

Introduction

- The prevalence of ADRD is increasing, with disproportionate burden in women. Blood-based biomarkers enable minimally invasive assessment of AD-related pathology.
- Cardiovascular (CV) risk factors are modifiable risk factors of dementia ; however, limited studies have assessed their associations with changes in plasma ADRD biomarkers.

Objectives

- Examine associations of modifiable CV risk factors with baseline levels and longitudinal changes in plasma ADRD biomarkers

Methods

- 2,784 cognitively unimpaired women enrolled in the Women’s Health Initiative Memory Study (WHIMS; 1996-1999) with baseline biomarker data. 967 had a repeat biomarker measurement ~15 (SD, 0.6) years later.
- Exposures include clinical CV risk factors (diabetes, hypertension, total cholesterol, high-density lipoprotein [HDL] cholesterol, and low-density lipoprotein [LDL] cholesterol) and lifestyle behaviors (smoking, alcohol consumption, self-reported sleep duration, self-reported moderate-to-vigorous physical activity [MVPA]).
- Outcomes were 5 plasma ADRD biomarkers: amyloid beta 42 to 40 ratio (Aβ42:Aβ40), tau phosphorylated at threonine 181 (p-tau181), tau phosphorylated at threonine 217 (p-tau217), neurofilament light (NfL), and glial fibrillary acidic protein (GFAP).
- We used linear mixed-effects models to examine associations of CV risk factors with baseline levels and longitudinal changes in plasma ADRD biomarkers.
- Models adjusted for age, race, ethnicity, education, hormone therapy treatment arm, and time-varying BMI and eGFR.

Results

- Diabetes, hypertension and elevated total and LDL cholesterol were associated with faster increases in p-tau217, with greatest increase observed in diabetes. Hypertension was also associated with faster increases in NfL and GFAP. Among behavioral risk factors, only long sleep duration was associated with greater increases in p-tau217.

Table 1. Baseline characteristics (N = 2,784)

Characteristic	Mean (SD) or No. (%)
Age	69.9 (3.8)
White	1,993 (73.1%)
Hispanic or Latino	202 (7.3%)
College graduate or higher	861 (31.0%)
BMI (kg/m²)	28.6 (5.6)
eGFR (ml/min/1.73 m²)	83.6 (13.6)
APOE	
ε2 carrier	193 (12.5%)
ε4 carrier	403 (26.2%)
Cardiovascular disease	135 (4.8%)
Diabetes	196 (7.1%)
Hypertension	1,874 (67.3%)
Total cholesterol ≥ 200 mg/dL	2,043 (81.3%)
HDL cholesterol < 50 mg/dL	1,015 (40.4%)
LDL cholesterol ≥ 160 mg/dL	914 (39.6%)
Current smoker	150 (5.5%)
Alcohol use	
Current drinker (< 7 drinks per week)	1,473 (53.5%)
Current drinker (≥ 7 drinks per week)	259 (9.4%)
Sleep duration (hours)	
< 7	1,136 (41.1%)
7 - 8	1,519 (55.0%)
> 8	109 (3.9%)
MVPA Meets Guidelines (≥ 7.5 MET/week)	677 (24.4%)

Abbreviations: APOE: apolipoprotein E; BMI: body mass index; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; LDL: low-density lipoprotein; MET-hour: metabolic equivalent task hour; MVPA: moderate-to-vigorous physical activity.

Conclusions

Clinical CVD risk factors and long sleep duration appear to be associated with accumulating AD neuropathology. Plasma biomarkers, particular p-tau217 may offer a critical tool for identifying when neuropathologic changes associated with CVD risk factors may begin to emerge and accumulate during the life course.

