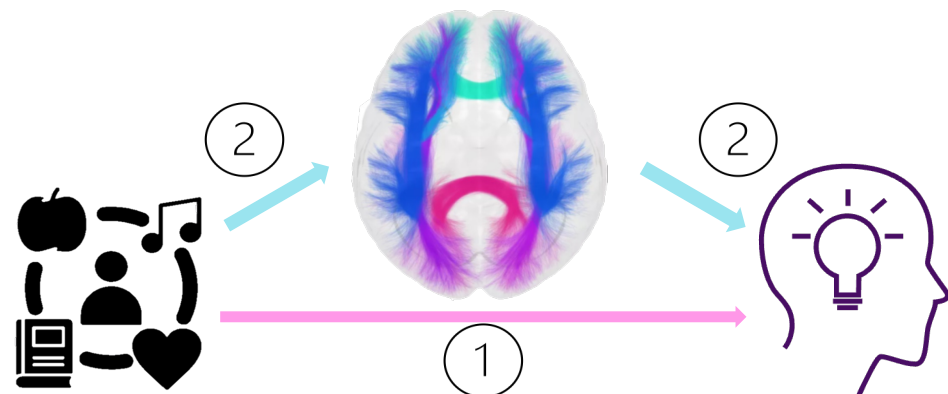
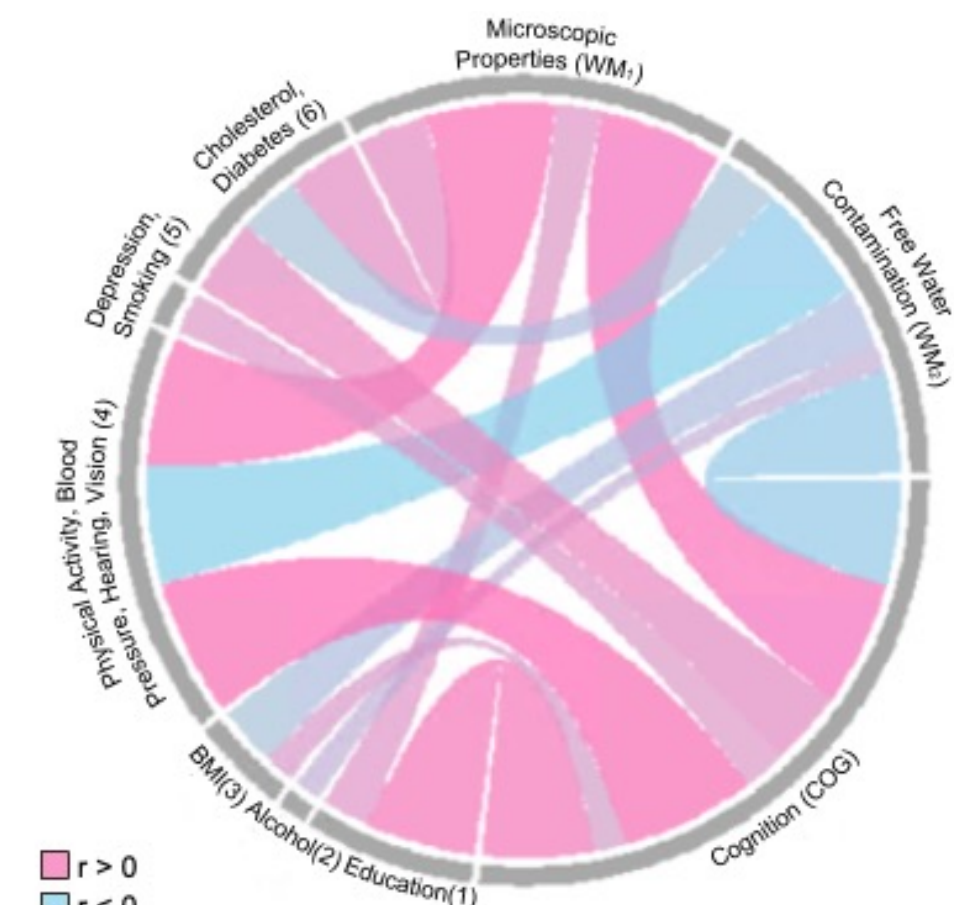
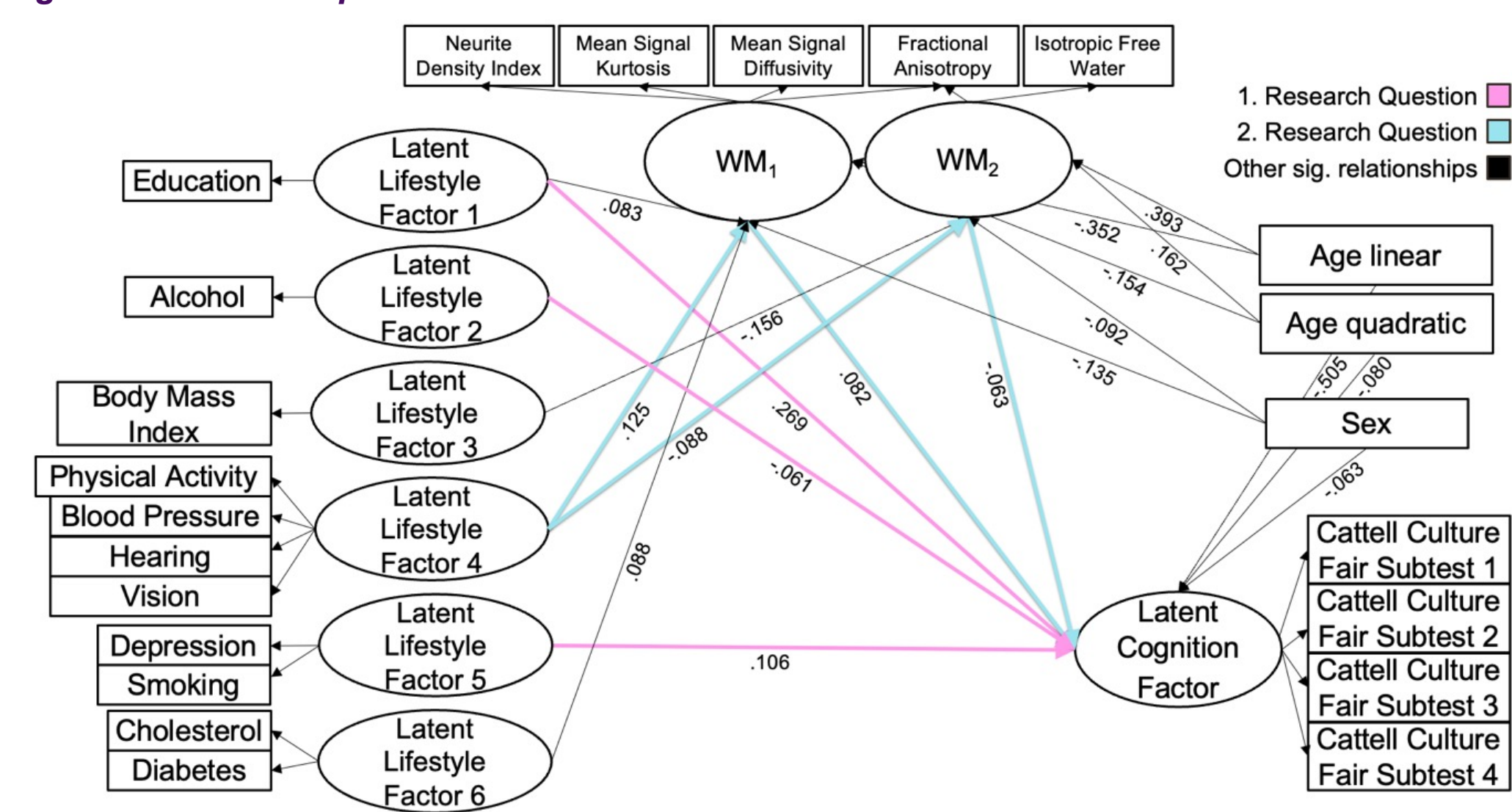


Exploring Lifestyle Factors and Cognition: A Structural Equation Modelling Approach to White Matter Mediation

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Analyses of the CamCAN cohort showed that only education, alcohol consumption, smoking, and depression were associated with cognition; no significant associations were observed for the remaining lifestyle factors. No strong evidence was found that white matter mediated the relationship between lifestyle and cognition

INTRODUCTION	METHODS	RESULTS	CONCLUSION	REFERENCES																				
Livingston et al.¹ identified 14 modifiable lifestyle factors that could prevent 45% of dementia cases. However, few studies have examined their combined effects or explored shared neurobiological mechanisms.^{2,3,4} This study asks: 1. Do individual lifestyle factors retain their significant effects on cognition when modelled together? 2. Does white matter mediate these effects? 	Fig.1 Materials. CamCAN Cohort⁵ N = 706 18-88 years Lifestyle: 34 Questionnaire Items White Matter: Diffusion-weighted MRI Metrics⁶ Fluid IQ: Cattell Culture Fair Test Confirmatory and exploratory factor analyses were conducted to derive two latent white matter factors, one latent cognition factor, and six latent lifestyle factors from eleven