



**WP4**  
**Interrogating biological  
pathways to understand  
how environment exposure  
influence cognitive  
health/ageing**

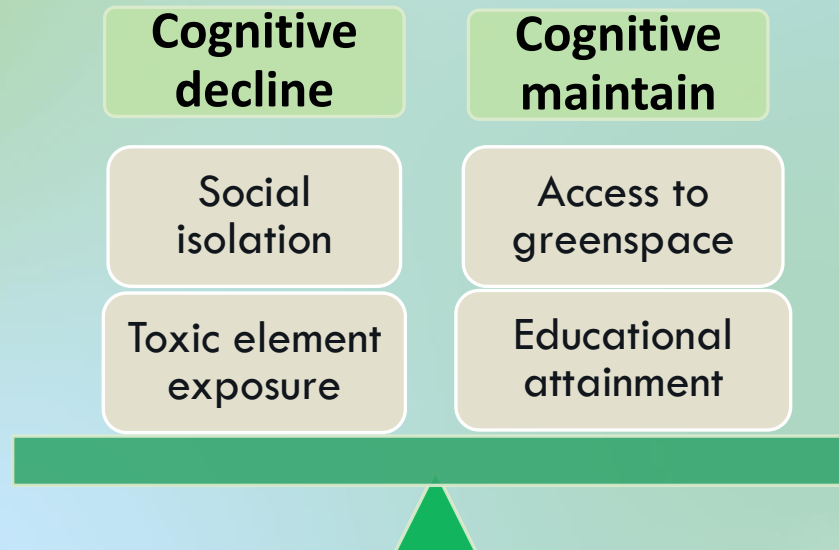
This work was supported by **UK Research and Innovation** [ES/V016075/1]





# OUR HEALTH IS LINKED TO THE ENVIRONMENT where we are born, live, and work

How do factors in our external environment get 'under the skin' to change our biology and affect health outcomes?



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# OUR HEALTH IS LINKED TO THE ENVIRONMENT where we are born, live, and work



Decreased risk of disease  
Increased longevity  
Maintenance of biological processes



DNA methylation  
Histone modification  
Changes in chromatin structure



Increased risk of disease  
Disease progression  
Age acceleration  
Biomarker of risk or disease

Biological changes in response to environmental stimuli

Epigenetic changes (DNA methylation) can be risk factors or protect against disease...some **damage is reversible!**

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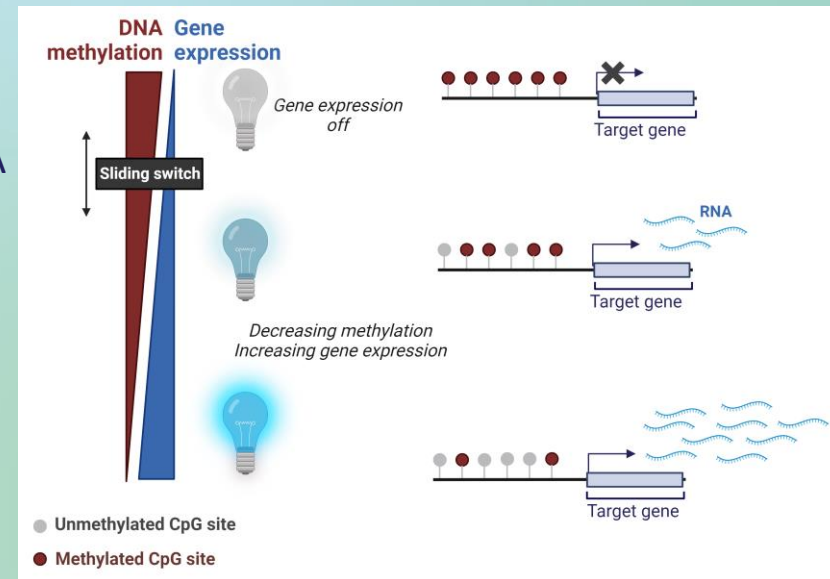


