

WP2 Biomarkers of Aging

WP2: Integrated molecular assessment of biological ageing using

- 1. Cellular senescence & inflammatory biomarkers
- 2. Epigenetic clocks and methylation-based ageing measures

Objectives

- Identify biomarkers of biological ageing linked to lifestyle, health, and functional decline based on analysis of **large, population-based cohorts**.
- Evaluate **causal** relationships between lifestyle interventions and ageing biomarkers using twin data.
- **Compare and integrate** epigenetic, inflammatory, and senescence-associated biomarkers.
- Develop **scalable and minimally invasive** biomarker strategies for population studies and intervention trials.

Knowledge, Expertise and skills within WP

- Cellular senescence and SASP biology
- Inflammatory and proteomic biomarkers
- DNA methylation and epigenetic clocks
- Twin cohorts and longitudinal population studies
- Causal inference and Mendelian randomization
- Biomarker integration and validation

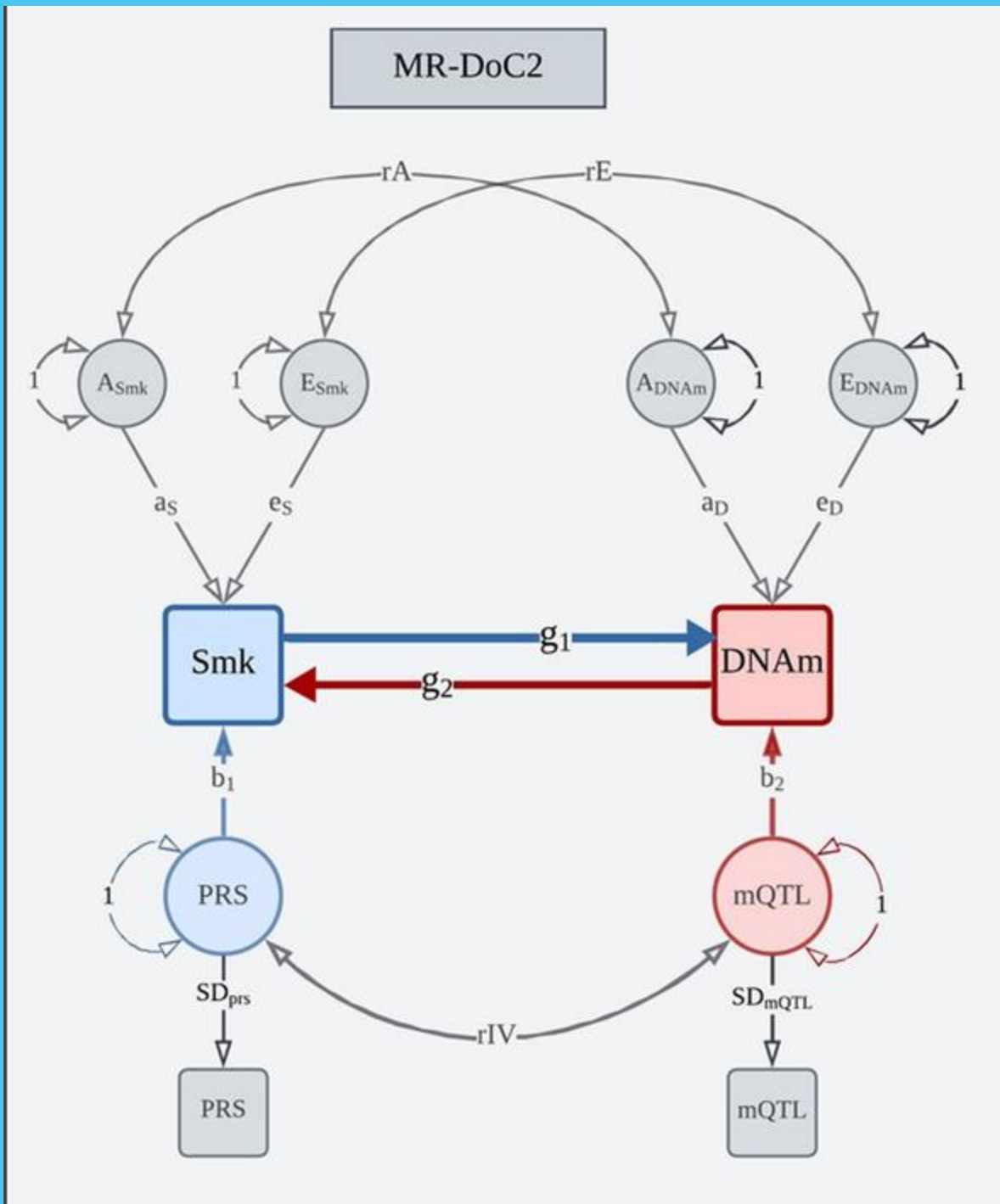
Figure 1 The power of twin study designs



