EMBODIMENT AND HISTORIC PLACE-BASED FACTORS: REDLINING AND STRESS IN ADOLESCENTS

by

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A Dissertation Submitted in

Partial Fulfillment of the

Requirements for the Degree of

Doctor of Philosophy

in Epidemiology

at

The University of Wisconsin-Milwaukee

December 2023

ABSTRACT

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The University of Wisconsin-Milwaukee, 2023
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Stress is a common human experience; however, chronic stress is socially patterned in the United States. Exposure to stress during sensitive periods of development, including adolescence, can result in lifelong negative health outcomes including immune dysregulation, mental health outcomes, and cardiovascular disease. Historic economic and political policies and processes resulting from structural racism have contributed to present-day health inequities, with one prominent example being historic redlining. Historic redlining has shaped the characteristics of present-day neighborhoods. Redlining has resulted in potentially harmful health exposures including reduced residential investment, racial residential segregation, and limited resources in neighborhoods subjected to redlining practices. However, it is not well understood if historical processes of structural racism impact determinants of adolescent stress levels in present-day. This dissertation examined the association between historic structural determinants, specifically redlining practices, and stress outcomes in adolescents.

Using data from the Future of Families and Child Wellbeing Study, we sought to: 1) examine the association between historic redlining, one form of structural racism, and perceived stress in adolescents; 2) evaluate the association between historic redlining

and biological stress, measured via cortisol output from hair, in adolescents; and 3) determine the association between historic redlining and biological aging, measured via DNA methylation “epigenetic clocks”, in adolescents. This research can help to elucidate pathways through which structural racism gets “under the skin”, leading to health inequities in adolescents.

The findings from this dissertation indicate that structural racism, measured via historic redlining is associated with present-day stress outcomes in adolescents. We found that exposure to redlining, particularly high redlining, was associated with subjective and biological measures of stress. We also found evidence that present-day neighborhood sociodemographic characteristics may mediate the relationship between historic redlining and stress. This dissertation used a cross-sectional study design; therefore, future research may consider examining the longitudinal effects of exposure to structural racism or assess whether there are potentially critical or sensitive periods where exposure may be more severe. Implications from the findings of this dissertation help to identify potential upstream determinants which impact adolescent stress measures in present-day. Furthermore, these findings may help to encourage equity-based policy options such as increased equitable lending opportunities in formerly redlined neighborhoods to address the impacts of structural racism and subsequent disinvestment from redlining practices.

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To my family,
especially my biggest supporter, Jerett.

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotrophic hormone
ANS	Autonomic nervous system
CAR	Cortisol awakening response
CI	Confidence interval
DAC	Daily average cortisol
DCS	Diurnal cortisol slope
CDBG	Community Development Block Grants
CpG	Cytosine-phosphate-guanine
CRF	Corticotrophin releasing factor
CVH	Cardiovascular health
DNA	Deoxyribonucleic acid
DNAmAA	DNA methylation accelerated aging
DNMT	DNA methyltransferase
FFCWS	Future of Families and Child Wellbeing Study
FHA	Federal Housing Administration
HCC	Hair cortisol concentration
HOLC	Home Owners' Loan Corporation
HPA	Hypothalamic-pituitary-adrenal axis
PSS	Perceived Stress Scale
SAND	Study of Adolescent to Adult Neural Development
SD	Standard deviation
SEM	Structural equation modeling
SNAP	Supplemental Nutrition Assistance Program
TANF	Temporary Assistance for Needy Families

ACKNOWLEDGEMENTS

I have been very fortunate to have such a wonderful dissertation committee who have supported me throughout this process. Dr. Helen Meier is the reason that I became interested in pursuing a degree in epidemiology, and I cannot thank her enough for support over the past four years. She went above and beyond what is required of an advisor and has taught me so much. Her confidence in me has helped me gain confidence in myself and I will be forever grateful for that.

Dr. Lorraine Halinka Malcoe took a chance on me as an advisee, and I am so thankful for that. She has urged me to think more critically about my research topics and has helped me become a better epidemiologist. I feel so fortunate to have been able to learn from her throughout my dissertation journey.

Dr. Linnea Laestadius has been such a supportive and knowledgeable dissertation committee member. She has a wonderful way of asking questions that encourages me to step back and think more deeply about my research topic. Her expertise has been greatly appreciated.

Dr. Anne Bonds has such a wealth of knowledge, and it has been a pleasure to learn from her over the past year and a half. Her enthusiasm and encouragement mean so much to me.

Thank you to the Zilber faculty and staff who have supported me since I began the MPH program in 2018. I am proud to be a graduate of the UW-Milwaukee Joseph J. Zilber College of Public Health.

A huge thank you to my family and friends for supporting me throughout this process, especially my husband Jerett who has been the greatest source of support that

I could ever ask for. I truly could not have done this without him. Also, a special thank you to my parents who have always supported my educational goals.

Finally, I would like to thank the participants and staff of the Future of Families and Child Wellbeing Study as well as the Study of Adolescent to Adult Neural Development Study. Their dedication and commitment to advancing population health is commendable.

Chapter 1

Introduction

1.1 Background

Chronic stress is socially patterned in the U.S. and a known determinant of negative health outcomes.[1,2] Chronic stress exposure varies by neighborhood factors,[3-7] but is it is not known if historical processes of structural racism are associated with present-day indicators of stress in adolescents. Furthermore, it is not well understood how structural determinants, such as historic redlining, impact health outcomes during periods of sensitive growth and development, for example during adolescence, or how these determinants could potentially impact health outcomes throughout the lifecourse. Using data from the Future of Families and Child Wellbeing Study,[8] a birth cohort from urban U.S. cities, this dissertation addressed these gaps by examining the association during adolescence between historic redlining, a measure of structural racism, and several indicators of stress, including 1) perceived stress, 2) hair cortisol, and 3) accelerated biological aging.

1.2 Specific Aims and Hypotheses

Aim 1: Examine the association between historic redlining, one form of structural racism, and perceived stress in adolescents.

Hypothesis 1a: Individuals living in historically redlined neighborhoods (proxied by census tracts) will have higher levels of perceived stress.

Hypothesis 1b: Census tract sociodemographic factors will partially mediate the association between historic redlining and perceived stress.

Aim 2: Evaluate the association between historic redlining and biological stress, measured via cortisol output from hair, in adolescents.

Hypothesis 2a: Individuals living in historically redlined neighborhoods will have higher biological stress reactivity.

Hypothesis 2b: Census tract sociodemographic factors will partially mediate the association between historic redlining and biological stress reactivity.

Aim 3: Determine the association between historic redlining and biological aging, measured via DNA methylation “epigenetic clocks”.

Hypothesis 3: Individuals living in historically redlined neighborhoods will have greater accelerated biological aging.

1.3 Structural Racism

Structural racism, refers to “the totality of ways in which societies foster racial discrimination, through mutually reinforcing inequitable systems”.[9] Race is socially constructed, and often differences in outcomes observed by race indicate impacts of racism.[10] The categorization of socially constructed groups into hierarchical levels by race perpetuates differential access to power, resources, and opportunities and contributes to harmful normative beliefs including stereotypes and prejudices.[11] Structural racism is “historically rooted and culturally reinforced” where historic policies and practices have contributed to present-day health inequities.[9] The colonization of North America as well as the enforcement of slavery and the subsequent policies and laws that established formalized practices of discrimination, have resulted in inequitable outcomes which are maintained by present-day institutions.[9] Therefore, structural racism can be seen through the multitude of ways in which racial discrimination and

marginalization are embedded into institutional systems including public policy, education, housing, societal values, and healthcare services in the U.S.[9,11]

Structural racism in the United States limits opportunities for people of color while simultaneously bolstering opportunities and outcomes for white populations.[9,11] Multiple systems reinforce structural racism through policies, values, practices, and laws. These systems then perpetuate racist outcomes, which may adapt over time, persisting beyond previous forms of discrimination that may have been deemed illegal.[11] Through interlocking institutional systems and processes over time, structural racism has resulted in the inequitable distribution of present-day resources, power, and opportunities, which ultimately contribute to health inequities.[9,11]

One example of persistent structural racism in the U.S. that has shaped the distribution of present-day resources is residential segregation.[9] Racial residential segregation refers to the physical separation of racial and ethnic groups resulting in the homogeneous composition of neighborhoods.[11] Racial residential segregation has been found to be associated with various negative health outcomes including chronic disease, health care access, and birth outcomes.[7,9,12] Government agencies, as well as private institutions backed by the federal government formalized racialized processes of housing discrimination including mortgage discrimination, redlining, and restrictive covenants, which have contributed to present-day racial residential segregation in the United States.[11,13-15]

In response to the economic crisis brought on by the Great Depression, the federal government created economic agencies as part of the New Deal to address housing finance instability.[16] The impacts of these federal agencies, including the Home

Owners' Loan Corporation (HOLC) established in 1933 and the Federal Housing Administration (FHA) established in 1934, have contributed to present-day residential segregation and disinvestment.[16-18] The HOLC conducted City Surveys between 1935 and 1940 among neighborhoods in over 200 urban cities throughout the United states to determine residential investment risk.[16] Through these City Surveys, neighborhoods that were deemed "risky for investment" were given the lowest grade ("D") and outlined in red on the "residential security maps" created by HOLC; this process became known as "redlining".[19] The assessment of neighborhoods were racially motivated and produced discriminatory results, particularly targeting Black and immigrant neighborhoods with hazardous grades.[16,19] Black Americans experienced targeted discrimination from racialized housing policies as additional housing restrictions, such as racial covenants and deeds, prevented them from purchasing homes in certain neighborhoods.[19,20]

The consequences of historic redlining practices can be seen through present-day neighborhood economic disparities and racial residential segregation.[17,18,21] HOLC redlining logic influenced FHA lending practices, which discriminated against Black Americans by restricting the sale of subsidized suburban housing to white populations and by limiting the distribution of home loans, particularly in regions deemed "hazardous", disproportionately harming Black communities.[13,17,20] Through these mechanisms, white populations were able to afford larger homes, move to suburban areas, and build equity in their homes.[13,20,22] As a consequence, white populations were aided by the U.S. government and various institutions and institutional actors to build generational wealth, while Black populations were simultaneously denied those same opportunities.[23,24]

Application of ecosocial theory

The U.S. remains highly segregated, particularly in metropolitan areas. Segregation, in turn, has been shown to lead to disparities in economic opportunities, educational attainment, and health outcomes.[9,11,12] Drawing on ecosocial theory, we are able to better understand how structural forces, specifically discriminatory housing policies, have contributed to inequitable health outcomes. Ecosocial theory was first introduced by Nancy Krieger in 1994.[25] One aspect of ecosocial theory posits that individuals embody social and environmental exposures, which in turn can lead to the dysregulation of biological outcomes.[25,26] Ecosocial theory emphasizes the importance of identifying pathways that have contributed to health inequities, and then using this information to hold institutions accountable.[27] Although embodiment is only one part of ecosocial theory, it provides a novel understanding of "biological expressions of racism", and the pathways through which our environment impacts the population distribution of health outcomes, including socioeconomic deprivation, limited access to resources (e.g., health care access), and discrimination.[26,27] As seen in Figure 1.1, racism can lead to harmful outcomes including discrimination, which may then lead to the biological expression of racism, and ultimately health inequities.[26] Racism can operate not only through multiple domains ranging from individual to global levels, but also across the lifecourse.[26] This understanding of ecosocial theory can be used to explain population distributions of health outcomes, such as chronic stress. Harmful pathways of embodiment, such as environmental and social stressors, which are driven by racism, disproportionately impact people of color. These pathways can then lead to the biological expression of racism, and subsequent racial and ethnic health inequities, such as inequities in chronic stress outcomes.[26]

Ecosocial theory affirms the importance of macro-level structures, which impact social, economic, and political pathways in driving the population distribution of health outcomes.[26] Understanding how our social environment can get "under the skin" helps researchers identify structural determinants that may impact health, including public policies, housing segregation, and discriminatory economic policies.[26] With this understanding, we are able to discern how individuals may literally incorporate external structural exposures, such as racial residential segregation, and how these may impact our biological outcomes, including stress levels.[28]

