DIFFERENTIAL ASSOCIATIONS BETWEEN MACROSCOPIC AND MICRO-STRUCTURAL WHITE MATTER INJURY WITH CONSTANT AND PULSATILE BLOOD PRESSURE COMPONENTS: AN ANALYSIS OF THE UK BIOBANK COHORT.

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WSO-ESO Conference
7th November 2020

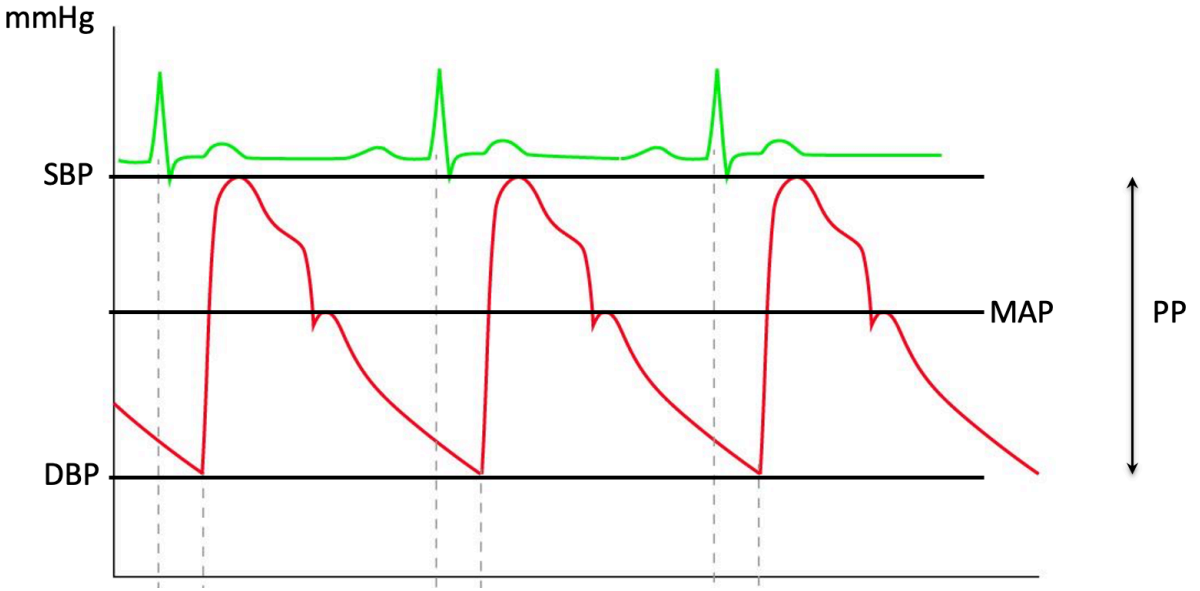
Background

White matter injury is evident macroscopically on magnetic resonance imaging (MRI) as white matter hyperintensities (WMHs), whilst microstructural injury is detectable on diffusion imaging (dMRI). Although WMHs and microstructural injury share genetic components and are associated with ageing and hypertension

, it is unknown if they differ in their relationship with the pulsatile blood pressure, represented by pulse pressure (PP) and steady blood pressure, corresponding to mean arterial pressure (MAP).

Aims

To determine the cross-sectional and predictive associations between PP and MAP and the the severity of WMHs.



