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Structural Racism, Discrimination and Epigenetics: How Social Inequality May Become Biologically Embedded

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Expats & Immigrants B.V.

Abstract: This article examines the relationship between structural racialisation, discrimination, social inequality, and epigenetic processes, with particular attention to the concept of biological embedding. Rather than conceptualising race as a biological characteristic, the analysis treats racialisation as a socially constructed process through which historical, institutional, economic, and environmental conditions can generate unequal exposures across populations. Social epigenetics provides a potential framework for understanding how socioeconomic disadvantage, neighbourhood conditions, environmental hazards, unequal healthcare access, racialised discrimination, and chronic psychosocial stress may influence physiological regulation, including DNA methylation and measures of epigenetic ageing. The available evidence suggests associations between adverse social conditions and epigenetic measures of biological ageing, although findings vary across populations, exposures, methodologies, and epigenetic clocks. Consequently, epigenetic differences observed between racialised populations should not be interpreted as evidence of inherent biological differences; rather, they may reflect differential exposure to socially structured environments. This perspective shifts the analytical focus from presumed biological differences between populations towards the processes through which racialised social environments create unequal biological exposures and potentially divergent health trajectories. Particular caution is required regarding intergenerational and transgenerational epigenetic inheritance. Although historical racialisation, enslavement, colonialism, socioeconomic inequality, and other forms of adversity can produce consequences extending across generations, current human evidence does not justify assuming that such effects are routinely transmitted through inherited epigenetic modifications. Intergenerational persistence can instead occur through family relationships, socioeconomic resources, neighbourhood environments, cultural memory, institutional arrangements, continuing discrimination, and renewed exposure to adversity in each generation. Epigenetic processes may contribute to these pathways but should not be presumed to constitute their principal mechanism. This article therefore advances a non-deterministic interpretation of social epigenetics: social inequality can become biologically embedded without becoming biologically predetermined. This framework has important implications for research and policy because it locates potential biological inequalities not in racialised populations themselves, but in the unequal social, economic, institutional, and environmental conditions to which populations are differentially exposed.

Keywords: social epigenetics, structural racialization, racialised inequality, discrimination, biological embedding, DNA methylation, epigenetic ageing, weathering, socioeconomic inequality, social determinants of health, health inequalities, intergenerational transmission, transgenerational epigenetic inheritance, colonialism, social adversity.

INTRODUCTION

Structural racism and discrimination are generally conceptualised as social, political and institutional phenomena. Epigenetics adds an important biological dimension to this analysis by investigating how social and environmental experiences can influence the regulation of gene activity without altering the underlying DNA sequence. The emerging field of **social**

epigenetics therefore raises an important question: can persistent exposure to discrimination, socioeconomic disadvantage, environmental hazards and chronic stress become biologically embedded and thereby contribute to health inequalities?

Race is understood in this article not as a discrete biological characteristic, but as a socially constructed system of classification. Accordingly, the terms racialisation, racialised populations, and racialised inequalities are used where they more accurately describe the social processes under investigation.

A growing body of research suggests that this is plausible. Social adversity—including socioeconomic disadvantage, neighbourhood conditions, psychosocial stress and experiences of racialised discrimination—has been associated with differences in DNA methylation and measures of epigenetic ageing (Lawrence et al., 2022). A major 2026 systematic review and meta-analysis encompassing 140 studies, 65,919 participants and 1,065 effect sizes provides further evidence that socioeconomic position and racialised social circumstances are associated with epigenetic measures of biological ageing, although associations differ according to the epigenetic clock and methodological characteristics used (Willems et al., 2026).

These findings require careful interpretation. Epigenetic research does not demonstrate that socially constructed racial groups possess fundamentally different biological essences. Nor does current evidence establish that the trauma of enslaved people or colonialism is routinely transmitted through epigenetic mechanisms over many human generations. Rather, the strongest contemporary interpretation is that: Persistent exposure to social environments characterised by racialised and socioeconomic inequalities may become biologically embedded through physiological and epigenetic processes. This distinction is crucial for understanding the relationship between structural racialisation and biology.

FROM GENETICS TO EPIGENETICS

DNA contains genetic information, but genes do not function independently of their cellular and environmental context. Epigenetic processes help regulate whether and how strongly particular genes are expressed. Important mechanisms include DNA methylation, histone modifications and non-coding RNAs.

DNA methylation is especially prominent in human social-epigenetic research. It involves chemical modifications associated with the regulation of gene activity and can be influenced by development, ageing, environmental exposures and behavioural and social conditions.

This produces a conceptual shift from the simplistic model: genes → health towards a more dynamic model: genes × environment × social experience → biological regulation → health

Social epigenetics investigates part of this interaction. It asks how experiences such as poverty, stress, discrimination, violence, neighbourhood disadvantage or environmental contamination may become biologically embedded. Lawrence et al. (2022), reviewing this literature, identify socioeconomic position, racialised and social inequality, psychosocial stress and neighbourhood environments as social exposures associated with DNA-methylation patterns relevant to health inequality.

Structural Racism as an Exposure System

A particularly important theoretical development follows from distinguishing interpersonal discrimination from structural racialisation. Interpersonal discrimination concerns interactions between individuals.