Structural determinants, including historic redlining, have contributed to the present-day characteristics of neighborhoods.[17,21,29,30] Drawing on the work by Krieger et al. (2020), we are able to better understand how historic housing policies, specifically redlining practices, have contributed to intermediary pathways, such as neighborhood demographics and resources, and ultimately present-day health inequities in adolescent stress outcomes.[29]

As seen in Figure 1.2, historic redlining practices, which were driven by structural racism, impacted the trajectory of neighborhood investment as well as other upstream factors including racial residential segregation and homeownership opportunities. Previous literature has found that historically redlined areas continue to report lower homeownership rates, particularly for minoritized populations, as well as increased racial residential segregation and decreased access to mortgage lending opportunities.[31-33]

An intermediary pathway contributing to inequitable health outcomes is via place-based resources critical for health promotion as well as neighborhood

sociodemographic characteristics. Access to place-based resources may be directly impacted via structural racism or through downstream mechanisms from historic redlining policies. The pathway between historic housing practices and current neighborhood characteristics is particularly critical to understand, as area of residence has been cited as a key determinant of health outcomes.[7,34,35] Historic redlining practices have directly impacted the built environment of neighborhoods, including factors such as healthy food access,[36,37] air quality,[38] tobacco and alcohol outlet density,[39-41] and tree coverage.[42] These intermediary determinants can have direct impacts on health outcomes. Access to food has been cited as a critical determinant of health outcomes including obesity, cardiovascular disease, and diabetes.[43-45] Furthermore, access to green space, including parks, trees, and open space, has been found to impact respiratory health,[46] cardiovascular disease,[47] and mental health outcomes.[46,48] Unsurprisingly, access to health care serves as an important indicator for health outcomes, with individuals living in areas with worse access to affordable, safe, and efficient care reporting worse health outcomes or lower utilization of services.[49,50]

Neighborhood characteristics driven by historic policies can also contribute to unequal stress by embodied exposures of discrimination and material deprivation.[21,29] As a result, inequities in health outcomes may arise. Historic redlining has been found to be associated with a variety of adverse health outcomes including cardiovascular disease,[24] birth outcomes,[29,31,51,52] cancer,[53,54] neighborhood safety,[55-57] COVID-19 risk,[58] and mental health outcomes.[31] Although these policies were initiated over 80 years ago, the subsequent negative repercussions have persisted, and continue to shape present-day neighborhoods and their development.[17,21] Furthermore, these

policies have contributed to present-day inequitable exposure and health outcomes among marginalized populations, highlighting an environmental and social justice issue. Despite a growing body of research examining the pathways and determinants linking historic redlining to inequities in health outcomes, no study has examined the impacts of historic redlining on stress outcomes in adolescents.

1.4 Stress and Health

Individual-level stress is one health outcome hypothesized via embodiment to be influenced by historic processes. Stress refers to an individual's perception of an internal or external threat to homeostasis.[59] Although stress is an inevitable life experience impacting all individuals regardless of social condition, prolonged stress or chronic stress is socially patterned.[3] Previous research has identified an association between exposure to chronic stress and a variety of health outcomes including cardiovascular disease,[60] mental health outcomes,[61] and harmful health behaviors.[62] Stress may also directly impact health outcomes via neuroendocrine responses.[1] Chronic stress has been found to be associated with immune dysregulation, including impacting immuno-pathology and immuno-suppression, which in turn may increase susceptibility to disease and infection.[63,64] Exposure to chronic stressors can result in the dysregulation of biological processes, which could potentially result in lifelong adverse health consequences, especially if children and adolescents are exposed to chronic stressors during sensitive periods of development.[3,65] Despite the potential for stress exposure in adolescence to have negative effects throughout the lifecourse, there is limited research examining structural determinants of stress among this population. Without examining the impact of structural determinants such as economic and social

policies on risk of chronic stress outcomes, important sources of stress may not be included or addressed, contributing to inequities in health outcomes, such as racial and ethnic health disparities.

Stress pathways

A variety of factors may impact susceptibility to increased stress. Discriminatory or marginalizing experiences disproportionately place minoritized racial and ethnic populations at an increased risk of elevated stress levels.[66] Socioeconomic indicators may also play an important role in reducing or amplifying stress. Whitely et al. (2022) found higher individual socioeconomic position mitigates the impact of negative neighborhood-level factors on cumulative stress in a sample of adults from the United Kingdom.[67] They found that individuals with the highest educational attainment living in the most deprived neighborhoods reported lower cumulative stress levels, measured via allostatic load, than those with the lowest educational attainment in the least deprived neighborhoods.[67] Finkelstein et al. (2007) reported similar findings among adolescents where lower reported parental education was associated with higher perceived stress.[68]

Interpersonal relationships also play a key role in teen and adolescent stress levels. Doom et al. (2022) examined the relationship between adolescent stress, measured via hair cortisol concentrations at age 15, and parental behaviors, including parental harshness and disengagement.[69] Among their sample of 171 adolescents, they found cumulative parental harshness between ages 1 – 15 was associated with higher cortisol levels while parental disengagement between ages 1 – 15 was associated with lower cortisol levels.[69] The authors hypothesize that these findings may be driven by the difference in timing of parental behaviors, where parental harshness is more

unpredictable, while parental disengagement can occur over a longer period of time, for example daily, resulting in chronic stress and ultimately lower cortisol levels.[69]

Neighborhood factors, including neighborhood socioeconomic status, social cohesion or collective efficacy, and access to social support services may also influence stress levels. Children with stronger support systems have been found to report lower levels of stress.[3,70] Furthermore, neighborhoods with greater connectedness or social cohesion have been found to buffer the effects of stressful life events for adolescents.[4] Neighborhood safety also plays an important role in influencing stress levels in children and adolescents. Theall et al. (2017) examined the association between neighborhood violence and crime and stress levels, measured via telomere length and cortisol functioning, in adolescents aged 5 to 16 years old from New Orleans between 2012 – 2013.[5] They found that neighborhood violence and crime, defined as exposure to higher density of liquor stores, violent crime, and domestic violence were significantly associated with telomere length and cortisol functioning.[5] Understanding the potential mechanisms that may drive inequitable stress exposure can help to target public health intervention efforts to certain populations at disproportionate risk or among populations at unique risk of the adverse effects of stress exposure, such as children and adolescents.

Stress in adolescents

Adolescence is a sensitive period of growth and development where harmful exposures play a particularly crucial role in determining later-life health outcomes. Thoits (2010) argues that early-life stressors, specifically those experienced during childhood, can proliferate throughout the lifecourse or even across generations, which perpetuates health disparities among marginalized populations. Individuals who

experience higher levels of stress in childhood and adolescence may be at a greater risk of adverse health outcomes in adulthood, including mental health outcomes, metabolic functioning, inflammatory responses, and cardiovascular risk.[3,65,71] Previous research has found that individual characteristics and circumstances, including socioeconomic status, social support, and self-esteem, may buffer against the adverse effects of stress in adolescence.[3] Although there is potential to buffer or reverse the effects of exposure in adolescence, given the documented health outcomes linked to early-life stress exposure, it is important to understand all potential risk factors, including structural determinants.

1.5 Future of Families and Child Wellbeing Study (FFCWS)

The Future of Families Child and Wellbeing Study (FFCWS) is a longitudinal cohort study with a baseline sample size of 4,898 U.S. children and caregivers who were followed over six waves: 1) birth (1998-2000), 2) age 1 (1999-2001), 3) age 3 (2001-2003), 4) age 5 (2003-2006), 5) age 9 (2007-2010), and 6) age 15 (2014-2017). Data collection at age 22 is currently in progress. The FFCWS oversampled for unmarried mothers and recruited from 75 hospitals among 20 large cities throughout the U.S. (population ≥ 200,000).[72] Approximately 75% (n = 3,710) of mothers enrolled in FFCWS reported not being married to the child's father at baseline. FFCWS participants were also over-sampled to include a larger proportion of Black and Hispanic participants as well as low-income families.[72] At baseline, the distribution of mother's race/ethnicity was 21% (n = 1,030) non-Hispanic white, 27% (n = 1,336) Hispanic, and 47% (n = 2,326) non-Hispanic Black. Furthermore, approximately 35% (n = 1,699) of mothers reported having less than a high school education, compared to 30% (n = 1,480) having

a high school education or equivalent, 24% (n = 1,189) with some college, and 11% (n = 524) with a college degree or greater, at baseline.

The core goal of the FFCWS was to assess the relationships, policies, and environments of children and caregivers. The FFCWS core study had four overarching questions of interest: 1) What are the conditions and capabilities of unmarried parents, especially fathers?, 2) What is the nature of the relationships between unmarried parents?, 3) What factors impact unmarried parents?, and 4) How do policies and environmental conditions affect families and children?[72] Individual demographic characteristics, neighborhood characteristics, and additional cognitive and behavioral diagnostics were collected at each wave by either the child, caregiver(s), or both (Figure 1.3).

Study population

This study sample comes from a sub-set of the FFCWS cohort via the Study of Adolescent to Adult Neural Development (SAND), which was collected during wave 6 of the FFCWS. The goal of the SAND sample was to provide a better understanding of adolescent brain structure and function in relation to their behaviors.[74] The SAND sub-sample of FFCWS participants includes 237 families with adolescents aged 15 – 17 years old who lived in or near Detroit, Toledo, or Chicago.[69] Aims 1 and 2 used the FFCWS SAND sub-sample collected at wave 6, while Aim 3 used the full FFCWS sample from wave 6.

1.6 Measure of stress in FFCWS

A strength of this dissertation is that it examined both participant's perceived stress and biological measures of stress. Examining multiple measures of stress allows

for a deeper understanding of how structural determinants impact both subjective and objective measures of stress during a sensitive period of growth, such as adolescence.

Perceived Stress Scale

A common measure of perceived stress is the Perceived Stress Scale (PSS), which was created by Cohen, Kamarck, and Mermelstein in 1983.[75] The PSS provides a global measure of perceived stress and is one of the most common psychologic tools used to measure stress levels.[39] The PSS was created as a 14-question survey (PSS-14) that asked participants to identify how often certain stressful responses or circumstances occurred within the past month.[75] Participants respond to the PSS-14 using a five-level Likert scale ranging from 0 = “never” to 4 = “very often”. Cohen et al. (1983) examined the validity of the PSS-14 among three college student samples. They found evidence of good internal consistency, reporting Cronbach’s alphas of .84, .85, and .86 among the three samples.[75] Participants of SAND were asked to respond to the PSS-14. Previous literature has identified that increased levels of perceived stress may result in later life adverse health outcomes including harmful health behaviors and poor mental health outcomes.[76,77]

Hypothalamus-pituitary-adrenal axis and cortisol

Cortisol is a useful measure of the hypothalamic-pituitary-adrenal (HPA) axis, which is a mechanism that regulates biological processes in response to stressors via the endocrine system, including the hypothalamus, pituitary glands, and adrenal glands.[59,78,79] When an individual experiences an external stressor, the hypothalamus, the region of the brain that regulates the autonomic nervous system (ANS), is activated and releases corticotrophin releasing factor (CRF), a peptide hormone.[59] CRF then enters the blood stream, activating the pituitary gland. The pituitary gland then releases

adrenocorticotrophic hormone (ACTH), which then reaches the circulatory system via the adrenal cortex where glucocorticoid cortisol, commonly referred to as the “stress hormone”, is produced.[59] This hormone then triggers a variety of biological processes in response to stress, including the slow-down of the digestive system, the break-down of glucose to send to muscles and the brain, and an increase in blood pressure and heart rate variability.[1]

Cortisol levels are a useful measure of stress because they capture acute and chronic stress, and it has been hypothesized that cortisol regulation can impact later-life health outcomes.[80] Cortisol can be measured via a variety of biological markers including saliva, blood, urine, and hair samples. Cortisol levels vary during the day, and on average, peak approximately 30 – 40 minutes after waking, and then diminish throughout the remainder of the day, reaching their lowest point at the end of the day.[80] This production cycle is known as the diurnal pattern of cortisol and can be measured via the daily average cortisol levels (DAC), the post-awakening surge of cortisol known as the cortisol awakening response (CAR), or by the change in cortisol levels from morning to night known as the diurnal cortisol slope (DCS).[1,80] Diurnal patterns of cortisol production can signal disruptions in biological processes, and have been shown to be associated with potential adverse health outcomes including mental health outcomes and cardiovascular disease.[80]

Hair cortisol concentration (HCC) is a particularly useful measure of longer-term cortisol levels, and a 3-cm hair segment can be used to assess average cortisol output over at least 3 months.[1,69] HCC is also less likely than saliva, blood, and urine cortisol measures to be influenced by factors such as sleep and diet.[1,69] HCC has been found to

be a validated measure of HPA axis activation in children.[81,82] Hair samples were collected among SAND participants and used to examine HCC.