# WHAT IS EPIGENETICS?

- *Epi* = on top of
- *Genetics* = your genes that are typically inherited from parents
- Epigenetics describes the influence of chemical changes to DNA that lead to modifications in gene expression
- Epigenetics explains how a person's environment interacts with their genetics

## DNA METHYLATION

- regulates gene expression like dimmer switch without altering DNA sequences
- is the most studied and therefore the best understood epigenetic modification



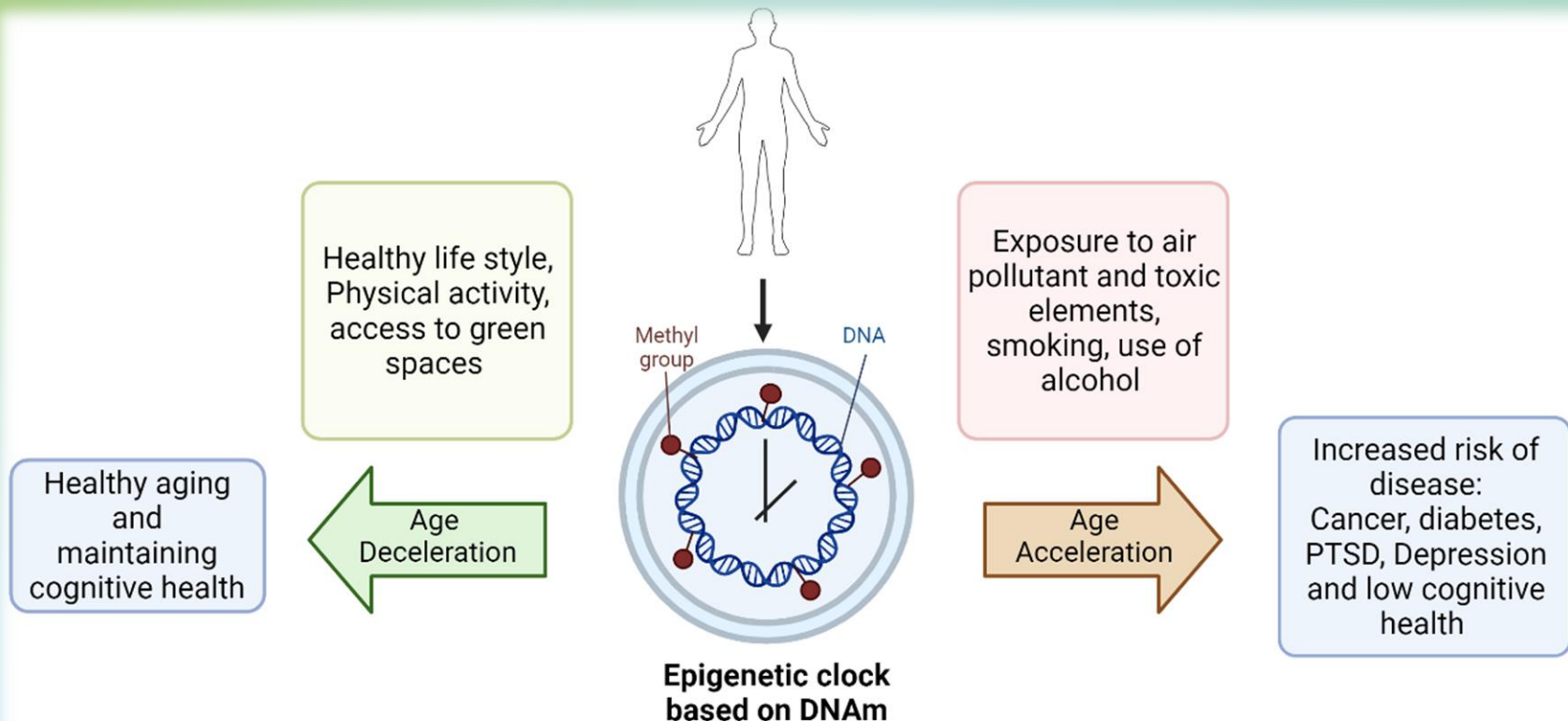
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# DNA METHYLATION (DNAm) AGE

- Epigenetic clocks are biomarker signatures that estimate biological age compared to years of life.
- Eleven epigenetic clocks have been generated for NICOLA.
- These clocks will help to demonstrate what environmental features lead to accelerated biological ageing & poor health outcomes.