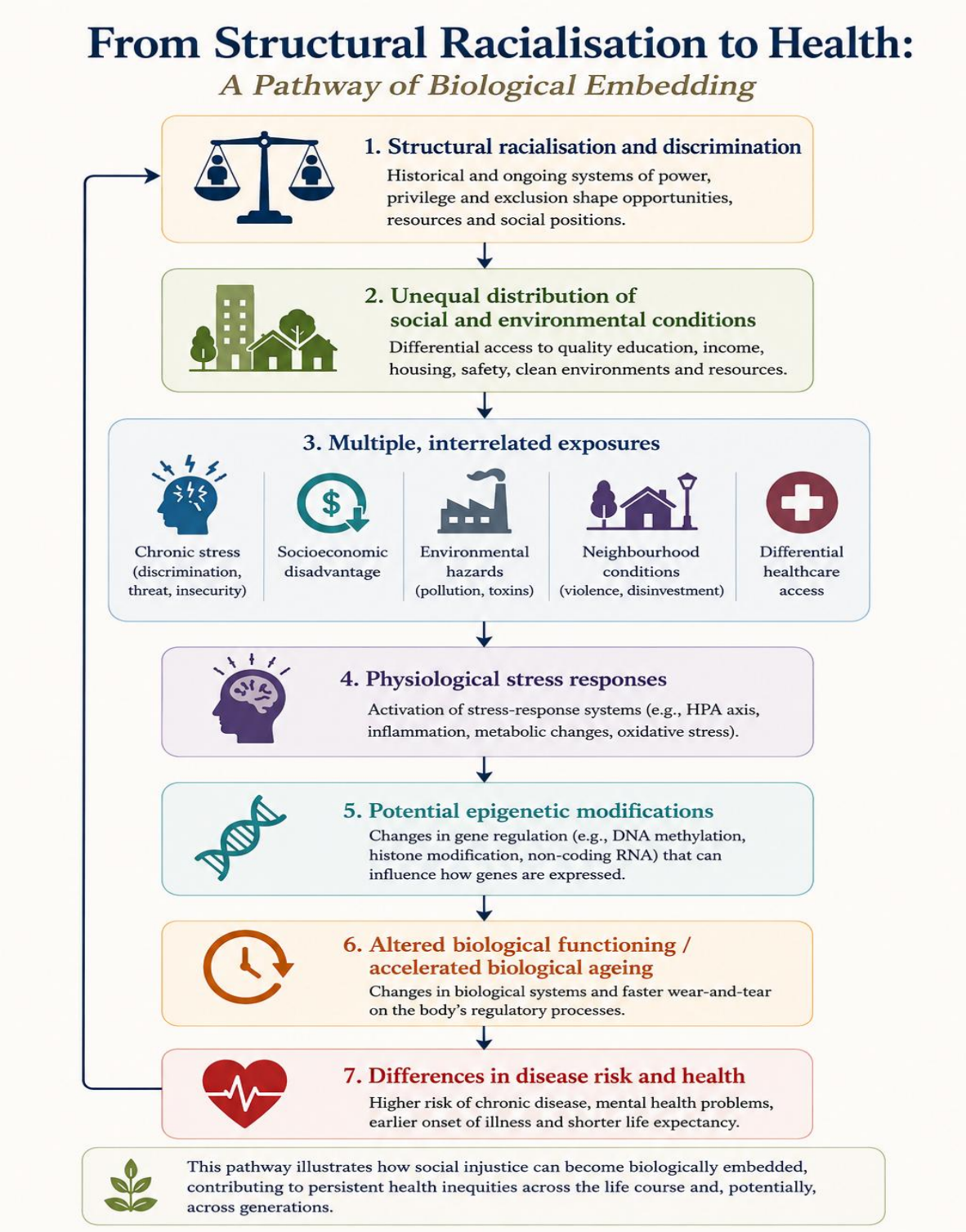

Figure 1: From Structural Racialisation to Health (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

Structural racialisation operates through interconnected institutions, historical arrangements and distributions of resources. These may include residential segregation, labour-market discrimination, unequal educational opportunities, environmental inequality, differential policing, healthcare access and unequal exposure to economic insecurity. Structural racialisation should therefore not be conceptualised as a single biological exposure. Rather, it can generate multiple downstream exposures. A useful model can be found below.

This model is consistent with the emerging social-epigenetic literature but should be regarded as a framework of interacting and probabilistic pathways rather than a deterministic chain.

Discrimination and Chronic Stress

A pathway involves chronic psychosocial stress. Discrimination may generate repeated experiences of threat, vigilance, uncertainty, exclusion and reduced control. These experiences can activate biological stress-regulation systems, including the hypothalamic–pituitary–adrenal axis and related inflammatory and neuroendocrine processes.

An isolated discriminatory event may be stressful, but structural discrimination can produce something more consequential: repeated exposure across multiple domains and over extended periods.

For example, the same individual might experience disadvantage in: education → employment → income → housing → neighbourhood conditions → healthcare.

These exposures can accumulate across the life course. Epigenetics provides one possible molecular mechanism through which such social experiences become biologically embedded. A systematic review by Lim et al. (2022) examined studies of trauma, racialised discrimination and epigenetic ageing. The evidence was heterogeneous, but several studies associated trauma, post-traumatic stress or discrimination with accelerated epigenetic ageing. The authors also emphasised the small number of studies and methodological limitations of the evidence base.

Thus, the scientifically defensible conclusion is not that discrimination inevitably changes DNA methylation, but that chronic racialised discrimination represents a plausible social exposure capable of influencing stress-related biological processes, including epigenetic regulation.

Evidence from Racialised Discrimination

Several empirical studies provide more direct evidence. Research reviewed by Lawrence et al. (2022) found evidence linking perceived racialised discrimination (discrimination operating through socially constructed racial categories) with DNA methylation and epigenetic ageing. For example, longitudinal research involving ´black´ adolescents found that greater exposure to racialised discrimination was associated with accelerated epigenetic ageing in young adulthood. Importantly, supportive family environments appeared capable of moderating some of these associations.

This latter observation is theoretically significant. It suggests that biological embedding should not be interpreted as irreversible biological damage. Social exposures may create risk, while protective social environments may buffer that risk.

More recent research from the Black Women's Health Study[1] provides further evidence. In an epigenome-wide study involving 384 participants, racialised-related or discrimination-related exposure/stress were associated with methylation differences at particular CpG sites. Greater reported exposure to racism was also associated with accelerated ageing according to more than one epigenetic clock. The researchers concluded that discriminatory experiences may affect the epigenome and potentially contribute to earlier disease development (Coogan et al., 2024).

These studies do not prove that racism-related experiences alone caused the observed epigenetic differences. They do, however, strengthen the evidence that racialised-related or discrimination-related exposure/stress can correlate with measurable biological processes.

The Weathering Hypothesis and the Epigenetic Clocks

Social epigenetics also intersects with Geronimus's influential concept of weathering. The weathering hypothesis proposes (Forde et al. 2023) that chronic exposure to social, economic and racial disadvantage/ exclusion can cause physiological deterioration to accumulate more rapidly among marginalised populations. The metaphor is useful: just as material exposed repeatedly to harsh environmental conditions can weather more rapidly, human biological systems subjected to persistent adversity may exhibit earlier deterioration.