Epigenetic signatures of accelerated aging

DNA methylation is a mechanism that can be used to assess epigenetic signatures of accelerated aging at the cellular level.[83] Clusters of CpG dinucleotides, known as CpG islands, are the main location for DNA modification, specifically the site where DNA methylation is most likely to occur.[83] DNA methylation refers to the transfer of a methyl group (CH_3) to a cytosine nucleobase, which occurs through DNA methyltransferase (DNMT).[84] DNA methylation is caused by a family of DNMTs, including DNMT1, DNMT3a, and DNMT3b. DNMT3a and DNMT3b conduct *de novo* methylation, meaning they activate a new methylation pattern on DNA that is unmodified, while DNMT1 maintains the pattern of DNA methylation from the parent strand to the daughter strand.[84,85] DNA methylation can then either act as an amplifier or suppressor of gene expression.[83]

Internal or external stressors may impact DNA methylation and have been found to be associated with epigenetic aging.[94,95] Furthermore, exposure to early-life stressors have been found to be associated with lasting effects on methylation, which could potentially continue into adulthood.[96] Epigenetic “clocks” are used to predict epigenetic age by examining methylated CpG sites and are useful measures of biological aging, as opposed to chronological aging,[95] and are an indicator of cellular stress.

A total of eight epigenetic clocks are included in the FFCWS at wave 6 (age 15), and a description of each epigenetic clock can be seen in Table 1.1. All clocks were computed from DNA methylation (DNAm) EPIC and 450k assays using saliva samples. The eight epigenetic clocks calculated in the FFCWS include: 1) Hannum,[86] 2) Horvath

Pan-Tissue Estimator,[87] 3) DNAmPhenoAge,[88] 4) Skin and Blood Clock,[89] 5) DNAm GrimAge,[90] 6) Pediatric-Buccal-Epigenetic Clock,[91] 7) Dunedin Pace of Aging Methylation,[92] and 8) DunedinPACE.[93] Despite the majority of clocks being trained on adult samples using tissue samples other than saliva, previous literature has validated the use of epigenetic measures of aging derived from adult samples in pediatric saliva samples.[97]

1.7 Public Health significance

To the best of our knowledge, this dissertation is the first to examine the impact of structural racism, measured via historic redlining, on stress measures in adolescents. The current body of literature that focuses on stress determinants in children and adolescents includes some recognition of neighborhood factors as potential exposures.[4,5,98] However, no prior studies have examined the effects of structural determinants, such as structural racism measured via historic redlining, on stress outcomes of adolescents. This dissertation fills that gap by examining the impact of historic redlining practices, measured via the Home Owners' Loan Corporation (HOLC) redlining maps, on stress outcomes among adolescents in a birth cohort of U.S. children from the Future of Families and Child Wellbeing Study (FFCWS). Specifically, this dissertation sought to determine in adolescents: 1) the association between historic redlining, one form of structural racism, and perceived stress, 2) the association between historic redlining and biological stress, measured via cortisol output from hair, and 3) the association between historic redlining and biological aging, measured via DNA methylation "epigenetic clocks".

A benefit of this dissertation is that it utilized a unique study sample comprised of populations that are often disproportionately under-represented in study samples including low-income families and racially minoritized populations. Because a main aim of this study is to examine how structural determinants, specifically structural racism, has impacted present-day health outcomes, it is crucial to incorporate populations that have faced greater marginalization or discrimination into the study sample. Furthermore, the impact of redlining on health outcomes is still an emerging topic within public health and this dissertation expands beyond the work previously conducted by examining an adolescent sample and utilizing stress as the outcome of interest.

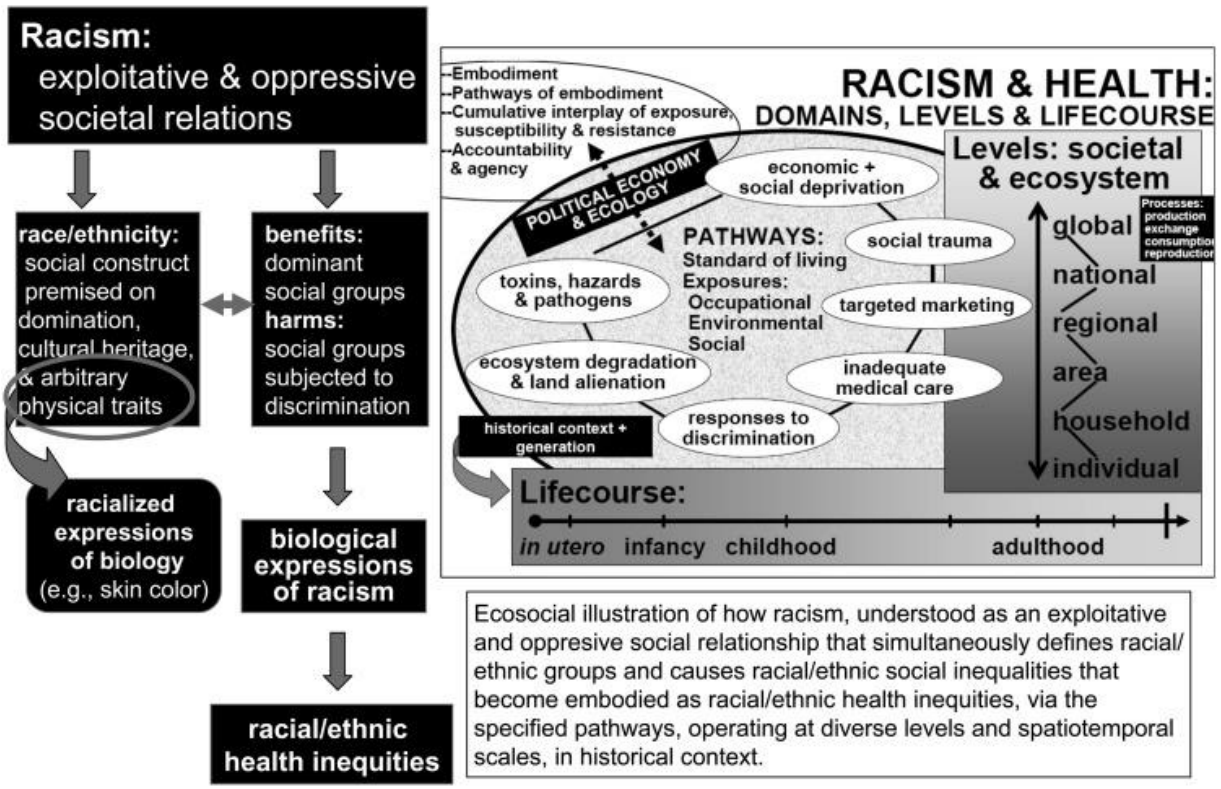
This dissertation applied ecosocial theory to understand how upstream, structural determinants may impact chronic stress outcomes. It is crucial for public health researchers to understand not only that disparities in exposure exist, but to investigate structural factors and systems that have created these inequities. Equipped with this knowledge, we can then target policy action to identify and eliminate structural determinants to reduce disparities, as well as hold accountable the systems that created these disparities.

1.8 Tables and Figures

Table 1.1 Future of Families and Child Wellbeing Study epigenetic clocks

Epigenetic Clock	Sample/Population	Outcome	Tissue
Hannum[86]	N = 656 adults aged 19 – 101 years old	Chronological age	Whole blood
Horvath[87]	N = 8,000 samples from 82 DNA methylation array datasets	Chronological age	Multi-tissue (51 healthy tissues and cell types)
Pheno Age[88]	N = 456 participants from Invecchiare in Chianti (InCHIANTI) study aged 21 – 100 years old	Phenotypic age	Whole blood
Horvath Revised (Skin/Blood)[89]	N = 2,222 across 26 datasets	Chronological age	Blood, skin, saliva, and fibroblast
Grim Age[90]	N = 2,356 from Framingham Heart Study	Mortality risk estimator	Whole blood
PedBE[91]	N = 1,721 samples from 11 pediatric cohorts aged 0 – 20 years old	Chronological age	Buccal
Dunedin Pace of Aging (38)[92]	N = 954 from Dunedin Study 1972 – 1973 birth cohort	Changes in 18 biomarkers	Whole blood
Dunedin Pace of Aging (45)[93]	N = 1037 from Dunedin Study 1972 – 1973 birth cohort	Changes in 19 biomarkers	Whole blood

Figure 1.1 Ecosocial theory: Racism and health



Ecosocial illustration of how racism, understood as an exploitative and oppresive social relationship that simultaneously defines racial/ethnic groups and causes racial/ethnic social inequalities that become embodied as racial/ethnic health inequities, via the specified pathways, operating at diverse levels and spatiotemporal scales, in historical context.

Image Source: Krieger (2012)[26]

Figure 1.2 Conceptual framework linking historic redlining and present-day adolescent stress outcomes*

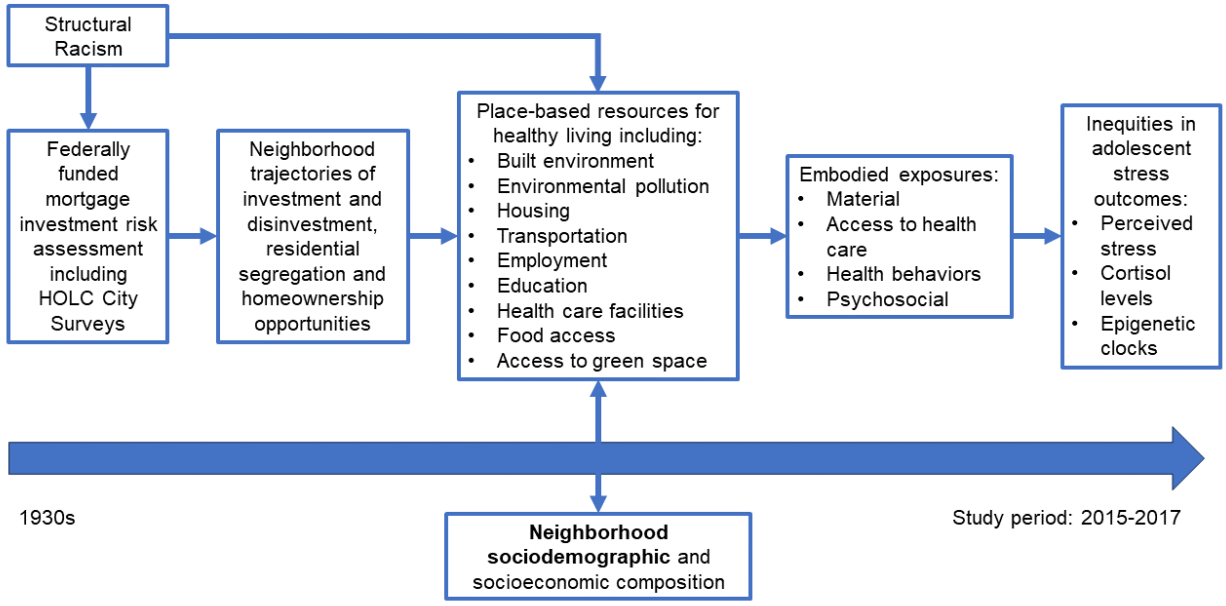


*Image adapted from: Krieger et al. (2020)[29]