# HOW CAN EPIGENETIC CLOCKS BE USED TO UNDERSTAND ENVIRONMENTAL INFLUENCE ON OUR DNA?

Discrepancies between epigenetic and chronological ages indicate accelerated ageing

Assess impact of environmental exposures over time

Identification of high-risk individuals susceptible to adverse effects of environmental exposures

**Epigenetic  
Clock  
Analysis**

Identify links between molecular biology, environmental exposures and overall health

Biomarkers of past environmental exposures

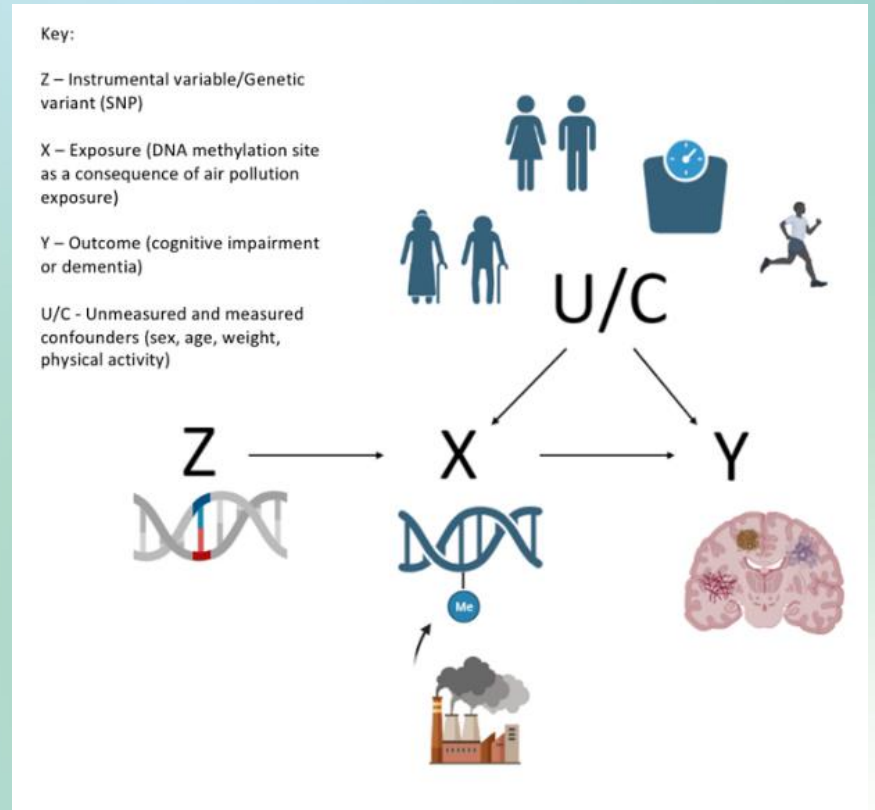
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# MENDELIAN RANDOMISATION (MR)

- MR can be used to find **causal associations** between a particular exposure (such as pollution) (X) and an outcome (such as dementia) (Y).
- This is possible because our **genetic** make-up does not change over our life course, so we are able to determine genetic correlations between an exposure and an outcome.
- A fundamental basis of MR is that our genetic make-up is defined at conception, before the influence of **confounders** (U/C).
- Our **epigenetic** make-up does change over our lifetime, so we can't use epigenetic markers (X) directly in MR analysis. However, we can use the genetic changes that we know alter particular epigenetic changes (Z) as substitutes.



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# SPACE

SUPPORTIVE ENVIRONMENTS FOR  
PHYSICAL & SOCIAL ACTIVITY,  
HEALTHY AGEING & COGNITIVE HEALTH

# Thank you

*Figures created with Biorender.com*

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