Research by Simons et al. (2021), for example, examined biological ageing among African Americans using the GrimAge epigenetic measure[2]. Income, education, neighbourhood conditions and unequal treatment/discrimination/exclusion predicted accelerated biological ageing, providing evidence consistent with the weathering hypothesis. Epigenetic clocks therefore provide one potential method for investigating whether unequal social environments are associated with differences in the pace of biological ageing. This does not mean that socially disadvantaged groups are genetically programmed to age faster. The interpretation is almost the opposite: different social environments may contribute to different biological trajectories.

Epigenetic clocks[3] are mathematical models (Appendix 1: AI https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa) that measure the precise biological age of an organism by analysing chemical changes on the DNA. While your chronological age simply counts the number of birthdays you have celebrated, an epigenetic clock measures the actual cellular wear and tear of your body. Here is an overview of how they work, the different generations of clocks, and how they expose social inequality. How does an epigenetic clock work? Most epigenetic clocks are based on a process called DNA methylation:

1. **Chemical switches**[4]: Your DNA contains millions of sites called CpG sites[5]. These are specific spots where tiny chemical molecules (methyl groups) attach themselves to the DNA. They act like "light switches" that turn genes on or off.

2. **Predictable patterns**: As we grow older, the pattern of these switches changes in a highly predictable manner (Satapathy et al. 2026).
3. **Algorithms**: Scientists use artificial intelligence and machine learning to analyse the patterns of thousands of individuals. The software selects the most reliable DNA locations and calculates your biological age based on them (Brighton, 2023).

When your biological age is higher than your calendar age, scientists refer to this as epigenetic age acceleration (EAA). This is a strong predictor of age-related diseases and premature mortality.

The Evolution of the Clocks (Three Generations)

Not every clock measures the same thing. The science has made enormous leaps forward over the last few years:

Generation	**Notable Examples**	**What does it measure?**	**What was it trained on?**
1st Generation *(The Chronological Estimators)*	Horvath's Clock Hannum's Clock	Your actual calendar age.	Trained to guess a person's birth year based on DNA markers.
2nd Generation *(The Health and Mortality Risk Clocks)*	PhenoAge GrimAge	Your risk of illness and death.	Trained on blood values (such as inflammatory markers) and the remaining lifespan of test subjects.
3rd Generation *(The Speedometers)*	DunedinPACE	The *pace* at which you are ageing right now.	Trained by following the same cohort of people for decades to see how quickly their organs decline.

Why the 3rd Generation Epigenetic Clocks Proves the 'Weathering' Concept?

The first generation of clocks was revolutionary, but it missed the profound impact of social stress. Because they were trained on chronological age, they often mistook a 40-year-old who had lived a harsh life for an average 40-year-old.

Research demonstrates that newer generations of clocks (such as DunedinPACE) are exceptionally sensitive to social inequality:

1. **Sensitive to poverty and discrimination (unequal treatment/ exclusion)**: Individuals exposed to systemic disadvantage, chronic stress, or racism-related experiences or discrimination-related exposure/stress show a drastic acceleration on these biological speedometers.
2. **The biological echo of childhood**: Large-scale meta-analyses show that growing up in poverty or facing childhood adversity leaves a permanent scar on the epigenome. Even if someone becomes financially successful or secure later in life, the epigenetic clock often keeps ticking faster due to that early-life stress.
3. **Visible in children**: Whilst older clocks detected no ageing in children, 'speedometers' now reveal that socioeconomic disadvantage activates biological ageing even in young children.

Can the Clock be Turned Back?

Unlike your fixed DNA sequence, the epigenome is highly adaptable. Recent clinical studies suggest that the clock can be slowed down or even partially reversed through targeted interventions. Factors such as intense stress reduction, exposure to green spaces, a healthy diet, and trauma-informed therapy can favourably influence DNA methylation and decelerate the biological clock.

