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Are housing circumstances associated with faster epigenetic ageing?: a commentary on Clair et al

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We read the article by Clair et al. (2023) reporting an association between housing and biological ageing with great interest [1]. This publication built upon preliminary work on how the physically built environment associates with DNA methylation (DNAm) [2] by focusing on DNAm age (also known as epigenetic age or epigenetic clock).

However, we note the authors investigated only one DNAm age measure: DunedinPACE. The authors argued that DunedinPACE was selected due to its greater association with mortality and morbidity than other measures of epigenetic age. Whilst the paper they cited did indeed show that DunedinPACE predicted mortality better than the Hannum, Horvath, and Levine clocks [3], it did not compare the performance of DunedinPACE to GrimAge, a more recently developed epigenetic clock for mortality.

Associations between exposures and DNAm age vary widely according to which clocks are used. Hence, we sought to replicate the finding reported by Clair et al. using both GrimAge (acceleration) and DunedinPACE measures of DNAm age in an independent cohort of children. We tested whether housing quality predicted GrimAge acceleration and DunedinPACE, in a sample of 782 children in the Avon Longitudinal Study of Parents and Children (ALSPAC) [4, 5], with housing quality measured in early childhood (birth to 2.75 years) and DNAm age at 7 years. This dataset contrasts the sample of adults used by Clair et al. (mean age=55.4 years, N=1420).

Using these data and the DunedinPACE clock, we replicated the association between poor housing quality and epigenetic ageing, as reported in Clair et al. (Table 1). By contrast, we

found no association between housing quality and GrimAge acceleration, suggesting housing quality may associate with rates of ageing, rather than ageing-related processes linked to mortality.

Table 1. *Associations between poor housing quality in early childhood (birth to 2.75 years) and DNAm age at age 7 in ALSPAC (n=728).*

Measure of DNAm Age	Standardised estimate (95% CI)	<i>p</i> value
DunedinPACE	0.060 (0.016, 0.103)	0.007
GrimAge acceleration	0.481 (-0.295, 1.256)	0.255

Note. GrimAge acceleration is defined as the difference between GrimAge and chronological age.

The variability in associations across different epigenetic clocks could be attributed to differences in the training datasets or outcomes used to create the clocks. For instance, DunedinPACE was trained to predict aging-related decline over a 19-year period in a sample from 26 to 45 years (n=817), while GrimAge was trained to predict mortality in a slightly older sample from 24 to 92 years (n=2754). It is also possible that DunedinPACE leverages CpG sites more strongly associated with housing than those included in GrimAge.

We hope our findings help readers better understand the complexity of epigenetic clocks, and how findings can differ depending on which clocks are used to estimate biological age.

Acknowledgments & Ethics

We are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team.

Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004).

Data Availability

Please note that the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool

(<http://www.bristol.ac.uk/alspac/researchers/our-data/>).

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