Methods

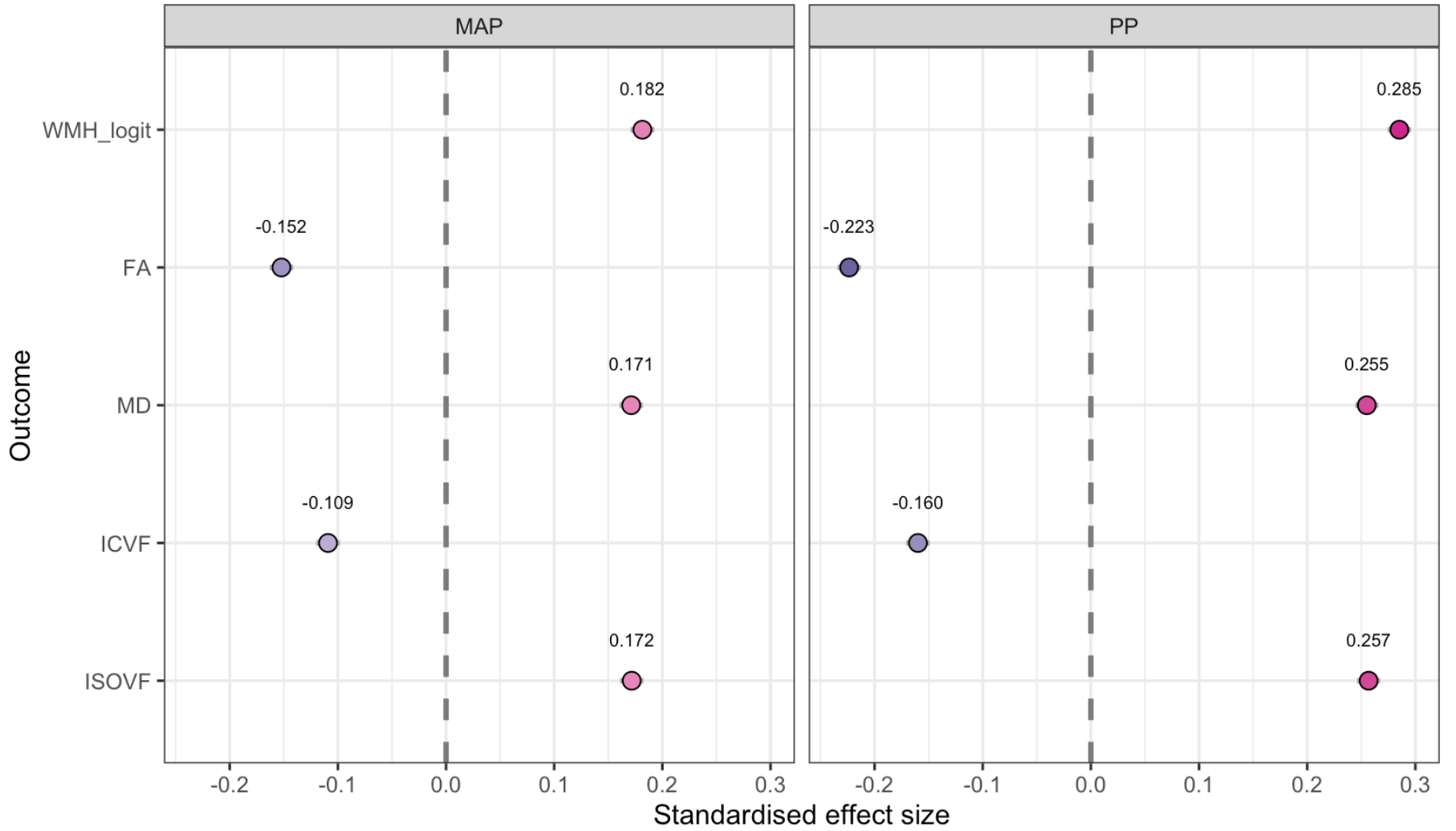
- UK Biobank is a prospective community-based cohort of >500,000, 40-69 year-old community-based people.
- 20,200 of whom had an MRI scan 4-12 years after baseline.
- WMHs were automatically segmented based on T1-weighted and T2-weighted FLAIR images using FSL tools (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/).