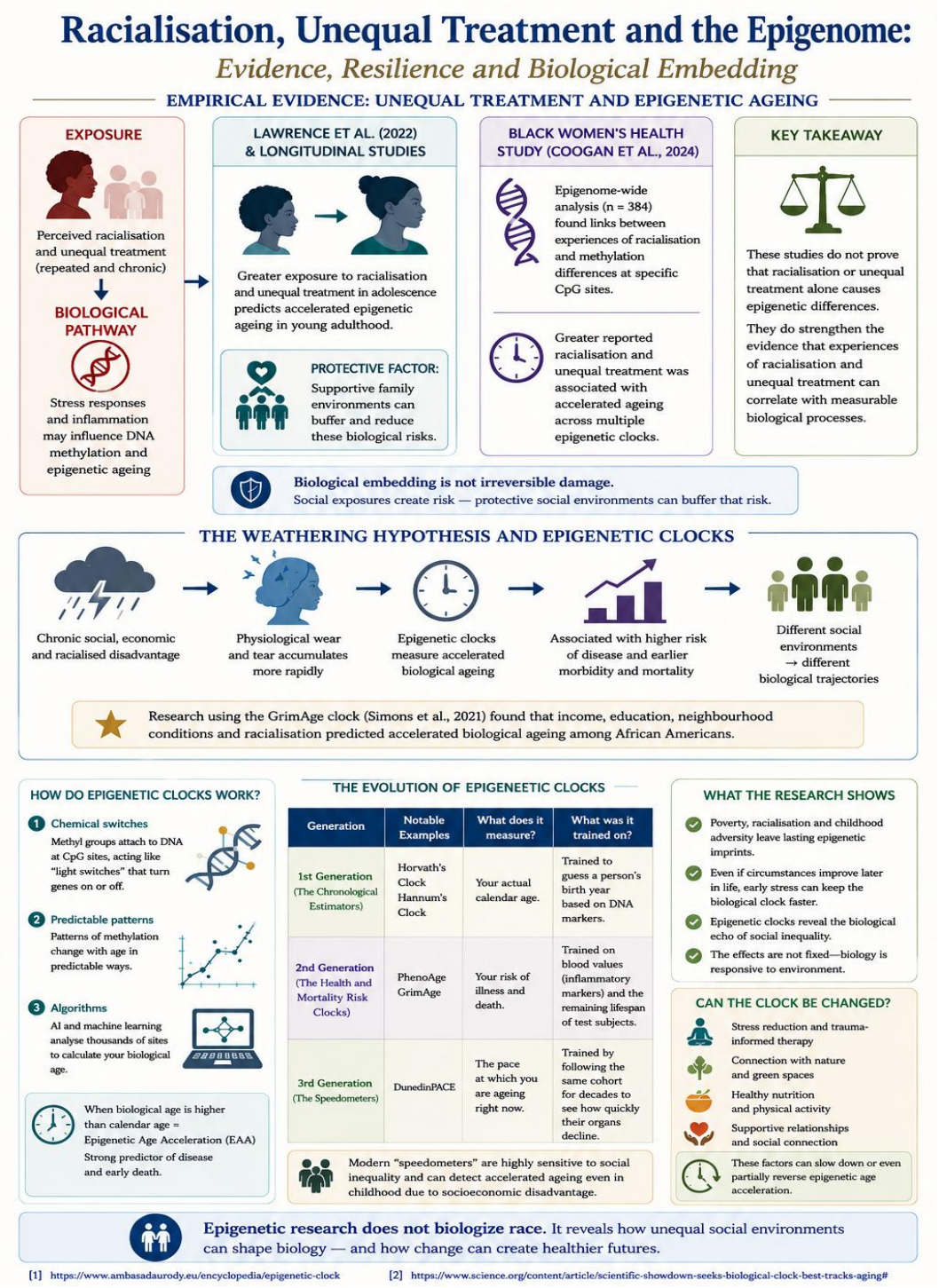

Figure 2: Racialisation, Unequal Treatment and the Epigenome (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

Socioeconomic Inequality as a Pathway

Structural racialisation and discrimination frequently intersects with socioeconomic inequality. Discrimination/ exclusion in education, employment, housing and access to capital can affect the distribution of income and wealth. Socioeconomic disadvantage/ exclusion can subsequently influence nutrition, housing quality, exposure to pollution, neighbourhood safety, healthcare access and chronic financial stress.

Figure 3: The Recursive Pathway from Structural Racism to Health Inequality (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

The 2026 meta-analysis by Willems et al. is particularly important here because it synthesised 140 studies investigating socioeconomic status and race/ethnicity in relation to epigenetic clocks. The findings strengthen the broader proposition that social determinants are associated with biological ageing, although the evidence varies by measure and much of the research remains concentrated in the United States.

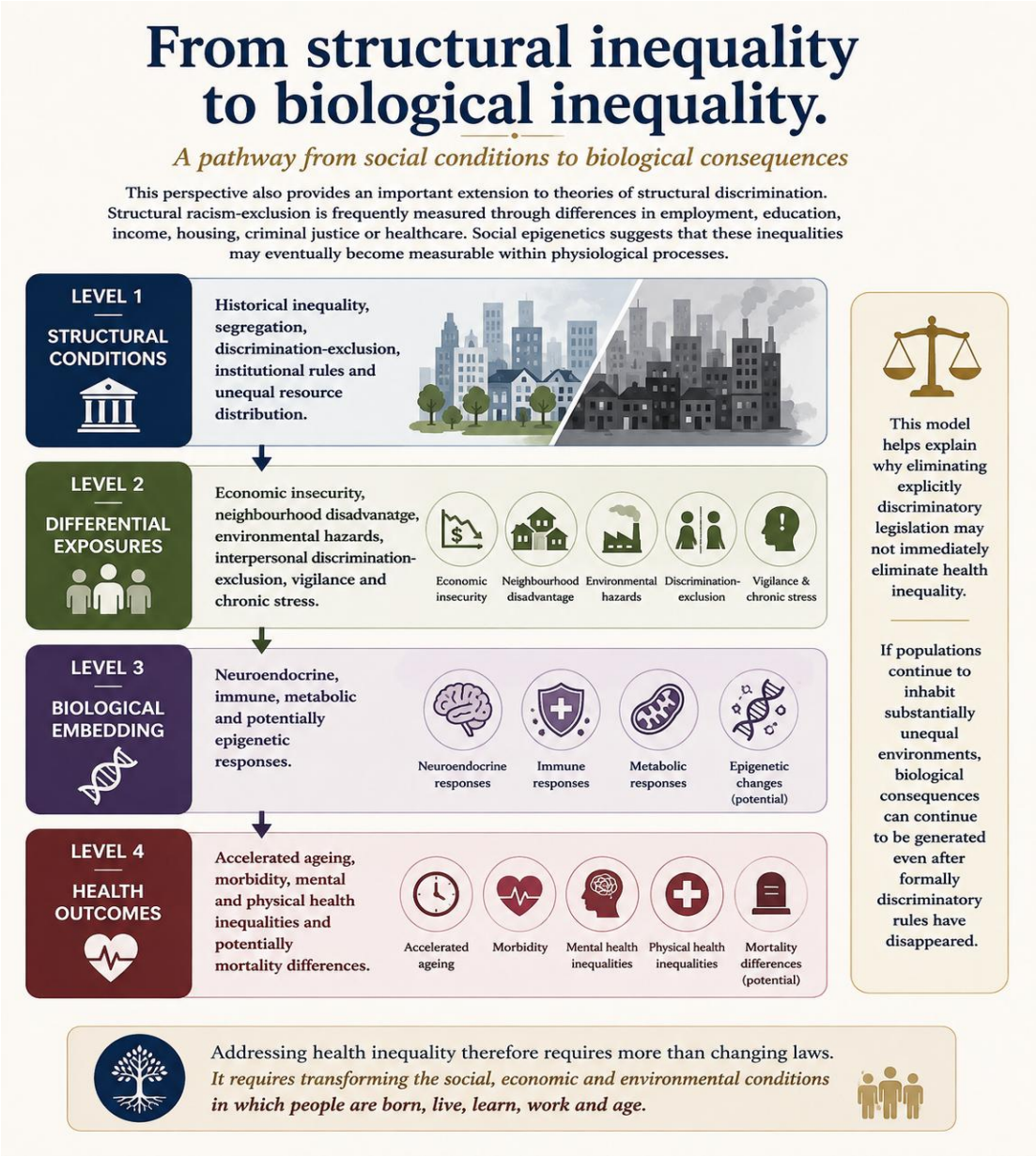

Figure 4: From structural inequality to biological inequality (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

Consequently, epigenetic differences associated with racialised populations should not automatically be interpreted as effects of "racialisation." They may instead reflect differences in **social exposures correlated with racialised classification**.