Figure 1.3 Future of Families and Child Wellbeing Study data collection by wave

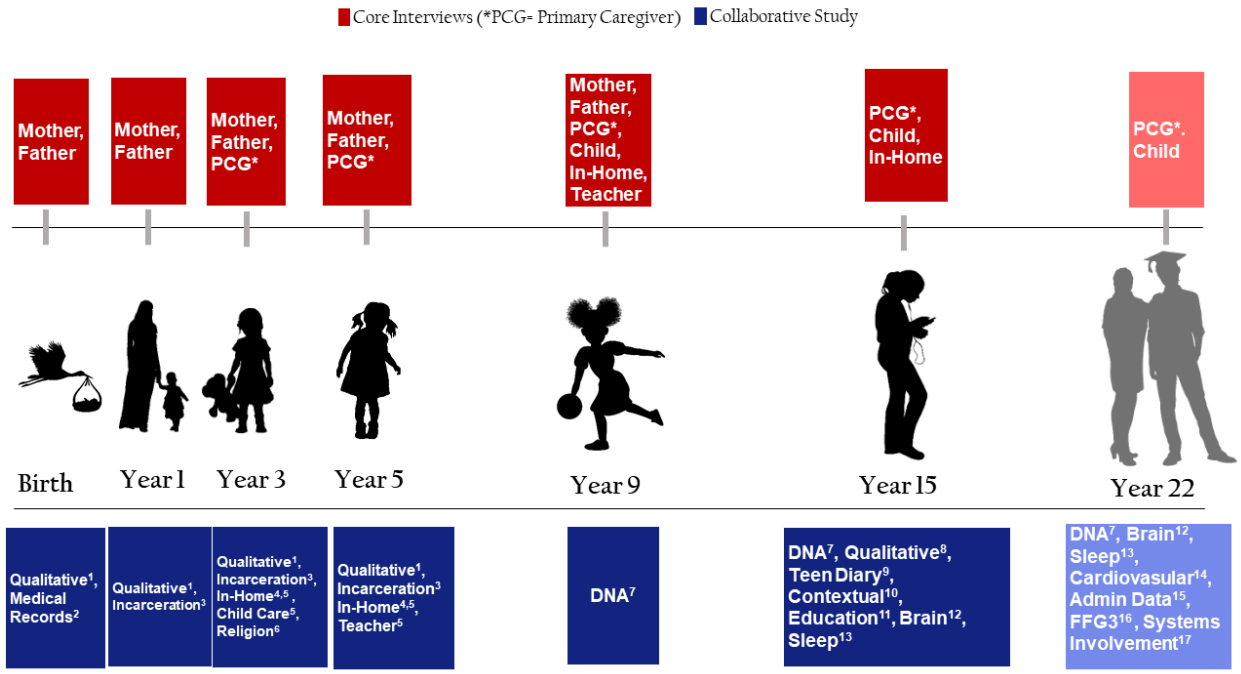


Image Source: Future of Families and Child-Wellbeing Study (n.d.)[73]

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Chapter 2

Historic structural racism and perceived stress in adolescents

2.1 Background

Adolescence is a period of rapid physical and psychosocial development. During this time, adolescents are at an increased risk of stress due to external burdens including social, physiological, and environmental factors.[1,2] Higher stress, particularly chronic stress that occurs over a prolonged period of time, has been found to be associated with adverse health outcomes, such as health risk behaviors[3,4] and reduced immune function.[4-6] Additionally, adolescents who experience chronic stress more often report mental health outcomes including anxiety and depression.[4,7,8]

Stress can be assessed using subjective or biological measures. Commonly used biological measures include cortisol functioning or allostatic load, whereas subjective measures can include an individual's perception of stress exposure or coping mechanisms. Perceived stress can help elucidate an individual's perception of stress severity and their ability to manage stress. Previous literature has found that perceived stress is a useful indicator of subsequent health outcomes in adolescents, particularly poor mental health. Lindholdt et al. (2022) found that adolescents with higher perceived stress reported greater odds of mental health diagnosis in the 12 months after follow-up.[9] Thorsén et al. (2022) showed similar findings where participants reporting higher levels of perceived stress reported more psychiatric symptoms.[10] Both studies highlight the growing concern that higher stress in adolescence contributes to subsequent adverse health outcomes.

Neighborhood-level social and environmental factors such as safety, access to greenspace, and social cohesion have been found to be associated with perceived stress.[11-15] Despite a large body of literature that examines intermediary factors associated with stress outcomes in adolescents, few studies have investigated associations between structural determinants, including structural racism, and perceived stress outcomes.

Historic redlining was one form of structural racism that has been associated with current neighborhood features.[17,18] Historic redlining refers to the inter-institutional discriminatory lending practices and policies that took place in the United States during the early 20th century where federal agencies and private financial institutions systematically denied mortgage lending in areas determined to be "risky for investment" based on racist ideology and assumptions.[19,20] One of the most commonly used methods to measure historic redlining is through the Home Owners' Loan Corporation (HOLC) residential security maps. The HOLC, a federal government agency, conducted City Surveys throughout urban regions of the U.S. in the 1930s.[19] The digitized HOLC maps provide historical documentation of the survey methods used to assess investment risk. A growing body of literature has linked these historic practices with present-day health outcomes, most often utilizing adult study samples.[17,21] However, no studies have examined associations between historic redlining and indicators of health in adolescents.

To address this gap, our study investigated the association between historic redlining neighborhood grades and present-day perceived stress levels among adolescents from urban regions of the U.S. Figure 2.1 displays the hypothesized causal

pathways linking structural racism – through historic redlining and other place-based opportunities, restrictions, and resources – to perceived stress outcomes among urban adolescents. Using this conceptual model adapted from Krieger et al. (2020),[16] we hypothesized that adolescents living in neighborhoods that faced greater historic redlining would report higher perceived stress than those living in areas not subjected or minimally exposed to historic redlining practices. Because previous literature has shown that historic redlining practices impact present-day neighborhood characteristics, including racial residential segregation and socioeconomic inequities,[18,22,23] we hypothesized that the association between historic redlining and perceived stress would be partially mediated by present-day neighborhood sociodemographic characteristics.

2.2 Methods

Study sample

Data come from the Study of Adolescent to Adult Neural Development (SAND), a sub-set of the Future of Families and Child Wellbeing Study (FFCWS). FFCWS is a longitudinal birth cohort study with a baseline sample of 4,898 U.S. children and caregivers who were followed over six waves: 1) birth (1998 – 2000), 2) age 1 (1999 – 2001), 3) age 3 (2001 – 2003), 4) age 5 (2003 – 2006), 5) age 9 (2007 – 2010), and 6) age 15 (2014 – 2017).[24] Participants of FFCWS come from 20 large cities (population ≥ 200,000) throughout the U.S. FFCWS participants were over-sampled to include a large proportion of Black and Hispanic participants as well as low-income families.[25] The SAND sub-study focused on understanding links between contextual factors and brain development. SAND data were collected during wave 6 of FFCWS (age 15) and included a total of 237 participants 15 –17 years old who lived in or near Detroit, MI,

Toledo, OH, or Chicago, IL. SAND is approved by the University of Michigan Institutional Review Board (HUM00167754).

Perceived Stress Scale (PSS)

One of the most commonly used psychologic tools used to measure perceived stress is the Perceived Stress Scale (PSS), which was created by Cohen, Kamarck, and Mermelstein in 1983.[26] The PSS was originally created as a 14-question survey (PSS-14) that asked participants to respond with their level of stress perception to events that occurred within the past month (Table S2.1). Cohen et al. (1983) examined the reliability of the PSS-14 using three samples, two college-aged participants (mean age: 19.01 and 20.75 years) and one sample drawn from a smoking cessation program (mean age: 38.4 years). They found good internal consistency, reporting Cronbach's alphas ranging from 0.84 – 0.86.[26] The validity of the PSS has been corroborated among multiple recent studies from a variety of settings.[27,28]

A total of 225 SAND participants completed the PSS-14 questionnaire. Participants responded to the 14 PSS questions using a five-level Likert scale, with responses ranging from 0 = "never" to 4 = "very often". Seven items were reverse coded due to positive wording (questions 4, 5, 6, 7, 9, 10, and 13) (Table S2.1). A total PSS score was calculated for each adolescent by summing the responses to all 14 questions. Participants missing over half the responses to the PSS were removed from the sample (n = 1). We used single mean imputation for participants missing less than half the PSS items (n = 6). For example, if a participant did not answer two questions from the PSS-14, and of the 12 questions they did answer they had a mean response value of three, we would replace the two missing values with a response of 3 to calculate the final total score. Higher total PSS scores indicate higher perceived stress.

We analyzed PSS scores as both a continuous and categorical variable. For descriptive purposes, participants were divided into three groups based on PSS score tertiles: "low perceived stress" (PSS score: ≤ 22), "moderate perceived stress" (PSS score: 23–27), and "high perceived stress" (PSS score: ≥ 28).

Historic redlining scores

Historic redlining scores come from the HOLC "residential security" maps and were computed by Meier and Mitchell (2022).[18] In the early 20th century, the HOLC assigned one of four grades to each neighborhood evaluated: A – "Best", B – "Still Desirable", C – "Definitely Declining", or D – "Hazardous".[29] To calculate historic redlining scores, neighborhoods identified by the HOLC as "Best" were given an initial score of 1, while "Still Desirable", "Definitely Declining" and "Hazardous" were scored 2, 3, and 4, respectively. Redlining scores were then multiplied by the total percentage of census tract area assessed by the HOLC. Tracts with <20% of their area assessed by HOLC were excluded. This procedure resulted in a continuous historic redlining score. A lower score indicates "low redlining", whereas a higher score indicates "high redlining". Historic redlining scores based on 2010 census tract boundaries were linked to the SAND sub-study by FFCWS staff using participants' reported addresses during wave 6 (age 15) of the FFCWS data collection.

We examined historic redlining scores as a categorical variable. Meier and Mitchell (2022) previously divided historic redlining scores into four intervals based on the national distribution of redlining scores: 1.00–1.749 (level 1), 1.75–2.49 (level 2), 2.5–3.249 (level 3), and 3.25–4.00 (level 4).[18] Areas not assessed by the HOLC, or with <20% of their area scored, were identified as "ungraded". We combined levels 1 and 2 into one category as these tracts were more favorably graded by HOLC surveyors. We

then combined levels 3 and 4 into another category as these tracts were deemed riskier for investment by HOLC appraisers. Our final three-level exposure variable consisted of "low redlining" (levels 1 and 2, historic redlining score range: 1.00–2.49), "high redlining" (levels 3 and 4, range: 2.5–4.00), and "ungraded".

Covariates

For descriptive purposes, we examined a variety of covariates. In wave 6 of FFCWS, participants were asked to self-identify their race/ethnicity by responding to the open-ended question: "What is your race and ethnicity?" Interviewers entered participant responses verbatim and responses were aggregated by the FFCWS staff to create race and ethnicity categories. For our study, race and ethnicity were split into four categories: Hispanic, non-Hispanic Black, non-Hispanic white, and other. The category "other" includes non-Hispanic participants who self-identified as more than one racial category or self-identified as American Indian, Alaska Native, Asian, and Native Hawaiian or Pacific Islander. Additional participant demographics examined included sex at birth (male or female, with no nonbinary response options available in FFCWS at baseline), participant age in years at FFCWS wave 6, and city at birth (Chicago, Detroit, Toledo, or Other). We included sex at birth as a covariate because previous literature has found gender differences in perceived stress outcomes.[30-34] We included city of residence at baseline as a covariate to account for potential differences in SAND sampling for each city.

Maternal characteristics included mother's age at baseline in years and maternal relationship with child's father at baseline (married, romantically involved/steady, or other, which includes on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another). We also examined socioeconomic position, measured

using maternal educational attainment at baseline (less than high school, high school or equivalent, some college or technical school, or college graduate), and household income at age 15 (reported in U.S. dollars). Neighborhood characteristics measured at the census tract-level included the percent of the population living below the federal poverty level and percent of the population that identified as non-Hispanic Black. Neighborhood indicators were based on the U.S. Census Bureau's American Community Survey 5-year estimates (2014-2018).[35]

Statistical analysis

All analyses were conducted using R version 4.2.1.[36] We used descriptive statistics to summarize the distribution of participant characteristics. A total of 24 participants (10.1%) were missing either perceived stress responses or historic redlining scores and were removed from the analysis. Seven (23.3%) of the 30 non-Hispanic white participants included in the SAND sample were missing location information so we were unable to assign these participants a historic redlining score. No other key variables were found to significantly differ between those who were missing data and those included in the final analytic sample (n=213).

