition (adjusted difference: **-135 (95% CI: -235, -34)** compared those who remained normal.
- A similar association was seen for individuals with impaired cognition who later transitioned to dementia (adjusted difference: **-99 (95% CI: -163, -35)** compared those who did not transition.
- The opposite association was observed for individuals with cognitive impairment who later reverted to apparent normal cognition compared to those who remained impaired (adjusted difference: **115 (95% CI: 32, 197)**).
- P-tau₁₈₁ (adjusted difference: **21 (95% CI: 11, 31)**) and T-tau (adjusted difference: **142 (95% CI: 67, 216)**) were higher in individuals with normal cognition who transitioned to cognitive impairment compared to those who did not transition.
- Associations between P-tau₁₈₁ or T-tau and transitions from cognitive impairment were in the expected direction but not statistically significant.

Conclusions

CSF ADRC biomarkers, particularly $A\beta_{42}$, may be predictive of future cognitive status transitions. More work is needed to evaluate the prospective predictive power of these biomarkers accounting for the specific time between measurements, as well as for their easier-to-measure counterparts in plasma.

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