Racialisation-related experiences must not be biologized. This point deserves particular emphasis. The emerging relationship between racism and epigenetics creates a

scientific danger: research intended to demonstrate the biological consequences of structural racialisation and social inequality can inadvertently be interpreted as demonstrating biological racialisation differences.

Those are fundamentally different propositions. King et al. (2024) specifically caution epigenetic researchers to examine how racialisation terminology is used. They recommend measuring social and structural conditions—including institutional inequality—rather than treating racialisation itself as an uncomplicated biological variable.

A preferable conceptual model is therefore:

- **Not: Exposure to socioeconomic disadvantage, unequal treatment, chronic psychosocial stress and other conditions associated with racialisation → epigenetic difference.**
- **But: racialisation / structural conditions → differential exposures → biological responses**

This shifts causal attention from supposed biological properties of populations to the social conditions under which populations live. In this sense, social epigenetics can potentially contribute to the **de-biologisation of racialisation** rather than its biological reification.

The Crucial Question of Intergenerational Transmission

The most controversial issue concerns whether epigenetic consequences of racialisation, slavery, colonialism or other historical trauma can be biologically transmitted across multiple generations. Here, considerable scientific caution is necessary. There is convincing evidence from animal research that certain environmental exposures can generate epigenetic effects that persist across generations under particular conditions. The molecular mechanisms of transgenerational epigenetic inheritance are an active field of research. See figure 5.

Figure 5: The crucial question intergenerational transmission (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

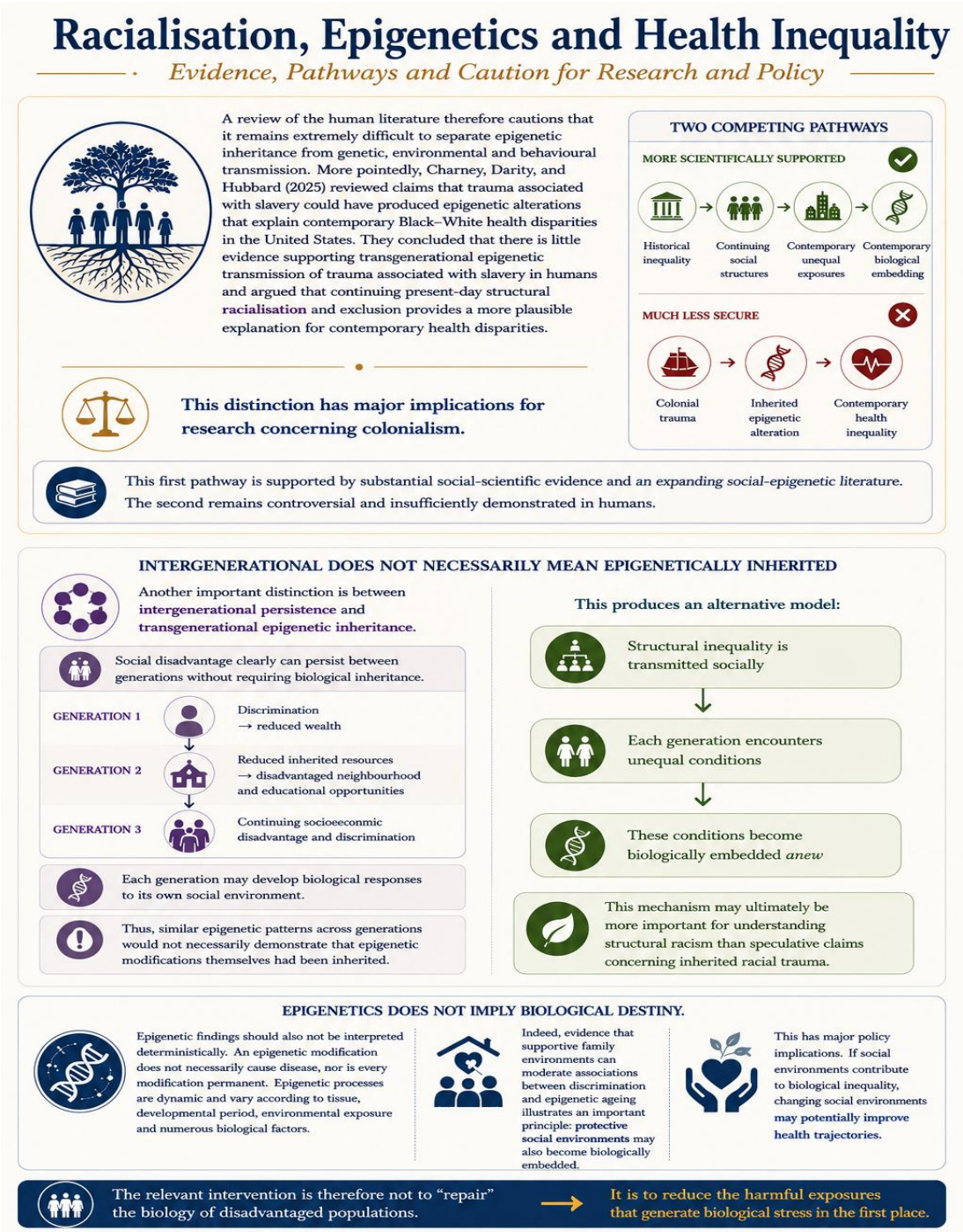

Figure 6: Racialisation, Epigenetics and Health Inequality (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

Implications for Structural-Racialised Research

Social epigenetics potentially strengthens structural analyses in three ways.

- **First**, it provides mechanisms through which social conditions may influence physical health. Structural discrimination is thereby connected to biological outcomes without reducing racialisation to individual prejudice.

- **Second**, it demonstrates why apparently abstract institutional inequalities can have tangible consequences. Housing discrimination, labour-market exclusion or neighbourhood segregation may ultimately influence exposure to stress, pollution, nutrition and healthcare—all of which can affect biological functioning.
- **Third**, it shifts the scientific question away from: *"Are racial groups biologically different?"* towards: ***"How do racialised social environments create different biological exposures?"***

That is a profound conceptual change. It treats racialisation as a potential **cause of biological difference**, rather than treating biological difference as a cause of racialised inequality.

CONCLUSION

The relationship between epigenetics and structural racialisation represents an important but still developing area of interdisciplinary research. Current evidence supports the proposition that social adversity, socioeconomic disadvantage and experiences of racialised discrimination can be associated with DNA methylation and epigenetic measures of biological ageing. Recent large-scale synthesis further indicates associations between social determinants of health and epigenetic ageing, although effect sizes, measures and study populations remain heterogeneous.

