

Association of retinal and OCT age gap and Multiple sclerosis

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Background

- Multiple sclerosis (MS) is a chronic autoimmune disease characterised by demyelination and progressive neurodegeneration of the central nervous system.
- Epidemiological trends show rising prevalence of MS among older adults [1]. However, chronological age fails to capture the variability in biological ageing among individuals.
- Existing biomarkers of biological ageing in MS** such as telomere length [2] cellular senescence, and MRI-derived brain age are invasive, costly, and impractical at scale.
- The retina offers a non-invasive window to the CNS via fundus photography and OCT imaging.
- Retinal age gap** (the difference between AI-predicted retinal age and chronological age) is an emerging biomarker of biological ageing.
- This study investigates whether retinal and OCT age gaps are elevated in individuals with MS compared to matched controls.

Methods

- This study used data from the **UK Biobank**, a prospective population-based cohort of over 500,000 recruited between 2006 and 2010.
- 298 participants** were included for retinal age gap analysis and **258** for OCT age gap analysis (Figure 1).
- MS was defined as the primary outcome, retinal age gap in the right eye was the primary exposure, and the left eye was used for sensitivity analysis.
- The development of Retinal and OCT age gap Deep learning models were described previously [3] [4] .
- Conditional logistic regression was matched on age, sex, ethnicity, and Townsend Deprivation Index, with additional adjustment for BMI and smoking.