We used linear regression to examine the association between historic redlining and continuous total PSS scores among adolescents. We first examined the unadjusted association between the 3-level historic redlining measure (low redlining, high redlining, and ungraded [reference category]) and total PSS score in the full sample. We then adjusted for baseline city of residence and participant sex sequentially. We used a similar modeling strategy to examine the association among non-Hispanic Black participants alone because associations between historic redlining and health outcomes

have been found to differ by race/ethnicity as the process of redlining specifically discriminated against Black neighborhoods.[37]

Previous literature has found that historic redlining has impacted the socioeconomic and demographic characteristics of present-day neighborhoods.[18,22,38] We investigated whether present-day neighborhood characteristics mediated the association between historic redlining and total PSS score using path analysis. We hypothesized that historic redlining influenced perceived stress via two different pathways, 1) a direct association independent of present-day neighborhood characteristics, and 2) an indirect association mediated through present-day neighborhood characteristics including percent of the population below poverty and percent of the population identified as non-Hispanic Black, which is used as a proxy for racial residential segregation. We used structural equation modeling (SEM) conducted in MPlus version 8.2 to examine these pathways.[39]

2.3 Results

Among the 213 participants in the analytic sample, the mean total PSS score was 24.4 (standard deviation [SD]: 6.6) (Table 2.1). Among those living in low redlined areas, 27.3% had low perceived stress, 38.6% had moderate perceived stress, and 34.1% had high perceived stress. Similar distributions were reported among those living in high redlined areas where 27.0% had low perceived stress, 32.4% had moderate stress, and 40.5% had high stress. Participants living in neighborhoods that were ungraded had higher rates reporting low stress (48.3%), while 25.9% had moderate stress, and 25.9% had high stress.

The majority (77.0%) of the sample identified as non-Hispanic Black, with 10.8% identifying as non-Hispanic white, 5.6% identifying as Hispanic, and 5.2% identifying as "other". The sample was fairly evenly split based on participant's sex at birth with 47.4% males and 52.6% females. Participant sex was associated with PSS score tertiles ($p = 0.044$). The mean age was 15.2 years with ages ranging from 15–17 years. Approximately two-thirds (65.7%) of participants reported living in Detroit at baseline, with the remainder living in either Chicago (14.6%), Toledo (16.9%), or another FFCWS sample city (2.8%).

The mean age of mothers at baseline was 25.5 years. Mother's age at baseline decreased as PSS increased ($p = 0.042$), from a mean maternal age of 26.6 years among adolescents with low PSS scores to 24.2 years among those with high PSS scores. At baseline, the majority of participants' mothers reported not being married to their child's biological father, and over half reported having a high school education or less at baseline. There was no association, however, between mother's relationship status and adolescent perceived stress. Mother's educational attainment at baseline was associated with adolescent PSS score tertiles ($p = 0.041$); in general, higher maternal educational attainment was paired with lower adolescent perceived stress, and lower maternal educational attainment was paired with higher perceived stress among adolescents.

The median household income was $35,700. There was a statistically significant difference in median household income by PSS score tertiles: adolescents with high PSS scores lived in households with the lowest median income at $28,000, whereas adolescents with low perceived stress lived in households with a median income of

$38,900. Neighborhood characteristics also differed by PSS score tertiles. Adolescents in the highest PSS tertile lived in census tracts with high poverty (30.6%) and with a high proportion of the population who identified as non-Hispanic Black (66.4%).

About half (52.1%) of participants resided in high redlining census tracts, 20.7% lived in low redlining tracts, and 27.2% lived in ungraded neighborhoods (Table 2.2). There was a statistically significant association ($p = 0.038$) between historic redlining categories and continuous total PSS scores. Participants in ungraded neighborhoods reported a mean total PSS score of 22.5, compared to 24.8 among those living in low redlining neighborhoods, and 25.2 among those living in high redlining neighborhoods. Race/ethnicity was associated with historic redlining score ($p < 0.001$): 73.9% of non-Hispanic white participants resided in ungraded tracts, 4.4% in low redlining, and 21.7% in high redlining tracts. In contrast, the majority of non-Hispanic Black (55.5%) and Hispanic (75.0%) adolescents resided in high redlining tracts. Maternal relationship status and maternal educational attainment at baseline were associated with historic redlining scores ($p = 0.008$ and $p < 0.001$, respectively). There was also a strong association between household income and historic redlining ($p < 0.001$): median household income was $58,500 in ungraded tracts compared to $31,000 in low redlining and $27,600 in high redlining tracts. Neighborhood characteristics were also associated with historic redlining categories ($p < 0.001$). Participants living in high redlining tracts reported a high mean percentage living below the poverty level (34.1%), compared to low redlining (31.8%) and ungraded tracts (11.2%). Ungraded census tracts had a significantly smaller proportion of residents who identified as non-Hispanic Black (19.7%) compared to low redlining (83.0%) and high redlining tracts (71.5%).

Historic redlining was associated with PSS scores in linear regression analyses, with participants living in high redlining tracts reporting statistically significantly higher PSS scores (β: 2.47; 95% CI: 0.35, 4.59), compared to their peers living in ungraded tracts, after adjusting for baseline city of residence and sex at birth (Table 2.3). There was no significant association between residence in low redlining tracts and PSS scores. Among non-Hispanic Black adolescents, those living in high redlining tracts reported higher PSS scores than those living in ungraded neighborhoods, after adjusting for baseline city and sex (β: 2.60; 95% CI: 0.06, 5.14). Similar to the full sample, there was no statistically significant association between residence in low redlining tracts and PSS scores.

Figure 2.2 shows the direct, indirect, and total effects of historic redlining on total PSS scores mediated by percent of the census tract below the poverty level. The total effect going from a low redlining tract to a high redlining tract was associated with a 0.165 standard deviation increase in perceived stress ($p = 0.013$). The total effect was then divided into the direct effect of historic redlining on perceived stress and an indirect effect of historic redlining mediated through census tract poverty. There was a statistically significant indirect effect mediated through current neighborhood poverty ($p = 0.043$). However, the direct effect of historic redlining on perceived stress was not statistically significant.

Figure 2.3 shows the direct, indirect, and total effects of historic redlining on PSS scores mediated by the percent of the census tract identifying as non-Hispanic Black. In this model we also found that the total effect going from a low redlining tract to a high redlining tract was associated with a 0.165 standard deviation increase in perceived

stress (p = 0.013). The indirect effect of redlining on total PSS through percent of the tract identifying as non-Hispanic Black was marginally significant (p = 0.059), while the direct effect of redlining on PSS score was not statistically significant.

2.4 Discussion

This study is the first to examine the relationship between historic redlining as a manifestation of structural racism and perceived stress among adolescents. We found that adolescents living in neighborhoods that were historically redlined reported higher total PSS-14 values compared with those living in ungraded neighborhoods not subjected or minimally exposed to redlining practices. These results support our initial hypothesis and are consistent with previous literature, which found an association between historic redlining practices and present-day health outcomes.[17,21] Our findings indicate that inter-institutional discriminatory lending practices and policies from the early 20th century continue to impact health outcomes of adolescents in the present-day.

Our study provides a novel investigation of the impacts of redlining relative to ungraded tracts within metropolitan areas. Census tracts classified as ungraded were mostly located outside urban city boundaries. Comparing ungraded tracts to low redlining and high redlined tracts provides valuable insight into the differential effects of mortgage lending policy, including investment promotion or deterrence, relative to areas that were not subjected, or minimally exposed to that policy. We used a three-level exposure variable and observed that census tracts graded least favorably by the HOLC (i.e., high redlining tracts) were associated with adolescent stress whereas there was no observed association with low redlining neighborhoods. Our findings indicate that those living in areas graded the worst by the HOLC continue to be disproportionately harmed

by historic policies driven by racist ideologies and practices despite decades having passed since these polices have been deemed illegal.

We theorized that historic redlining and perceived stress in adolescents would be partially mediated by present-day neighborhood sociodemographic characteristics. We found that the association between historic redlining and total PSS in adolescents was mediated by census tract-level poverty, but not by the proportion of the census tract identified as non-Hispanic Black. We found that 57.6% of the total effect between historic redlining and total PSS-14 values mediated by the proportion of the population living below poverty. These findings support our initial hypothesis and correspond with the theorized pathways through which redlining may impact neighborhoods. These intermediary pathways include disinvestment of redlined regions, increased racial segregation, and concentrated disadvantage, which can ultimately impact present-day health outcomes (Figure 2.1). Previous literature has found historic redlining to be associated with present-day neighborhood socioeconomic outcomes.[18,22,23] Additionally, socioeconomic position is a known determinant of stress in adolescents.[30,40] Therefore, the findings from this study provide that intermediary pathways which were driven by structural racism continue to impact adolescent stress outcomes, specifically via neighborhood socioeconomic disadvantage.

We hypothesized that redlining would be associated with increased total PSS values among a sub-sample of non-Hispanic Black adolescents because historic redlining practices specifically discriminated against predominantly Black neighborhoods.[19] Our findings support our initial hypothesis; we observed that high redlining exposure was significantly associated with higher total PSS-14 values,

compared to participants living in ungraded tracts, after adjusting for baseline city of residence and sex at birth. Mujahid et al. (2021) examined the association between HOLC grades and cardiovascular health (CVH) among adults and found that non-Hispanic Black participants living in redlined areas had lower CVH outcomes compared to areas graded more favorably by the HOLC, and the association between redlining and CVH was not observed among any other race/ethnicity group.[37] They theorized that this finding may be due to Black populations being disproportionately harmed by redlining practices because these policies unjustly discriminated against neighborhoods with high percentages of Black neighborhoods.[37] Although we observed a significant association among the full sample as well as the sub-sample of non-Hispanic Black adolescents, our findings are useful for understanding how redlining may not equally impact all individuals and how redlining can lead to subsequent health disparities among racially minoritized populations.

We found that historic structural racism, an upstream determinant of present-day urban neighborhood factors, was associated with individual-level health outcomes. This finding suggests that interventions to reduce health inequalities should consider historic structural racism. Taken together with previously documented associations of historic redlining and intermediary determinants of health, including individual-level, neighborhood-level, and place-based risk factors,[17] our findings support intervening on intermediary determinants may, in turn, reduce adolescent stress levels among those living in areas that were discriminated against by historic redlining policies. Previous literature has identified an association between socioeconomic status and adolescent stress outcomes,[11,30,40] and neighborhoods that were historically redlined continue to

face socioeconomic disadvantage in present-day due to sustained lending discrimination or disinvestment.[41] Programs that may buffer the adverse effects of policies via social support services or increased investment opportunities, such as tax incentives to revitalize neighborhoods subjected to redlined practices and expansion of public assistance programs including Temporary Assistance for Needy Families (TANF), Supplemental Nutrition Assistance Program (SNAP), and community development block grants (CDBG), should be made available in previously redlined neighborhoods.[42]

Strengths and limitations

Our study provides a novel examination of the impact of historic redlining, a manifestation of structural racism, on perceived stress outcomes among adolescents. Most previous literature that has examined the association between historic redlining and health outcomes has focused on impacts among adult populations, with limited studies focusing on child or adolescent health. Adolescence has been identified as a sensitive period where exposures during this time may uniquely impact development and can potentially lead to subsequent adverse health outcomes.[8,10] Given that exposure during adolescence can impact health throughout the lifecourse, it is critical to understand determinants and experiences of stress during this timeframe. Our findings extend the current understanding of how historic redlining impacts population health in the present-day.

Other strengths of our analysis include the use of a validated measure of perceived stress, the Perceived Stress Scale, which is one of the most commonly used psychological tools to assess subjective stress outcomes.[28] Additionally, our study sample includes a diverse birth cohort from urban cities in the United States. Our

findings are generalizable to adolescents living in urban areas of the United States and demonstrate the impacts of structural racism on stress outcomes among adolescents.

Despite the strengths of this study, there are some important limitations to note. First, 23.3% (n = 7) of non-Hispanic white SAND participants were missing location information at wave 6 (age 15) of FFCWS, so we were unable to assign them a historic redlining score and these participants had to be removed from the analysis. However, the FFCWS oversampled for non-Hispanic Black and Hispanic participants,[25] so although a sizable portion of the non-Hispanic white population were not eligible for the analysis, they only accounted for a small portion (3%) of the full SAND sample.