Figure 1. Associations of Baseline Clinical Cardiovascular Risk Factors with 15-Year Changes in Plasma Biomarkers

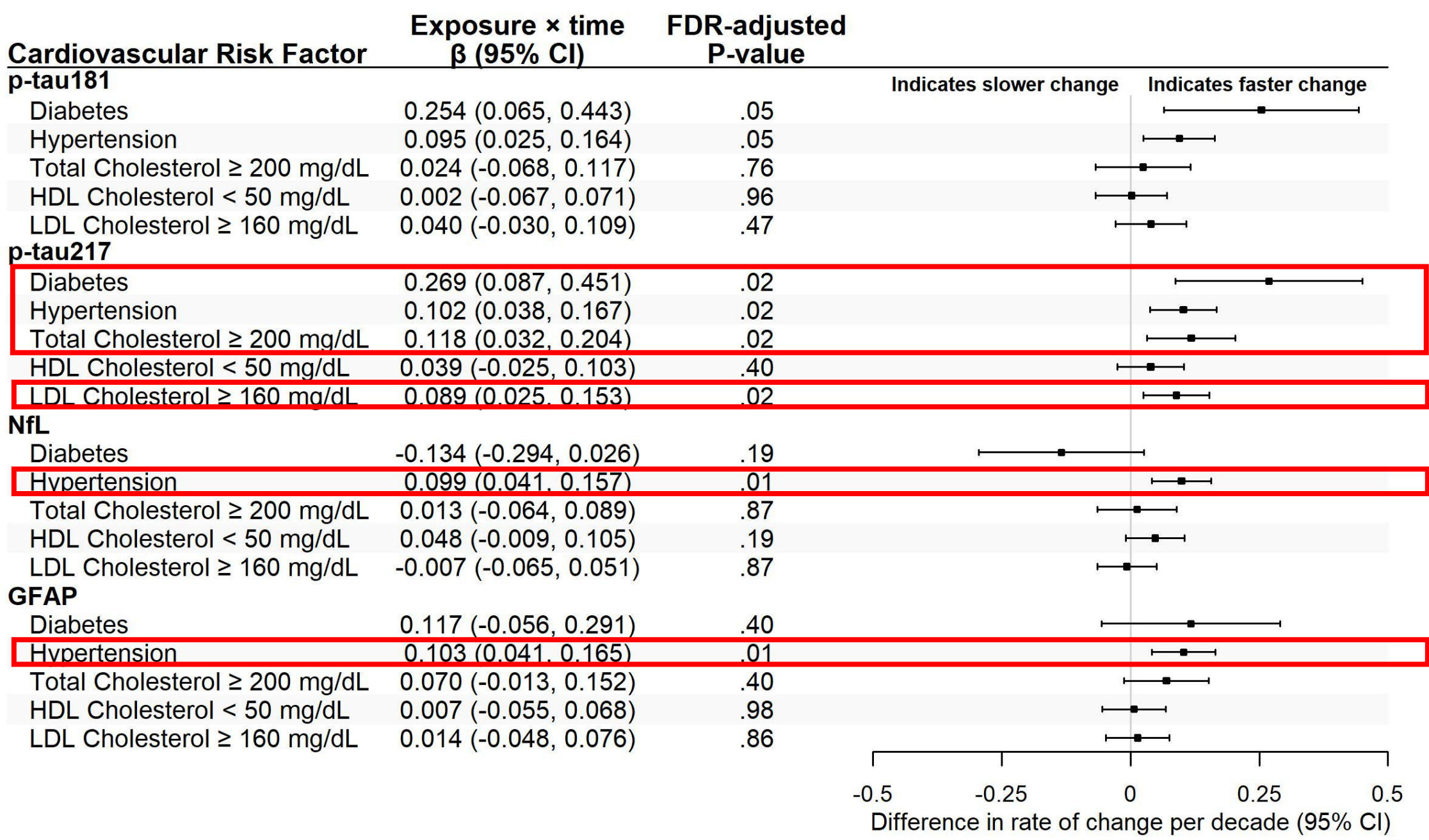
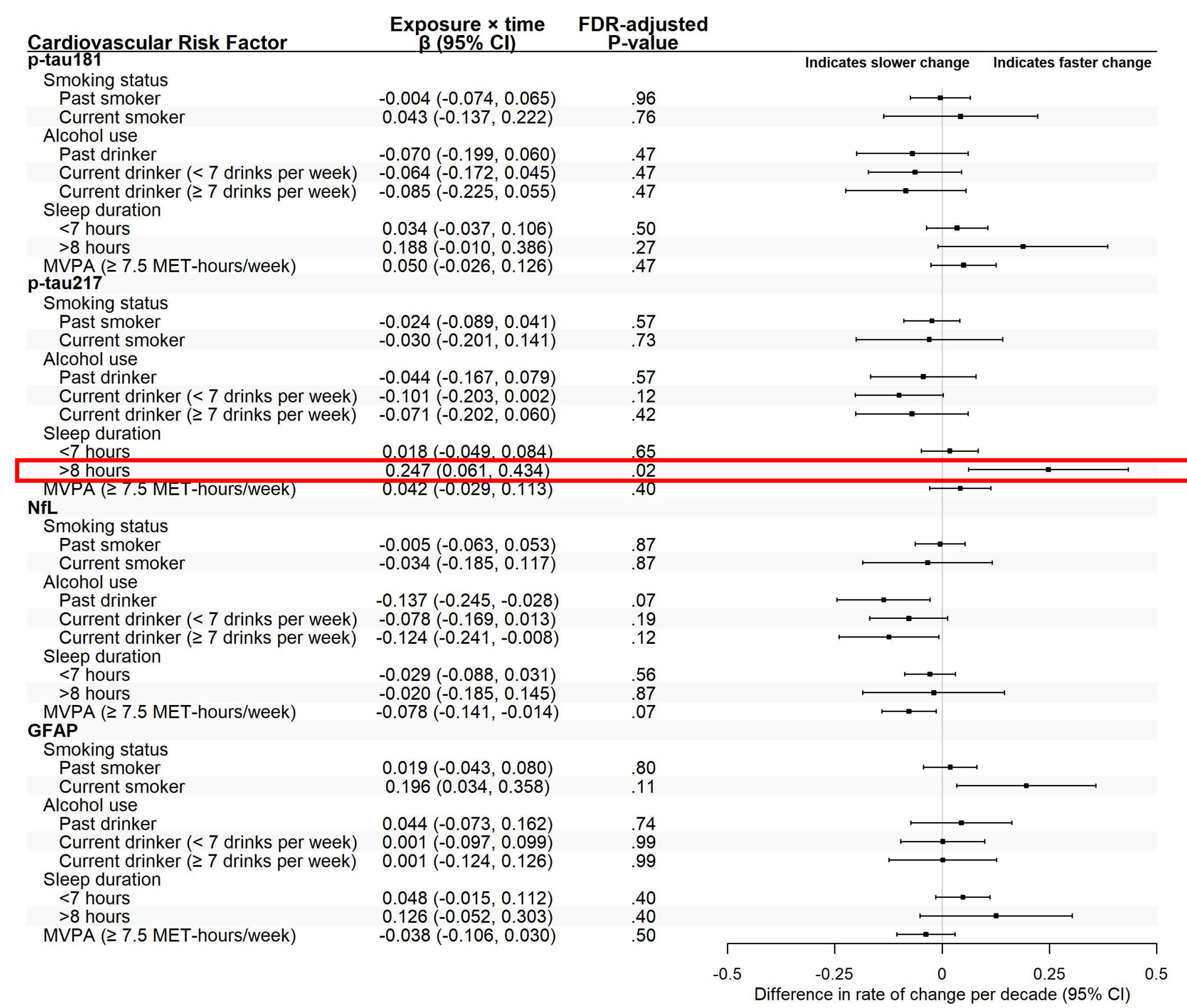


Figure 2. Associations of Lifestyle Behaviors with 15-Year Changes in Plasma Biomarkers



Effect estimates were reported per 1-SD increase in log₂ of plasma biomarker: Aβ42:Aβ40 (SD 0.32), p-tau181 (SD 0.62), p-tau217 (SD 0.93), NfL (SD 0.73), and GFAP (SD 0.68).

Figure 3. Longitudinal Trajectories of p-tau217 by Cardiovascular Risk Factors