The strongest interpretation of this literature is therefore one of **biological embedding**. Structural racialisation can shape the environments in which individuals live: their economic security, neighbourhoods, exposure to racialised discrimination, environmental hazards, healthcare access and chronic stress. These conditions can influence physiological processes, of which epigenetic regulation represents one possible mechanism. See figure 7.

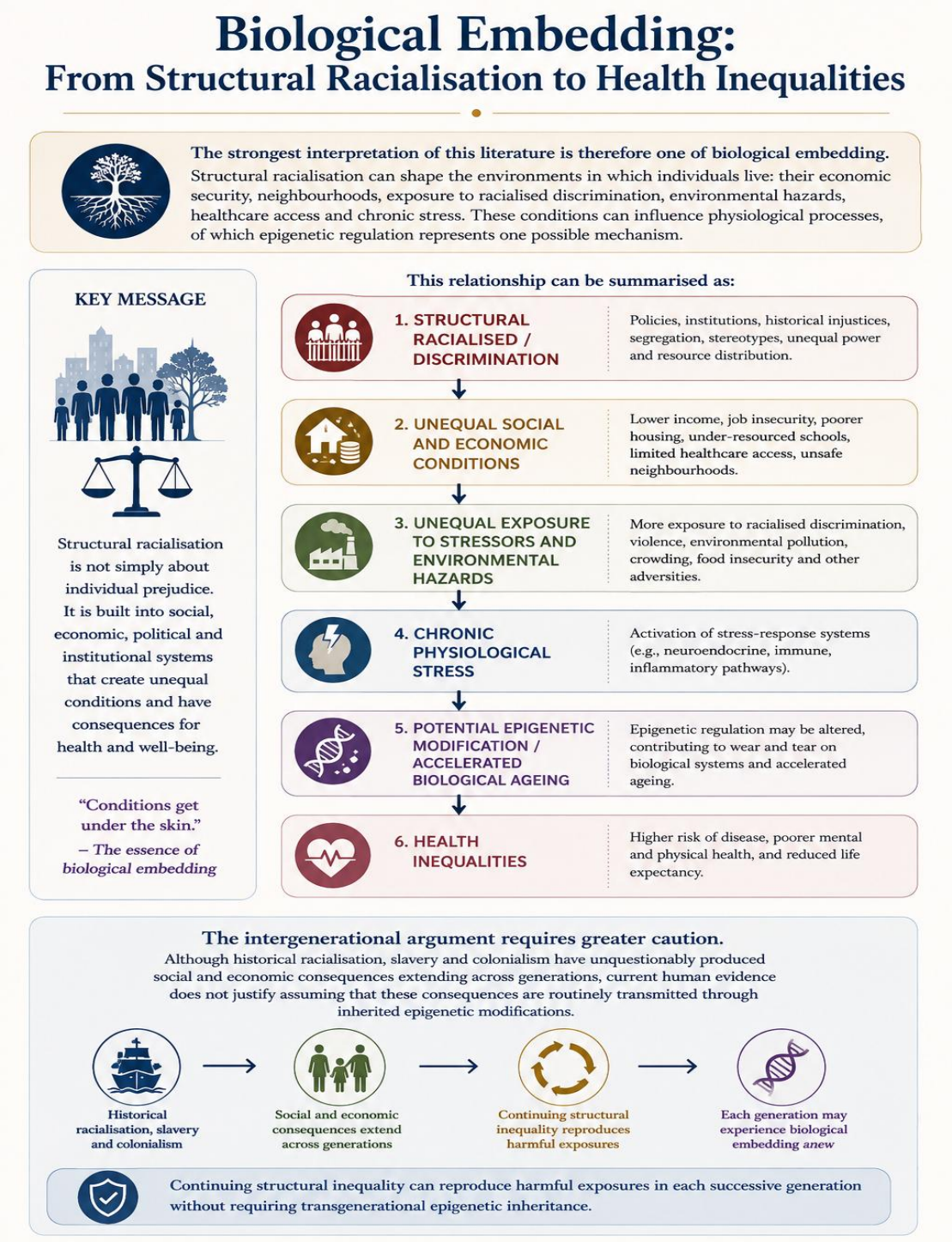

Figure 7: Biological Embedding: From Structural Racialisation to Health Inequalities (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

The intergenerational argument requires greater caution. Although historical racialisation, slavery and colonialism have unquestionably produced social and economic consequences extending across generations, current human evidence does not justify assuming that these consequences are routinely transmitted through inherited epigenetic modifications. Continuing structural inequality can reproduce harmful exposures in each successive generation without requiring transgenerational epigenetic inheritance.

The most defensible conclusion is consequently also the most socially significant: **social inequality can become biologically embodied without becoming biologically predetermined**. Epigenetics does not demonstrate that racialised inequality is natural. On the contrary, social epigenetics increasingly suggests that some biological inequalities may partly record the unequal environments that societies have created.

In that sense, the body should not be interpreted as evidence that racialised categories are biologically real. It can instead be understood as one place in which the consequences of **socially real racialisation and discrimination** may become measurable.

An Illustrative Example: It Didn't Start With You

The concept of intergenerational transmission of trauma has been popularised by Mark Wolynn in *It Didn't Start With You: How Inherited Family Trauma Shapes Who We Are and How to End the Cycle* (2016-2025). Wolynn proposes that unresolved traumatic experiences within families can influence subsequent generations, potentially manifesting as anxiety, depression, fears, behavioural patterns, physical symptoms, and difficulties for which individuals cannot identify an obvious cause within their own lives. His approach combines family-history reconstruction with psychological, neuroscientific, and epigenetic explanations of intergenerational trauma (Wolynn, 2016-2025).

One example described in connection with Wolynn's approach concerns a woman experiencing an intense fear that her child would die. Investigation of her family history revealed that her grandparents had lost two children before immigrating to the United States. Wolynn interprets cases such as this as illustrating how unresolved traumatic experiences may continue to influence emotional patterns within subsequent generations.