Another study limitation is that the SAND sample only includes participants who lived in either Chicago, Detroit, or Toledo at baseline or lived near these regions during SAND wave 1 data collection. Historic redlining practices varied throughout the United States, so these three cities may not be representative of the impact of historic redlining on adolescent stress outcomes in other urban regions in the U.S. Future studies may wish to examine the association of historic redlining and adolescent stress in other urban regions of the U.S., particularly outside the upper Midwest. Finally, the measurement of historic redlining is based on present-day census tracts, which do not directly correspond with historical neighborhood boundaries assessed by HOLC City surveyors.[43] There is a potential for misclassification of an individual's redlining exposure because participants were assigned redlining scores based on their census tract of residence rather than using the gold standard of complete address data to assign redlining exposure.[43]

2.5 Conclusion

Our study contributes to the growing body of literature examining the impacts of historic redlining on present-day health outcomes. Our findings show that adolescents living in areas that faced greater historic redlining reported higher perceived stress compared to their peers living in areas that were not subjected or minimally exposed to redlining practices. These findings persisted when examining the association among a sub-sample of non-Hispanic Black participants alone. We additionally observed no direct effect of historic redlining on perceived stress and a statistically significant indirect effect of redlining on perceived stress through neighborhood poverty. Future research should consider the impact of historic redlining exposure over time. As the FFCWS is a longitudinal cohort, future research could examine the relationship between historic redlining and stress outcomes using earlier wave of data (e.g., baseline – wave 5). For example, an accumulation lifecourse hypothesis would examine the sum of exposure to redlining over time. Utilizing this lifecourse approach would allow for examination of redlining exposure over time to see if prolonged exposure resulted in increased stress outcomes.[44] Given that adolescence is a period of critical growth and development, it is crucial that we implement interventions and policies aimed at addressing structural determinants of health to reduce health inequities.

2.6 Tables and figures

Table 2.1 Descriptive statistics for participant and census tract characteristics by tertiles of Perceived Stress Scale (PSS) scores (low vs. moderate vs. high)

	Low PSS (N=70; 32.9%)		**Moderate PSS** (N=68; 31.9%)		**High PSS** (N=75; 35.2%)		**Total Sample** (N=213)		**p-value[1]**
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
PSS-14									**< 0.001**
Mean (SD)	16.90	(4.42)	25.30	(1.29)	30.50	(3.43)	24.4	(6.55)	
Historic redlining score									0.052
Low redlining	12	27.27	17	38.64	15	34.09	44	100.00	
High redlining	30	27.03	36	32.43	45	40.54	111	100.00	
Ungraded	28	48.28	15	25.86	15	25.86	58	100.00	
Race/ethnicity[2]									0.334
Hispanic	7	58.33	3	25.00	2	16.67	12	100.00	
Non-Hispanic Black	49	29.88	55	33.54	60	36.59	164	100.00	
Non-Hispanic white	11	47.83	5	21.74	7	30.43	23	100.00	
other	3	27.27	3	27.27	5	45.45	11	100.00	
Missing	0	0.00	2	66.67	1	33.33	3	100.00	
Sex at birth									**0.044**
Male	39	38.61	24	23.76	38	37.62	101	100.00	
Female	31	27.68	44	39.29	37	33.04	112	100.00	
Age									0.297
Mean (SD)	15.10	(0.391)	15.20	(0.461)	15.30	(0.496)	15.20	(0.453)	
Baseline city of residence									0.249
Chicago	14	45.16	6	19.35	11	35.48	31	100.00	

	Low PSS (N=70; 32.9%)		Moderate PSS (N=68; 31.9%)		High PSS (N=75; 35.2%)		Total Sample (N=213)		p-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Detroit	38	27.14	51	36.43	51	36.43	140	100.00	
Toledo	16	44.44	9	25.00	11	30.56	36	100.00	
Other	2	33.33	2	33.33	2	33.33	6	100.00	
Mother's age at baseline									**0.042**
Mean (SD)	26.6	(5.64)	25.7	(6.20)	24.2	(5.20)	25.5	(5.73)	
Missing	0	0.00	1	100.00	0	0.00	1	100.00	
Mother's relationship status at baseline[3]									0.526
Married	18	40.91	15	34.09	11	25.00	44	100.00	
Romantically Involved	39	31.45	41	33.06	44	35.48	124	100.00	
Other	13	30.23	12	27.91	18	41.86	43	100.00	
Missing	0	0.00	0	0.00	2	100.00	2	100.00	
Mother's educational attainment at baseline									**0.041**
Less than high school	24	32.00	22	29.33	29	38.67	75	100.00	
High school or equivalent	11	19.30	24	42.11	22	38.60	57	100.00	
Some college or technical training	21	38.18	18	32.73	16	29.09	55	100.00	
College grad	14	56.00	4	16.00	7	28.00	25	100.00	
Missing	0	0.00	0	0.00	1	100.00	1	100.00	
Household income at 15 ($)									**0.033**
Median [Min, Max]	38900	[94.0, 500000]	37500	[2000, 289000]	28000	[1.00, 152000]	35700	[1.00, 500000]	
% Tract Below Poverty									**0.042**

	Low PSS (N=70; 32.9%)		Moderate PSS (N=68; 31.9%)		High PSS (N=75; 35.2%)		Total Sample (N=213)		p-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Mean (SD)	23.8	(17.2)	27.4	(14.6)	30.6	(16.1)	27.4	(16.2)	
% Tract non-Hispanic Black									**0.005**
Mean (SD)	48.0	(38.7)	64.7	(36.7)	66.4	(34.4)	59.8	(37.3)	

[1] P-value based on ANOVA test (continuous variables) or chi-squared/Fisher's exact test (categorical variables) comparing low vs. moderate vs. high total PSS-14 values

[2] Race/ethnicity = "other" includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = "Other" includes participants where mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child's father at baseline

Table 2.2 Descriptive statistics for participant and census tract characteristics by historic redlining categories (ungraded vs. low redlining vs. high redlining)

	Ungraded (N=58; 27.2%)		**Low redlining** (N=44; 20.7%)		**High redlining** (N=111; 52.1%)		**Total Sample** (N=213)		**p-value[1]**
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
PSS-14									**0.038**
Mean (SD)	22.5	(7.07)	24.8	(6.38)	25.2	(6.20)	24.4	(6.55)	
Race/ethnicity[2]									**< 0.001**
Hispanic	3	25.00	0	0.00	9	75.00	12	100.00	
Non-Hispanic Black	33	20.12	40	24.39	91	55.49	164	100.00	
Non-Hispanic white	17	73.91	1	4.35	5	21.74	23	100.00	
other	4	36.36	3	27.27	4	36.36	11	100.00	
Missing	1	33.33	0	0.00	2	66.67	3	100.00	
Sex at birth									0.511
Male	25	24.75	24	23.76	52	51.49	101	100.00	
Female	33	29.46	20	17.86	59	52.68	112	100.00	
Age									0.095
Mean (SD)	15.1	(0.307)	15.2	(0.424)	15.3	(0.517)	15.2	(0.453)	
Baseline city of residence									0.052
Chicago	8	25.81	3	9.68	20	64.52	31	100.00	
Detroit	31	22.14	33	23.57	76	54.29	140	100.00	
Toledo	16	44.44	7	19.44	13	36.11	36	100.00	
Other	3	50.00	1	16.67	2	33.33	6	100.00	
Mother's relationship status at baseline[3]									**0.008**
Married	9	20.45	15	34.09	20	45.45	44	100.00	

	Ungraded (N=58; 27.2%)		Low redlining (N=44; 20.7%)		High redlining (N=111; 52.1%)		Total Sample (N=213)		p-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Romantically Involved	26	20.97	65	52.42	33	26.61	124	100.00	
Other	9	20.93	29	67.44	5	11.63	43	100.00	
Missing	0	0.00	2	100.00	0	0.00	2	100.00	
Mother's educational attainment at baseline									**< 0.001**
Less than high school	15	20.00	14	18.67	46	61.33	75	100.00	
High school or equivalent	8	14.04	14	24.56	35	61.40	57	100.00	
Some college or technical training	17	30.91	13	23.64	25	45.45	55	100.00	
College grad	18	72.00	2	8.00	5	20.00	25	100.00	
Missing	0	0.00	1	100.00	0	0.00	1	100.00	
Mother's age at baseline									0.086
Mean (SD)	26.7	(5.93)	25.8	(6.10)	24.7	(5.40)	25.5	(5.73)	
Missing	0	0	0	1	100	1	100	(0.5%)	
Household income at 15 ($)									**< 0.001**
Median [Min, Max]	58500	[1800, 500000]	31000	[2620, 150000]	27600	[1.00, 155000]	35700	[1.00, 500000]	
% Tract Below Poverty									**< 0.001**
Mean (SD)	11.2	(9.7)	31.8	(10.9)	34.1	(14.9)	27.4	(16.2)	
% Tract non-Hispanic Black									**< 0.001**
Mean (SD)	19.7	(23.2)	83.0	(23.5)	71.5	(31.5)	59.8	(37.3)	

[1] P-value based on ANOVA test (continuous variables) or chi-squared test (categorical variables) comparing participants in low redlining vs. high redlining vs. ungraded census tracts

[2] Race/ethnicity = “other” includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = “Other” includes participants where mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child’s father at baseline

Table 2.3 Association between historic redlining score and continuous total Perceived Stress Scale (PSS) score among SAND participants

	Model 1: Unadjusted			Model 2: Adjusted for baseline city			Model 3: Adjusted for sex at birth			Model 4: Adjusted for baseline city and sex at birth		
Full Sample (n = 213)												
	β	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*
Low redlining	2.28	(-0.28, 4.83)	0.080	1.91	(-0.67, 4.49)	0.146	2.36	(-0.21, 4.92)	0.072	2.00	(-0.59, 4.60)	0.129
High redlining	2.66	(0.59, 4.73)	**0.012**	2.43	(0.31, 4.54)	**0.025**	2.69	(0.61, 4.76)	**0.011**	2.47	(0.35, 4.59)	**0.022**
Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Non-Hispanic Black Adolescents (n = 164)												
	Model 1: Unadjusted			Model 2: Adjusted for baseline city			Model 3: Adjusted for sex at birth			Model 4: Adjusted for baseline city and sex at birth		
	β	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*
Low redlining	0.89	(-2.02, 3.81)	0.546	1.08	(-1.87, 4.03)	0.470	0.96	(-1.97, 3.88)	0.519	1.15	(-1.81, 4.11)	0.443
High redlining	2.33	(-0.19, 4.85)	0.069	2.59	(0.05, 5.13)	**0.045**	2.32	(-0.20, 4.84)	0.071	2.60	(0.06, 5.14)	**0.045**
Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

Figure 2.1 Theorized pathways linking structural racism and historic redlining to adolescent perceived stress outcomes*