Methods

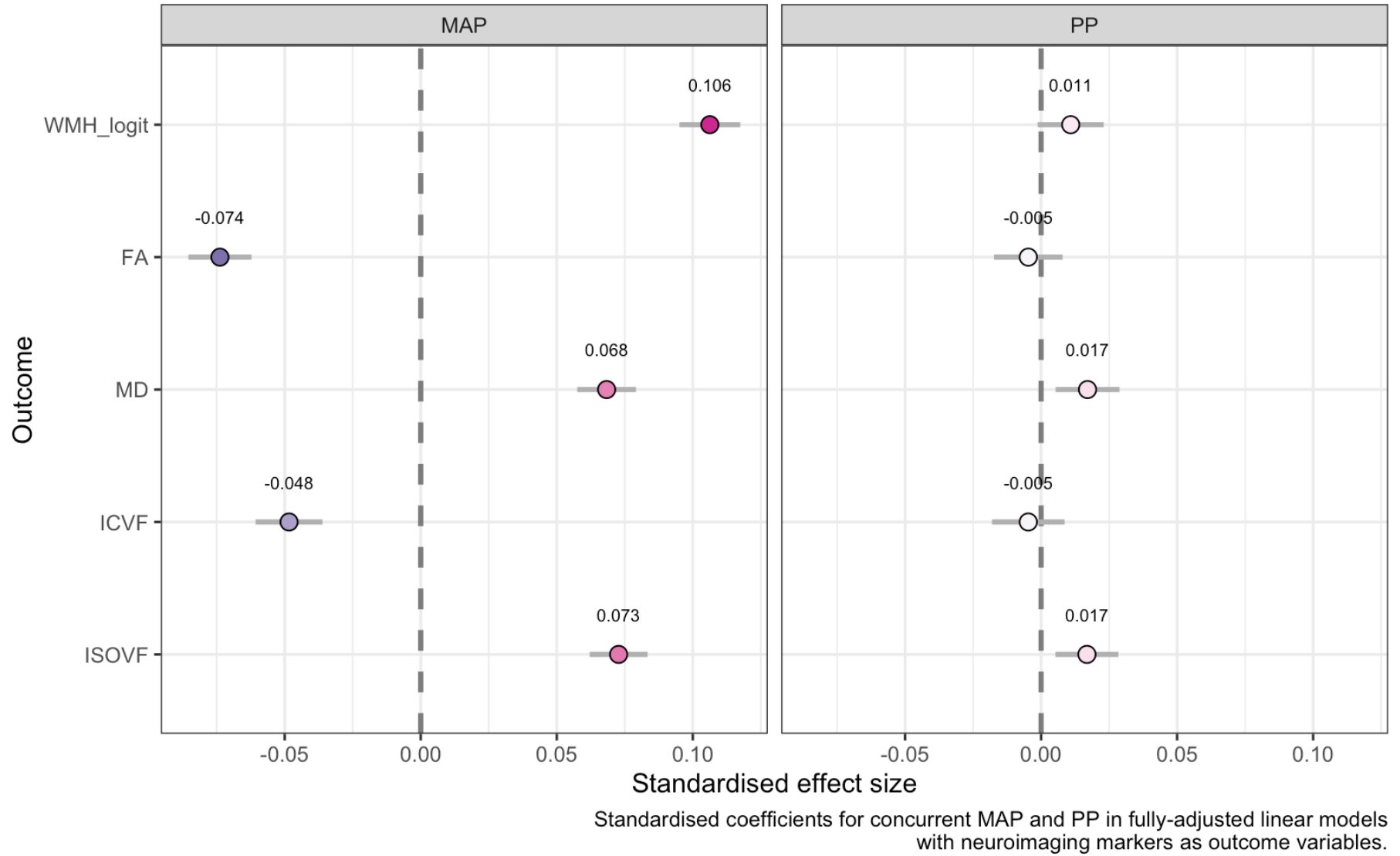
In linear models, associations between MAP and PP, adjusted for age, sex, diabetes and smoking, were determined for logit-transformed WMHs and dMRI measures including fractional anisotropy (FA), mean diffusivity (MD), NODDI-based intracellular (ICVF), and isotropic compartment (ISOVF) volume fraction.