This perspective can be connected to structural racism and discrimination, although the connection requires an additional analytical level. Consider, for example, a hypothetical family exposed to racial persecution, forced displacement, colonial violence or systematic discrimination. The first generation may experience severe insecurity, violence, poverty or loss. These experiences may influence psychological functioning, family relationships and physiological stress regulation. Their children may subsequently grow up not only within a family affected by those experiences but also, if structural discrimination continues, within social conditions that reproduce some of the original stressors. The pathway may therefore be represented as:

This formulation is important because the intergenerational effects described by Wolynn do not necessarily require epigenetic inheritance. Trauma can be transmitted between generations through parenting, attachment, family narratives, silence surrounding traumatic events, learned threat responses, socioeconomic conditions, neighbourhood environments, cultural memory and continuing discrimination. Epigenetic processes constitute one possible biological pathway among several.

A distinction must therefore be made between intergenerational trauma and transgenerational epigenetic inheritance. The former is well supported as a broad psychological and social phenomenon. The latter—particularly claims that specific trauma-induced epigenetic modifications are transmitted through the human germline across several generations—remains scientifically contested and difficult to demonstrate

conclusively. Contemporary research continues to investigate possible epigenetic mechanisms, including in PTSD, but substantial methodological and causal uncertainties remain.

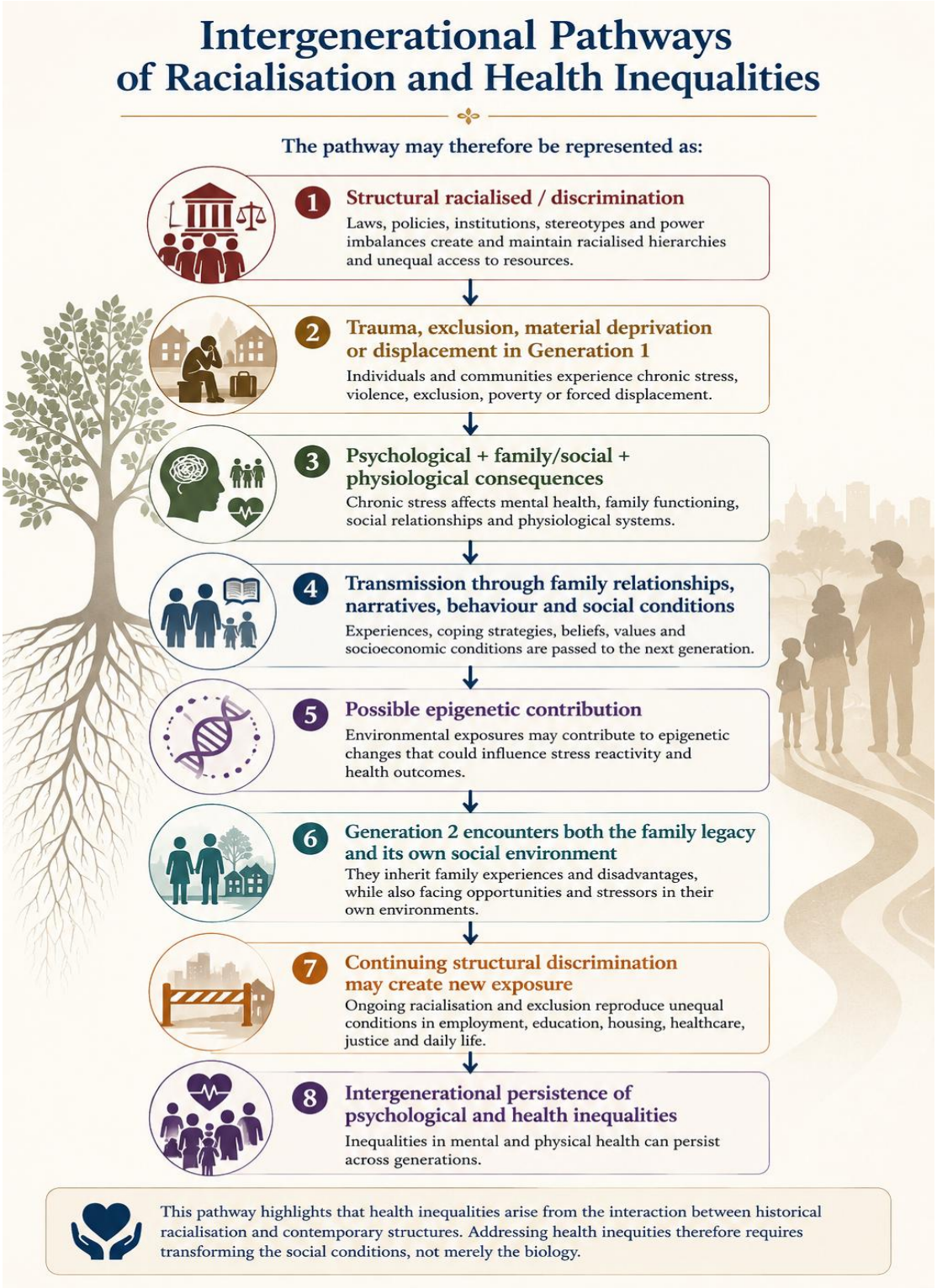

Figure 8: Intergenerational Pathways of Racialisation and Health Inequalities (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

This distinction becomes particularly important when applying Wolynn's ideas to slavery, colonialism and structural racism. It would be scientifically premature to argue that contemporary descendants necessarily carry an inherited epigenetic imprint of colonial or racial trauma.

Figure 9: A More Strongly Supported Model: How Historical Inequalities Persist Across Generations (AI: https://chatgpt.com/c/6a797ffa-6574-83eb-859f-4702ddb469fa)

This model does not exclude epigenetic inheritance, but importantly, it does not require it. Wolynn's work is therefore valuable as an accessible illustration of the proposition that an individual's psychological experience cannot always be understood independently of family history. For an academic analysis of structural racism, however, his model should be expanded from the family level to the societal level. Families do not transmit their histories in isolation; successive generations develop within political, economic and institutional environments. When discriminatory structures persist, what appears to be an inherited consequence of historical trauma may partly represent the renewed biological embedding of inequality in each generation.

In other words: the effects of trauma can travel across generations because families transmit experiences, relationships and resources, while societies transmit institutions, inequalities and environments. Epigenetic processes may contribute to this transmission, but they should not be assumed to constitute its sole—or even primary—mechanism.

In this sense, Wolynn's proposition that *"it didn't start with you"* can be extended to structural racialisation: some contemporary inequalities did not originate with the individuals currently experiencing them. Yet the scientific emphasis should remain on identifying the specific social, psychological, economic, environmental and biological pathways through which historical conditions continue to influence present generations.