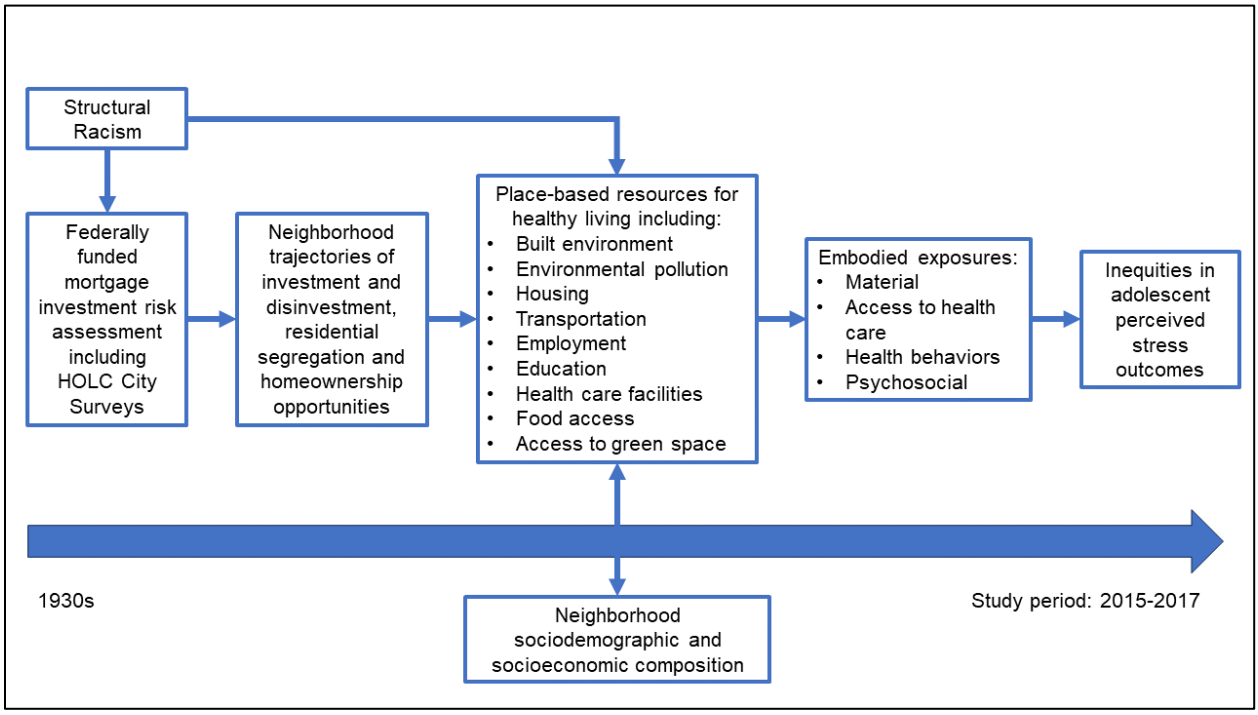

*Figure adapted from Krieger et al. (2020)[16]

Figure 2.2 Pathway between historic redlining and adolescent Perceived Stress Scale score, mediated via percent of census tract living below poverty level using ACS 5-year estimates (2014 – 2018) (n = 213)

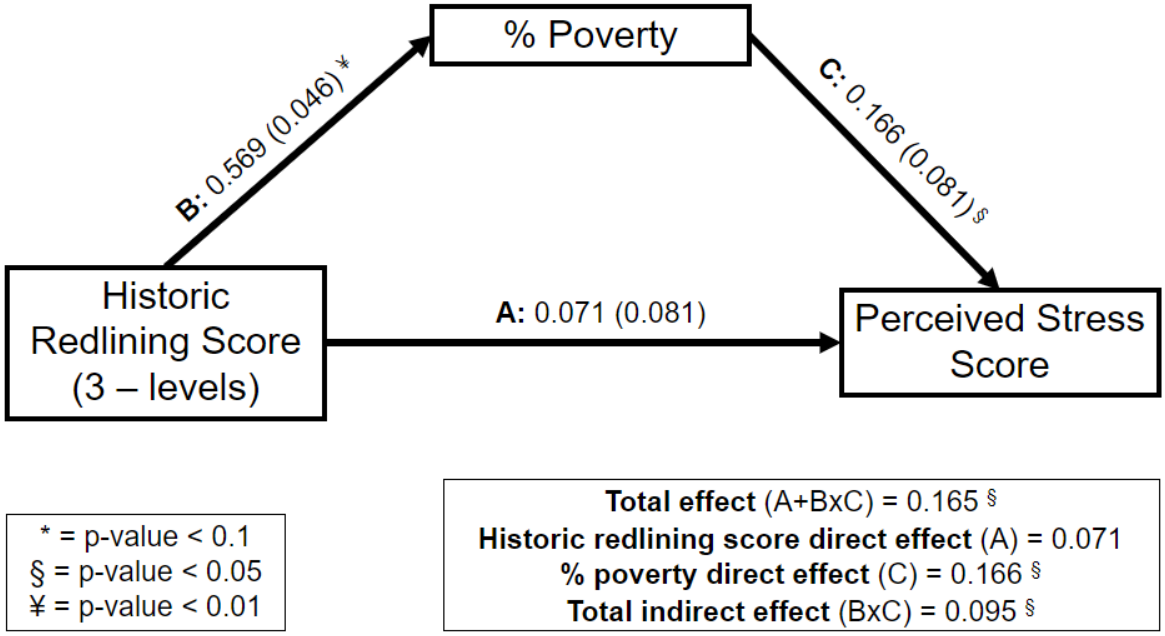

Figure 2.3 Pathway between historic redlining and adolescent Perceived Stress Scale score, mediated via percent of census tract identified as non-Hispanic Black using ACS 5-year estimates (2014 – 2018) (n = 213)

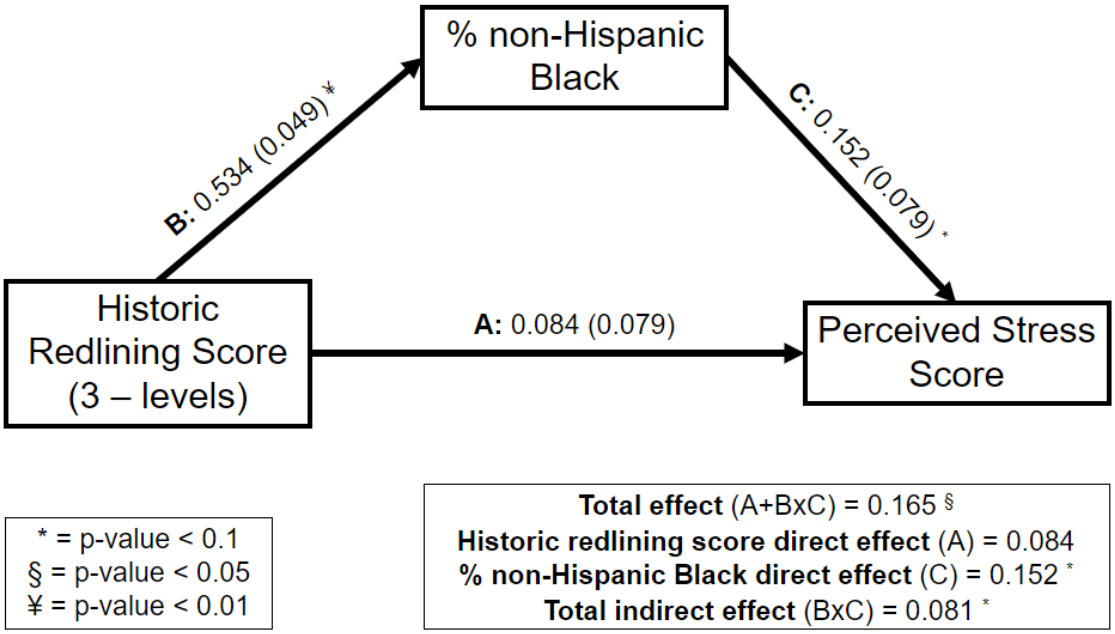

Table S2.1 Perceived Stress Scale (PSS-14) questionnaire[1]

1. In the last month, how often have you been upset because of something that happened unexpectedly?
2. In the last month, how often have you felt that you were unable to control the important things in your life?
3. In the last month, how often have you felt nervous and “stressed”?
4. In the last month, how often have you dealt successfully with irritating life hassles? *
5. In the last month, how often have you felt that you were effectively coping with important changes that were occurring in your life? *
6. In the last month, how often have you felt confident about your ability to handle your personal problems? *
7. In the last month, how often have you felt that things were going your way? *
8. In the last month, how often have you found that you could not cope with all the things that you had to do?
9. In the last month, how often have you been able to control irritations in your life? *
10. In the last month, how often have you felt that you were on top of things? *
11. In the last month, how often have you been angered because of things that happened that were outside of your control?
12. In the last month, how often have you found yourself thinking about things that you have to accomplish?
13. In the last month, how often have you been able to control the way you spend your time? *
14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

[1] PSS-14 questionnaire developed by Cohen et al. (1983)[26]

* Positive questioning: responses reversed before summing to create continuous score

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Chapter 3

Structural racism and hair cortisol levels in adolescents

3.1 Background

Psychosocial stress is a common experience for U.S. adolescents. During critical periods of growth and development, including adolescence, chronic stress can lead to lifelong health complications including poor mental health outcomes, risky behaviors, and reduced immune function.[1-5] Stress can arise from a variety of factors across interpersonal, neighborhood, and structural levels. Specifically, neighborhood factors including safety and urbanicity have been found to be associated with stress levels in children and adolescents.[6,7] Limited research has considered the impacts of structural factors, such as structural racism, as upstream determinants of current contextual neighborhood features on stress outcomes among adolescents.

Structural racism refers to historic and present-day ideologies, policies, and cultural practices that reinforce racial discrimination and racialized inequitable outcomes over space and time, including across generations.[8] Structural racism operates via interconnected institutional systems such as education, housing, the labor market, healthcare, and the criminal legal system[8] and results in differential access to power, resources, and opportunities for Black, Indigenous, and other people of color to the benefits of white populations. Structural racism has been posited as a fundamental cause of racial residential segregation, racialized socioeconomic disadvantage, and racial/ethnic health inequities.[8]

One proxy for historic structural racism is redlining. Historic redlining refers to racialized policies, procedures, and practices through which federal agencies as well as

private institutions systematically denied lending services in urban neighborhoods deemed “risky for investment”.[9] An example of government sanctioned historic redlining was through the Home Owners’ Loan Corporation (HOLC), established in 1933 by the U.S. federal government.[10] The HOLC conducted City Surveys between 1935 and 1940 among neighborhoods in over 200 urban cities throughout the United States to determine residential investment risk.[10] Areas identified as “risky for investment” were given the lowest grade and outlined in red on the “residential security maps” created by the HOLC. Thus, this process became known as redlining.[9] Many of the residential risk assessments were racially motivated, resulting in discriminatory lending practices against racially minoritized populations, specifically Black Americans and immigrants of color.[9-11]

The impact of redlining did not stop with lending in the HOLC era. Though the HOLC pioneered the logic of redlining, these racist policies and practices were incorporated into subsequent lending and investment strategies, including the Federal Housing Administration.[13,14] Over time, discriminatory lending practices are hypothesized to have shaped the distribution of people (racial residential segregation), goods, and investment opportunities across present-day neighborhoods (Figure 3.1).[12] Accordingly, historic redlining has shown to be associated with present-day neighborhood factors such as air quality,[15] access to food outlets,[16,17] tobacco and alcohol outlet density,[18-20] and tree coverage.[21] Historic redlining is also associated with present-day neighborhood socioeconomic outcomes and demographic distributions.[11,22-24] As present-day neighborhood social, economic and physical features are associated with health outcomes[25-27], it is not surprising that historical redlining would serve as a

determinant of health outcomes. Studies have now examined historic redlining in relation to cardiovascular disease,[28] birth outcomes,[12,29-31] cancer,[32,33] and neighborhood safety.[34-36]

One hypothesized pathway through which historic redlining may be associated with current health outcomes is through stress, but studies of historic redlining and individual-level health outcomes are few. To address this gap, we examined census tract historic redlining in relation to adolescent hair cortisol levels, an indicator of biological stress reactivity. We hypothesized that adolescents living in historically redlined tracts would have higher biological stress reactivity, measured via hair cortisol concentration, than individuals living in tracts that were not subjected or minimally exposed to racist redlining policies. Because historic redlining policies and practices have contributed to present-day segregation and neighborhood-level socioeconomic inequities[11,22-24] we further hypothesized that the association between historic redlining and hair cortisol concentration would be partially mediated by present-day census tract sociodemographic characteristics.

3.2 Methods

Study sample

Data for this study come from the Study of Adolescent to Adult Neural Development (SAND), a sub-set of the Future of Families and Child Wellbeing Study (FFCWS). FFCWS is a longitudinal cohort study with a baseline sample of 4,898 U.S. children and caregivers who were followed over six waves: 1) birth (1998 – 2000), 2) age 1 (1999 – 2001), 3) age 3 (2001 – 2003), 4) age 5 (2003 – 2006), 5) age 9 (2007 – 2010), and 6) age 15 (2014 – 2017).[37] Participants of FFCWS come from 20 large cities

throughout the US (population ≥ 200,000). FFCWS participants were over-sampled to include a large proportion of Black and Hispanic participants as well as low-income families.[38] The SAND sub-study, focused on understanding links between contextual factors and brain development, were collected during wave 6 of FFCWS (age 15) and included a total of 237 participants 15 – 17 years old who lived in or near Detroit, Toledo, or Chicago.