Results

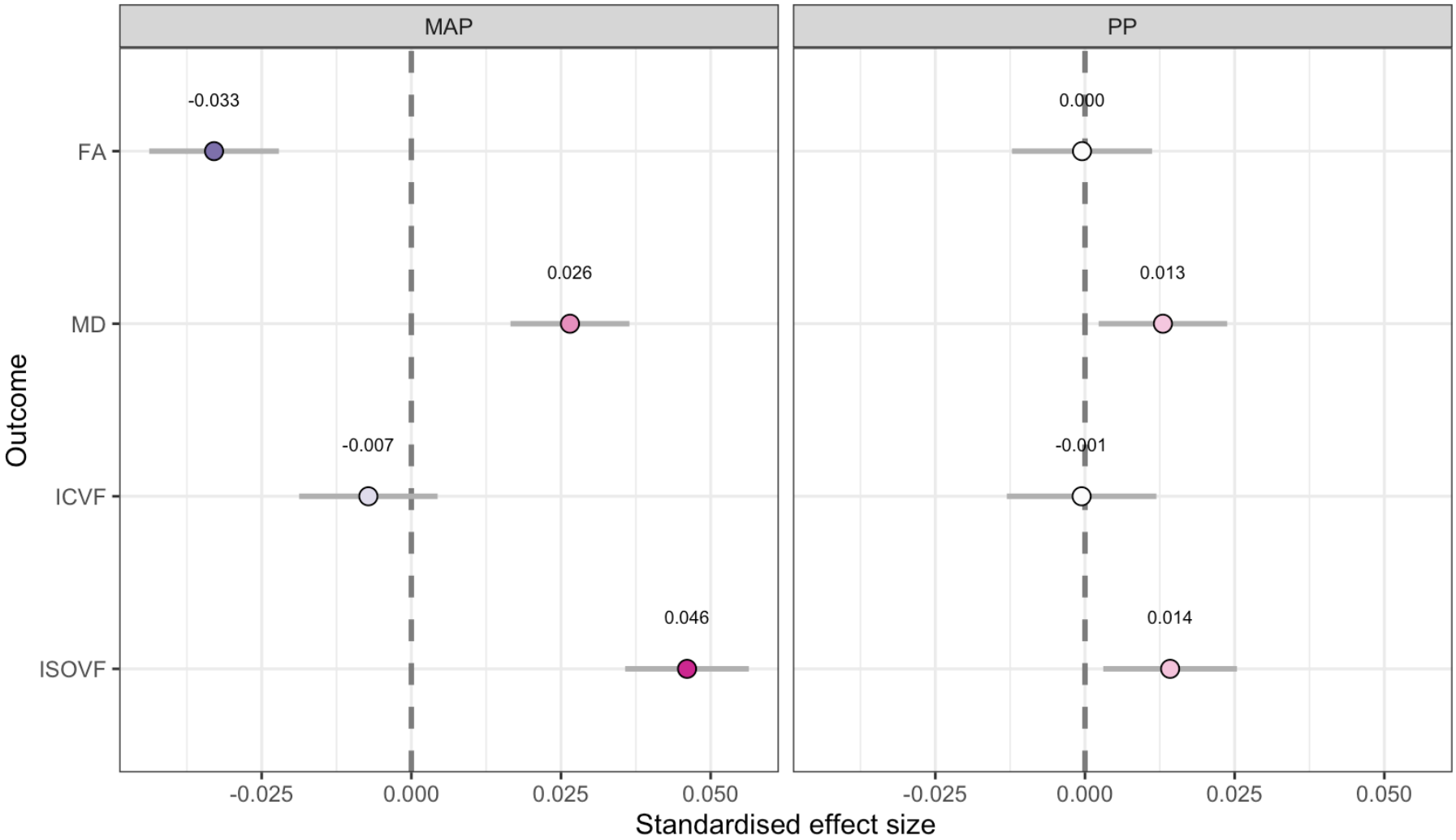
In N participants, concurrent MAP and PP were associated with microstructural injury (FA, MD) and free water fraction (ISOVF), with weak associations between baseline DBP and FA. DBP was associated with WM volume and decreased GM volume. In contrast, macroscopic WM damage (WMH) was associated with both MAP and PP, but with a stronger association with MAP.



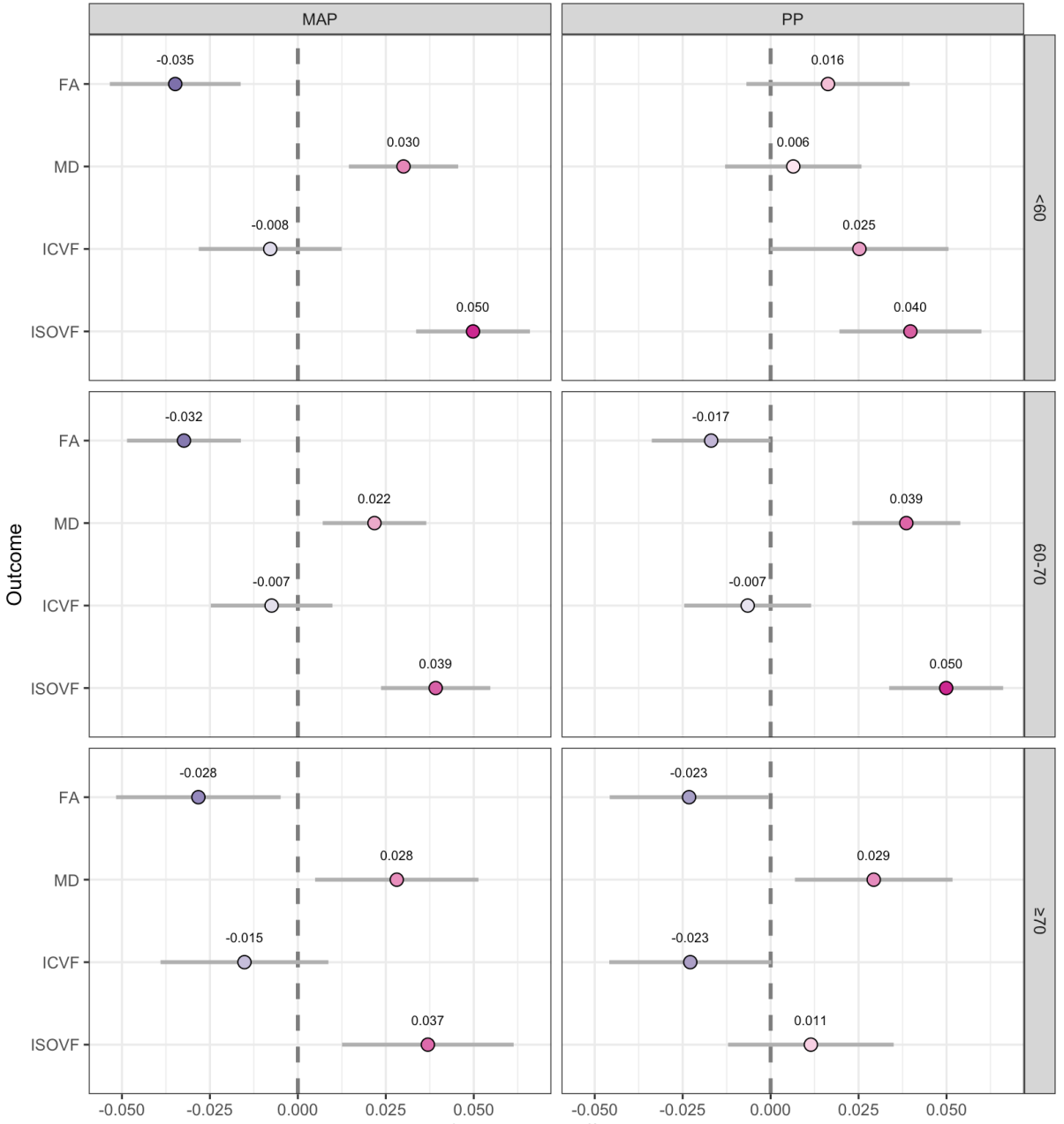
Standardised coefficients for concurrent MAP and PP in unadjusted linear models with neuroimaging markers as outcome variables.