a



b

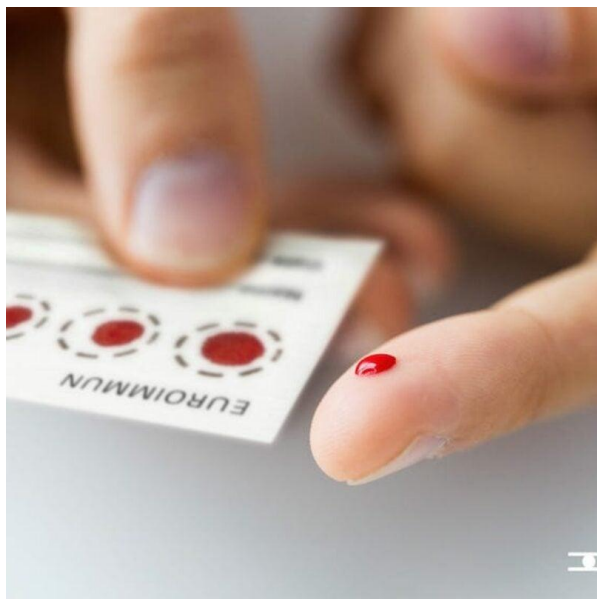


c

- a) Discordant twin design: Effect of lifestyle on (facial) ageing revealed in monozygotic (identical) twins discordant for smoking habits (Okada et al 2013)
- b) Intervention study in monozygotic twins. Poster from a 2024 Netflix documentary series exploring how diet impacts health.
- c) Mendelian Randomization Direction of Causation model to test **bi-directional causal relationships** between lifestyle and biomarkers of ageing using **large datasets** from twin cohorts (Singh et al 2025)

Outcomes

- Prioritized multimodal biomarker panel for biological ageing
- Mechanistic insight into lifestyle–ageing interactions
- Recommendations for biomarker implementation in clinical and population studies
- Cost-effective and scalable biomarker strategies for healthy ageing research



Collaboration with other WP's, enablers or stakeholders

- **WP1/4**: Interview and intervention study in monozygotic twin pairs
year 1: selection and invitation of twins by WP2 PhD student
year 3-4: Analysis of pre-and post intervention biomarker data by WP2 PhD student
- **WP3**: Priority List of Biomarkers
year 1: Collaboration on biomarker meta-analysis in cohorts
year 1-4: Develop recommendation for biomarker assessment

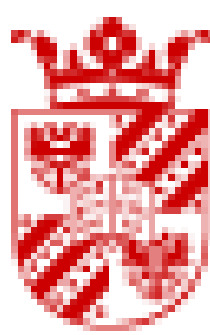
Key Stakeholders

- Adult, working-age, Dutch citizens of all socioeconomic classes (target age: 30-67)
- Organizations that aim to promote healthy ageing of employees / Dutch citizens

Key Challenges

- biomarker standardization across cohorts
- integration of multimodal ageing measures
- scalability and accessibility of biomarker assessment

Refs Okada et al Facial changes caused by smoking: a comparison between smoking and nonsmoking identical twins. Plastic and reconstructive surgery 132.5 (2013): 1085-1092
Singh M. et al Unidirectional and bidirectional causation between smoking and blood DNA methylation: evidence from twin-based Mendelian randomization. (2025)Eur J Epidemiol 40, 55–69



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