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APPENDIX 1: MATHEMATICAL FORMULAS OF EPIGENETIC CLOCKS

From DNA methylation to biological age, age acceleration, GrimAge and DunedinPACE

Most epigenetic clocks are weighted statistical models. DNA methylation measurements at selected CpG sites are multiplied by fitted coefficients and combined into an age- or ageing-related score. The clocks differ mainly in the outcome they were trained to predict.

Basic Mathematical Model

Let M_i denote the DNA methylation level at CpG site i. A generic DNA-methylation clock can be written as:

$$\hat{A}_{epi} = \beta_0 + \Sigma_{i=1}^{p} \beta_i M_i$$

$$\hat{A}_{epi} = \beta_0 + \beta_1 M_1 + \beta_2 M_2 + \cdots + \beta_p M_p$$

- $\hat{A}_{epi}$ = predicted epigenetic or biological age
- β_0 = intercept

- M_i = methylation level at CpG site i
- β_i = statistical weight assigned to that CpG
- p = number of CpG sites included in the model

How the Coefficients are Obtained

Many clocks use penalised regression, especially elastic-net regression. A simplified objective function is:

$$\hat{\beta} = \arg\min_{\beta} \left[\|y - X\beta\|_2^2 + \lambda_1\|\beta\|_1 + \lambda_2\|\beta\|_2^2 \right]$$

Here, y is the target outcome, X contains methylation measurements, and λ_1 and λ_2 penalise model complexity. This allows the model to select informative CpG sites from a much larger set of measured sites.

Horvath's Epigenetic Clock

Horvath's original multi-tissue clock uses 353 CpG sites. Conceptually, the methylation score is:

$$S = \beta_0 + \sum_{i=1}^{353} \beta_i M_i$$

Because chronological age was transformed during model development, the final age estimate can be represented conceptually as:

$$\text{DNAmAge} = g^{-1}\left(\beta_0 + \sum_{i=1}^{353} \beta_i M_i \right)$$

The inverse transformation g^{-1} converts the fitted methylation score back into years. The clock therefore detects a multivariate methylation pattern that statistically predicts chronological age.

Epigenetic Age Acceleration (EAA)

A simple measure of epigenetic age acceleration is:

$$\text{EAA} = \text{DNAmAge} - \text{Chronological Age}$$

Example:

$$\text{DNAmAge} = 56, \ \text{Chronological Age} = 50 \ \Rightarrow \ \text{EAA} = +6 \text{ years}$$

Researchers often use a residual-based measure. Epigenetic age is regressed on chronological age:

$$\text{DNAmAge}_i = \alpha + \beta \text{Age}_i + \varepsilon_i$$

$$\text{Age Acceleration}_i = \varepsilon_i$$

A positive residual indicates faster-than-expected epigenetic ageing relative to people of the same chronological age.

PhenoAge

Second-generation clocks changed the target from chronological age toward health and mortality risk. Phenotypic Age was first constructed from chronological age and clinical biomarkers. A published mortality-risk predictor is:

$$xb = -19.907 - 0.0336(\text{albumin}) + 0.0095(\text{creatinine}) + 0.1953(\text{glucose})$$
$$+ 0.0954\ \ln(\text{CRP}) - 0.0120(\text{lymphocyte \%}) + 0.0268(\text{MCV}) + 0.3306(\text{RDW})$$
$$+ 0.00188(\text{alkaline phosphatase}) + 0.0554(\text{WBC}) + 0.0804(\text{age})$$

This predictor is converted through a mortality-risk function and then mapped to a Phenotypic Age. DNAm PhenoAge was subsequently trained to predict this health-related phenotype from DNA methylation.

- **1st generation: methylation → chronological-age estimate**
- **2nd generation: methylation → health / mortality phenotype**

GrimAge

GrimAge incorporates DNA-methylation surrogates for physiological and mortality-related factors, together with a methylation-derived proxy for cumulative smoking exposure. A simplified representation is:

$$\text{GrimAge} = \alpha + \beta_1\text{Age} + \beta_2\text{Sex} + \sum_j \gamma_j(\text{DNAmProtein}_j) + \delta(\text{DNAmPACKYRS})$$

GrimAge acceleration is commonly represented as an age-adjusted residual:

$$\text{GrimAgeAccel} = \text{GrimAge} - E(\text{GrimAge} \mid \text{chronological age})$$

A positive value indicates that the mortality-related methylation profile appears older than expected for chronological age.

DunedinPACE: Measuring the Pace of Ageing

DunedinPACE differs conceptually from conventional age clocks because it estimates the pace of biological ageing. Its methylation algorithm contains 173 CpG sites:

$$\text{DunedinPACE} = \beta_0 + \sum_{i=1}^{173} \beta_i M_i$$

The scale is designed so that approximately:

$$\text{Pace of Ageing} = 1.0 \approx \text{1 biological year per chronological year}$$

Thus, a value below 1 indicates relatively slower ageing, whereas a value above 1 indicates relatively faster ageing. For example, DunedinPACE = 1.20 can be interpreted approximately as a pace of 1.20 biological years per chronological year.

Connecting Epigenetic Clocks to Structural Discrimination

Suppose D represents exposure to discrimination, S socioeconomic disadvantage, E environmental adversity, and P the pace of biological ageing. An empirical research model could be:

$$P_i = \alpha + \beta_1 D_i + \beta_2 S_i + \beta_3 E_i + \beta_4 \text{Age}_i + \beta_5 \text{Sex}_i + \cdots + \varepsilon_i$$

If $\beta_1 > 0$ after appropriate adjustment for relevant confounders, greater discrimination exposure is statistically associated with faster biological ageing. This does not by itself establish a deterministic causal law; it tests whether discrimination exposure predicts variation in the ageing measure after specified covariates have been considered.

Summary of the Major Clock Types

Clock	Mathematical target	Interpretation
Horvath / Hannum	CpGs → chronological-age estimate	How old the methylation pattern appears
PhenoAge	CpGs → phenotypic/health ageing	Health- and disease-related ageing
GrimAge	CpGs → mortality-related ageing	Mortality and morbidity-related risk
DunedinPACE	CpGs → pace of ageing	How rapidly ageing is occurring