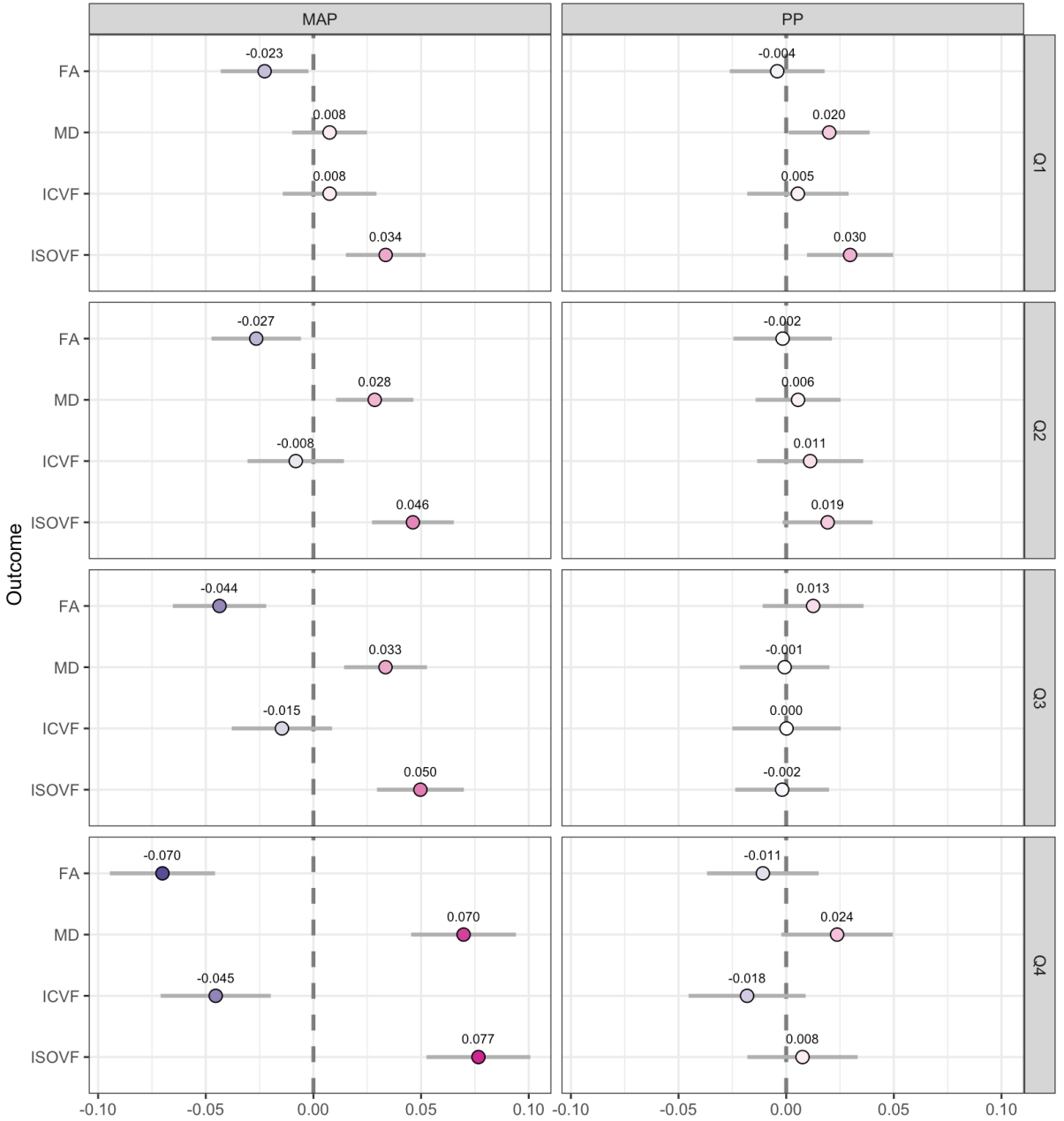
Standardised coefficients for concurrent MAP and PP in fully-adjusted linear models with neuroimaging markers as outcome variables.