Livingston modifiable risk factors. Correlation analyses informed subsequent structural equation modelling to examine the joint effects of the latent lifestyle factors on cognition and the mediating role of the latent white matter factors.	Fig.2 Latent factor correlations (Pearson's r, $p < 0.05$).  Table 1. Path estimates of SEM. <table><tr><th>Path</th><th>R²</th><th>Estimate</th><th>Sig.</th></tr><tr><td>Cognition ~ Factor 1</td><td>7.2%</td><td>0.269</td><td><0.001</td></tr><tr><td>Cognition ~ Factor 2</td><td>0.4%</td><td>-0.061</td><td>0.03</td></tr><tr><td>Cognition ~ Factor 5</td><td>1.1%</td><td>0.106</td><td><0.001</td></tr><tr><td>Indirect effect on Cognition ~ Factor 4 through WM₁ + WM₂</td><td>0.03%</td><td>0.016</td><td>0.02</td></tr></table> Fig.3 Structural Equation Model.  Only paths significant at $p < 0.05$ are shown. Latent factors were derived from exploratory factor analyses. WM₁ = Latent factor reflecting white matter microscopic properties; WM₂ = Latent factor capturing free water contamination.	Path	R ²	Estimate	Sig.	Cognition ~ Factor 1	7.2%	0.269	<0.001	Cognition ~ Factor 2	0.4%	-0.061	0.03	Cognition ~ Factor 5	1.1%	0.106	<0.001	Indirect effect on Cognition ~ Factor 4 through WM ₁ + WM ₂	0.03%	0.016	0.02	No strong support was found for the Livingston et al.