Figures

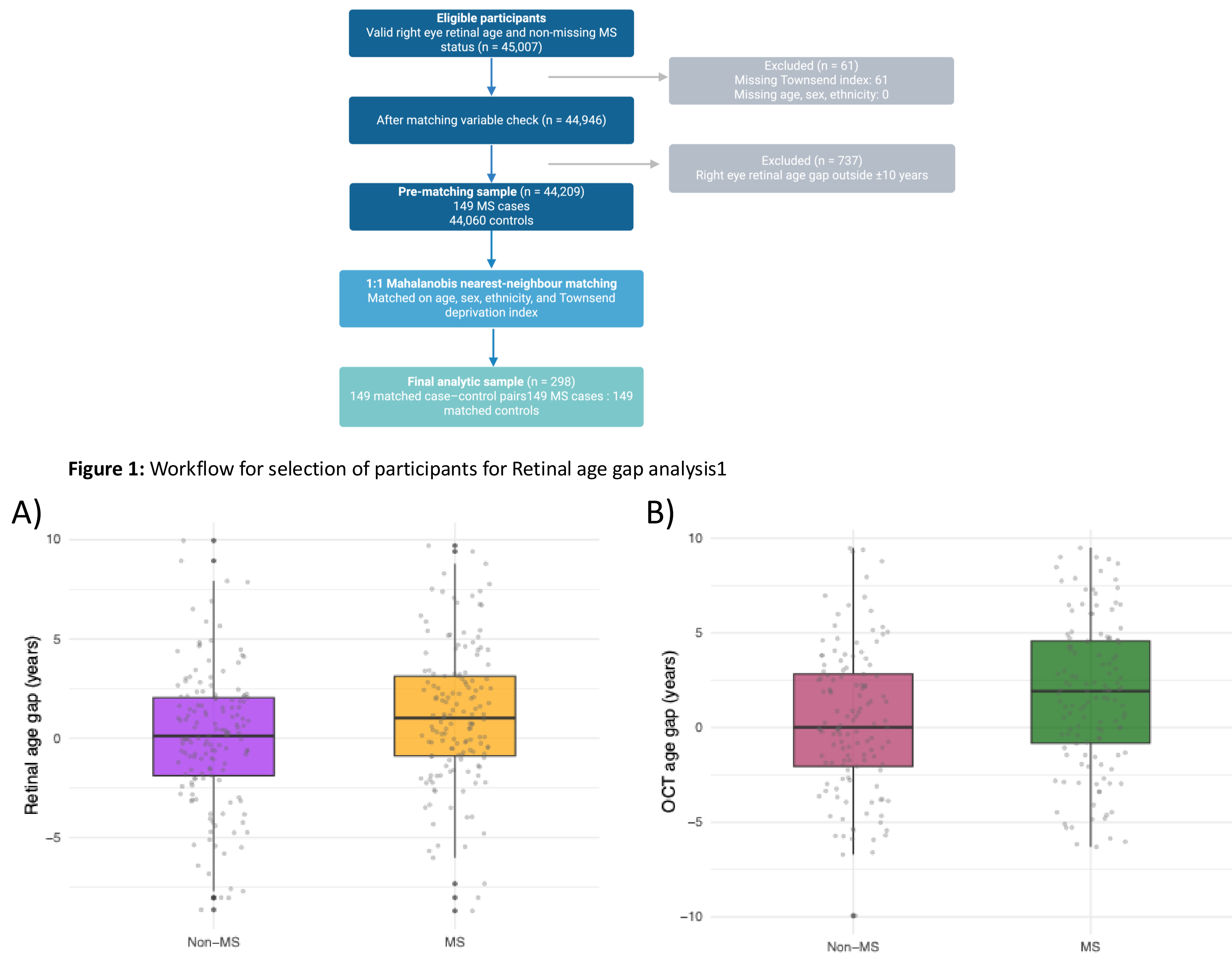


Figure 1: Workflow for selection of participants for Retinal age gap analysis1

Figure 2 : Box plots showing A) OCT in MS participants vs Non MS controls B) Retinal Age gaps in MS participants vs Non MS controls

	Model 1		Model 2	
	HR (95% CI)	P value	HR (95% CI)	P value
OCT age gap, per one age (yrs)	1.10	0.006	1.10	0.008
OCT age gap				
Tertile 1	Reference	–	Reference	–
Tertile 2	1.61	0.135	1.58	0.163
Tertile 3	2.46	0.009	2.24	0.021
Trending	1.57	0.008	1.50	0.021
Retinal age gap, per one age (yrs)	1.11	0.006	1.10	0.015
Retinal age gap				
Tertile 1	Reference	–	Reference	–
Tertile 2	1.19	0.527	1.14	0.641
Tertile 3	2.15	0.012	1.86	0.048
Trending	1.46	0.013	1.36	0.049

- Model 1 adjusted for age, sex, ethnicity and Townsend deprivation indices.
- Model 2 adjusted for covariates in model 1 + BMI, smoking status
- HR, HR ratio; CI, CI interval.

Table 1: Association between Retinal and OCT age gap with multiple sclerosis using Cox proportional hazards regression models

Results

- Participants with MS had a significantly higher **OCT age gap** (1.15 vs. 0.02 years, $p = 0.004$) (Figure 2A) and **retinal age gap** (1.70 vs. 0.30 years, $p = 0.004$) (Figure 2B).
- Each one-year increase in **OCT age gap** was independently associated with an **11%** increase in the odds of MS (OR 1.10, 95% CI, $p = 0.008$) after adjustment for BMI and smoking.
- Each one-year increase in **retinal age gap** was associated with a **10%** increase in MS odds (OR 1.10, $p = 0.015$).
- Participants in the highest tertile of OCT age gap had significantly greater odds of MS compared to the lowest tertile (OR 2.46, $p = 0.009$), as did those in the highest retinal age gap tertile (OR 2.15, $p = 0.012$).
- Sensitivity analyses using the left eye showed consistent directional effects.

Conclusion

- This study demonstrates that individuals with MS have significantly elevated retinal and OCT age gaps compared to matched controls.
- Retinal age gap may capture accelerated biological ageing in MS, potentially reflecting systemic ageing, neurodegeneration mirrored in the retina, or local structural changes such as RNFL and mGCIPL thinning.
- Unlike absolute retinal thickness measurements, retinal age gap accounts for expected age-related change, distinguishing MS-related neurodegeneration from physiological decline.
- Retinal imaging is non-invasive and low-cost, making retinal age gap a scalable and clinically accessible biomarker for disease monitoring in MS.
- Longitudinal studies are needed to determine whether baseline retinal age gap predicts disease progression, disability accumulation, or treatment response.

References:

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