Standardised coefficients for concurrent MAP and PP in fully-adjusted linear models with WMH with neuroimaging markers as outcome variables.



Standardised coefficients for concurrent PP and MAP in fully-adjusted linear models with neuroimaging markers as outcome variables per age decade with WMH.



Standardised coefficients for concurrent PP and MAP in fully-adjusted linear models with neuroimaging markers as outcome variables per WMH quartile.

Variable	FA	MD	ISOVF	WMH
MAP	-0.042 (-0.060 to -0.025)	0.041 (0.025 to 0.057)	0.064 (0.047 to 0.081)	0.116 (0.098 to 0.134)
PP	-0.001 (-0.020 to 0.018)	0.019 (0.002 to 0.036)	0.022 (0.004 to 0.041)	0.006 (-0.014 to 0.026)
Age	-0.219 (-0.230 to -0.207)	0.306 (0.296 to 0.317)	0.371 (0.360 to 0.383)	0.474 (0.463 to 0.485)
Age*MAP	**-0.003 (-0.015 to 0.009)**	**0.010 (-0.001 to 0.021)**	**0.005 (-0.006 to 0.016)**	**-0.003 (-0.014 to 0.007)**
Age*PP	**-0.015 (-0.027 to -0.002)**	**0.018 (0.007 to 0.029)**	**0.006 (-0.006 to 0.017)**	**0.011 (0.000 to 0.022)**
WMH	-0.382 (-0.393 to -0.371)	0.389 (0.379 to 0.399)	0.249 (0.239 to 0.259)	.

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WMH	-0.382 (-0.393 to -0.371)	0.389 (0.379 to 0.399)	0.249 (0.239 to 0.259)	.
WMH*MAP	-0.019 (-0.031 to -0.008)	0.017 (0.006 to 0.027)	0.015 (0.003 to 0.026)	.
WMH*PP	-0.051 (-0.063 to -0.039)	0.069 (0.058 to 0.080)	0.049 (0.037 to 0.060)	.
Antihypertensives	-0.148 (-0.172 to -0.125)	0.124 (0.103 to 0.146)	0.192 (0.170 to 0.215)	0.248 (0.224 to 0.273)
Antihypertensives*MAP	0.039 (0.015 to 0.064)	-0.020 (-0.042 to 0.003)	-0.012 (-0.036 to 0.012)	-0.029 (-0.055 to -0.004)
Antihypertensives*PP	0.001 (-0.022 to 0.024)	-0.012 (-0.033 to 0.009)	-0.031 (-0.053 to -0.009)	-0.038 (-0.062 to -0.014)

Conclusions

- Both MAP and PP are associated with micro- and macro-structural white matter injury.
- The patter of relationships between BP and neuroimaging markers was similar for FA, MD, and WMH
- ISOVF shows strong associations with MAP and PP that are age-independent and occur before development of WMH
- MAP is age independent while PP increases with age and also enhances the effect of age on microstructural white matter injury.

Acknowledgements