¹ framework: 1. Only a subset of lifestyle factors retained significant effects with cognition when modelled together 2. Weak evidence that white matter mediates the relationship between lifestyle and cognition Findings are limited by the cross-sectional design, and data-driven operationalization of lifestyle factors. However, the use of latent constructs and a unified SEM provides a valuable framework for future research.	- Livingston, G., et al. (2024). Dementia prevention, intervention, and care: 2024 report of the Lancet Commission. <i>The Lancet</i>, 404(10452), 572-628 - Heger, I., et al. (2021). Lifestyle for Brain Health Index and brain structure and cognition. <i>Neurology</i>, 97(13) - Salzman, T., et al. (2022). Associations of multidomain interventions with improvements in cognition in mild cognitive impairment: a systematic review and meta-analysis. <i>JAMA Network Open</i>, 5(5), e226744-e226744. - Lee, S. M., et al. (2023). Impact of a multidomain lifestyle intervention on white matter integrity: the SUPERBRAIN exploratory sub-study. <i>Frontiers in Aging Neuroscience</i>, 15, 1242295. - Shafto, M. A., et al. (2014). The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) study protocol. <i>BMC Neurology</i>, 14, 1-25 - Henriques, R. N., Henson, R., Cam-CAN, & Correia, M. M. (2023). Unique information from common diffusion MRI models about white-matter differences across the human adult lifespan. <i>Imaging Neuroscience</i>, 1, 1-25.
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