Hair cortisol concentration (HCC)

Cortisol levels were measured using cortisol output from hair samples among SAND participants. Hair cortisol concentration (HCC) is a validated measure of hypothalamic-pituitary-adrenal HPA axis activation in children.[39,40] HCC can be used to measure longer-term cortisol levels, where a 3-cm hair segment can be used to assess average cortisol output over at least three months.[41,42] Additionally, previous findings indicate that HCC is not associated with factors such as sleep and diet which can impact other biomarkers of cortisol, such as saliva, blood, and urine.[41]

A total of 175 SAND participants provided a hair sample. A detailed description of the methods used to obtain hair samples are described elsewhere.[42] Briefly, a research assistant collected three hair samples, which were then analyzed using liquid chromatography tandem mass spectrometry-based methods to determine HCC.[42] Cortisol levels were measured in picograms of cortisol per milligram of hair (pg/mg) and continuous cortisol levels were log-transformed to account for skewedness in measured values. HCC levels were categorized into tertiles for descriptive purposes and continuous HCC was used in regression analyses. Tertiles were based on the distribution of log-transformed cortisol values, resulting in a three-level outcome: “low”

cortisol (< 0.20 pg/mg), “moderate” cortisol (0.20 - < 3.21 pg/mg), and “high” cortisol (≥ 3.21 pg/mg).

Historic redlining scores

Historic redlining scores come from the HOLC “residential security” maps and were computed by Meier and Mitchell (2022).[43] In the early 20th century, the HOLC assigned one of four grades to each neighborhood evaluated: A – “Best”, B – “Still Desirable”, C – “Definitely Declining”, or D – “Hazardous”.[44] To calculate historic redlining scores, neighborhoods identified by the HOLC as “Best” were given an initial score of 1, while “Still Desirable”, “Definitely Declining” and “Hazardous” were scored as 2, 3, and 4, respectively. Redlining scores were then multiplied by the total percentage of census tract area assessed by the HOLC. For example, a tract graded 50% C and 50% B would receive a historic redlining score of 2.5 (3*0.5 + 2*0.5 = 2.5). Tracts with <20% of their area assessed by HOLC were excluded. This procedure resulted in a continuous historic redlining score. A lower score indicates “low redlining”, while a higher score indicates “high redlining”. Historic redlining scores based on 2010 census tract boundaries were linked to the SAND sub-study by FFCWS staff using participants’ reported addresses during wave 6 (age 15) of the FFCWS data collection.

We examined historic redlining as a categorical variable. Meier and Mitchell (2022) previously divided historic redlining scores into four intervals based on the national distribution of redlining scores.[43] This categorical historic redlining score used the following ranges to identify historic redlining intervals: 1.00 – 1.749 (level 1), 1.75 – 2.49 (level 2), 2.5 – 3.249 (level 3), and 3.25 – 4.00 (level 4).[43] Areas not assessed by the HOLC, or with <20% of their area scored were identified as “ungraded”. Historic

redlining score categories were combined to create a three-level exposure variable with the following ranges: “Low redlining” (levels 1 and 2, historic redlining score range: 1.00 – 2.49), “High redlining” (levels 3 and 4, range: 2.5 – 4.00), and “ungraded”.

Covariates

For descriptive purposes, we examined a variety of covariates. In wave 6 of FFCWS, participants were asked to self-identify their race/ethnicity by responding to the question: “What is your race and ethnicity?” Interviewers entered participant’s responses as an open-ended question and aggregated responses for race and ethnicity. In this study, race and ethnicity was then examined as four categories: Hispanic, non-Hispanic Black, non-Hispanic white, and other. The category “other” includes participants who identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander.

Additional participant demographics examined included sex at birth (male or female, with no nonbinary response options available in FFCWS at baseline), age in years, and city at birth (Chicago, Detroit, Toledo, or other). Maternal characteristics examined included mother’s age at baseline in years, maternal relationship with child’s father at baseline (married, romantically involved/steady, or other, which includes on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another), and maternal educational attainment at baseline (less than high school, high school or equivalent, some college or technical school, or college graduate). We also examined socioeconomic status, measured using household income at age 15 (reported in U.S. dollars). Neighborhood characteristics measured at the census tract-level included the percent of the population below the federal poverty level and percent

of the population that identifies as non-Hispanic Black alone. Neighborhood indicators were based on the U.S. Census Bureau's American Community Survey 5-year estimates (2014-2018).[45]

Statistical analysis

Descriptive statistics were reported to summarize participant and neighborhood characteristics of the study sample. Using listwise deletion, participants missing responses on either the exposure or outcome were removed (n = 73), resulting in a final sample of 164 participants (69.2% of total SAND sample). Individuals missing HCC values were more often male (71.0% vs. 40.0%), born to younger mothers at baseline (mean [SD]: 24.3 [5.44] vs. 26.2 [6.06]), and to have their mother report a baseline relationship status of "other" with the child's father (30.6% vs. 17.1%) (Table S3.1).

We used linear regression to examine the association between historic redlining scores and log-transformed HCC. We first examined the unadjusted association between HCC and historic redlining using a 3-level exposure (low redlining, high redlining, and ungraded [reference group]) among the full sample. In sequential models we first adjusted for city of residence at baseline, then mother's age at birth. City of residence at baseline was included as a covariate of interest as we wanted to control for potential differences in SAND sampling for each city. Finally, we adjusted for both city of residence at baseline and mother's age at birth. We used the same modeling strategy subset to non-Hispanic Black participants (n = 128). Finally, we examined the relationship between HCC and historic redlining unadjusted and adjusted for mother's age at birth only among participants who lived in Detroit at baseline (n = 113).

Descriptive statistics and linear regression modeling was conducted using R version 4.2.1.[46]

Studies have shown associations between historic redlining and current neighborhood sociodemographic characteristics. To determine whether present-day neighborhood sociodemographic characteristics mediated associations between redlining and HCC, we used path analysis. We hypothesized historic redlining to influence hair cortisol concertation via two different pathways, 1) a direct association independent of present-day census tract characteristics (percent poverty and percent non-Hispanic Black as proxy for racial residential segregation), and 2) an indirect association mediated through present-day census tract characteristics. We used structural equation modeling (SEM) conducted in MPlus version 8.2 to examine these pathways.[47]

3.3 Results

Among the 164 participants, over three-quarters (78.7%) identified as non-Hispanic Black, 10.4% as non-Hispanic white, 4.9% as Hispanic, and 4.9% as “other” (Table 3.1). Those identified as female at birth accounted for 59.8% of the sample. The mean age of participants at wave 6 of FFCWS was 15.2 years, and the majority (68.9%) of the sample lived in Detroit at baseline. The mean age of mothers at baseline was 25.9 years, and the majority of mothers reported not being married to the child’s father at baseline with 60.4% reporting being romantically involved or steady with the father. Approximately one-third of mothers at baseline reported having less than a high school education (34.1%), and the median household income was $35,000. On average, participants at wave 6 lived in census tracts that were majority non-Hispanic Black

(61.7%) and over one-quarter of the population living below the federal poverty level (26.5%).

In univariate analyses, there was a statistically significant association ($p = 0.01$) between hair cortisol levels and historic redlining score (Table 3.1). Participants with moderate or high cortisol levels more often resided in high redlining tracts, at 55.4% and 56.1%, respectively, compared to 33.3% of participants with low cortisol values. Individuals with low cortisol also more often resided in ungraded census tracts (47.1%), compared to those with moderate (23.2%) and high cortisol levels (17.5%). We also observed a statistically significant association between cortisol levels and race and ethnicity ($p < 0.001$), baseline maternal educational attainment ($p = 0.044$), household income at age 15 ($p = 0.006$), percent of census tract non-Hispanic Black ($p = 0.001$), and percent of census tract below poverty ($p = 0.005$).

Table 3.2 shows the distribution of participant sociodemographic characteristics by census tract historic redlining score comparing those living in ungraded census tracts (28.7%), low redlining census tracts (22.6%), and high redlining census tracts (48.8%). Non-Hispanic white participants more often resided in ungraded census tracts (82.4%), compared to their non-Hispanic Black peers (22.5%). The majority of non-Hispanic Black (51.9%) and Hispanic (75.0%) participants resided in high redlining census tracts. Among participants with mothers who had graduated from college at baseline, the majority (75%) resided in ungraded census tracts at age 15, whereas the majority of participants with mothers with a high school education (56.8%) or less (60.7%) resided in high redlining census tracts. Household income was associated with historic redlining category, with participants in ungraded tracts reporting a median household income of

$55,200, compared to $33,200 among participants in low redlining tracts, and $27,200 among participants in high redlining tracts. We observed a statistically significant association between historic redlining score and log-transformed cortisol levels ($p = 0.001$), race/ethnicity ($p < 0.001$), city at birth ($p = 0.018$), mother's age at baseline ($p = 0.04$), baseline relationship with father ($p = 0.013$), baseline maternal educational attainment ($p < 0.001$), household income at age 15 ($p = 0.013$), and census tract characteristics including percent non-Hispanic Black ($p < 0.001$), and percent below poverty ($p < 0.001$).

Table 3.3 reports estimates from linear regression analyses examining the association between the exposure of interest, historic redlining, and the outcome, log-transformed hair cortisol levels, in adolescents among three samples: full sample ($n = 163$), non-Hispanic Black participants ($n = 128$), and participants living in Detroit at baseline ($n = 113$). Model 1 is the unadjusted association. In the full sample, participants in high redlining tracts had statistically significantly higher cortisol levels than those in ungraded tracts ($\beta = 1.13$, CI: 0.55, 1.72). This association persisted in the fully adjusted model which included both baseline city of residence and mother's age at birth ($\beta = 0.88$, CI: 0.25, 1.51). Participants living in low redlining tracts also reported higher cortisol level compared to ungraded tracts for all models, including the fully adjusted model ($\beta = 0.76$, CI: 0.04, 1.48).

Among non-Hispanic Black participants, there was an association between cortisol levels and high redlining but not low redlining in the fully adjusted model. Participants in high redlining tracts had statistically significantly higher cortisol levels than those in ungraded tracts after adjusting for baseline city of residence and mother's

age at birth (β = 0.78, CI: 0.01, 1.55). Similarly, among the Detroit at baseline sample, participants living in high redlining (but not low redlining) census tracts had statistically significantly higher cortisol levels compared to those living in ungraded tracts after adjusting for mother's age at birth (β = 0.89, CI: 0.05, 1.73). These results differed from the full sample as low redlining was no longer statistically significantly associated.

Figure 3.3 shows estimates of the direct, indirect, and total effects of historic redlining on hair cortisol concentrations mediated by percent of the census tract below the poverty level. An increase in historic redlining score (e.g., going from a low redlining census tract to a census tract with high redlining) was associated with greater biological stress reactivity. A one-unit increase in historic redlining resulted in a 0.278 standard deviation increase in hair cortisol concentration ($p < 0.01$). This total effect was decomposed into a direct effect of historic redlining score on hair cortisol concentration and an indirect effect mediated through the percent of the census tract below the poverty level. There was a statistically significant direct effect of historic redlining on hair cortisol concentration independent of current census tract socioeconomic indicators (β = 0.193, $p = 0.022$). Mediation of the total effect through percent below poverty was marginally significant (β = 0.085, $p = 0.051$).

Figure 3.4 depicts the direct, indirect, and total effects of historic redlining on hair cortisol concentration mediated by the percent of the census tract identified as non-Hispanic Black. For a one-unit increase in historic redlining, there was a 0.278 standard deviation increase in hair cortisol concentration ($p < 0.01$). There was no significant direct effect of historic redlining on hair cortisol concentration independent of current census tract demographics (β= 0.147, $p = 0.084$). However, there was mediation of the

total effect through percent of census tract that was non-Hispanic Black (β= 0.132, p = 0.005). Both SEM models are just-identified, so fit statistics are not reported as they are not applicable.

3.4 Discussion

The current study provides a novel investigation of the impact of historic structural factors on biological stress reactivity among a sample of adolescents living in urban areas of the U.S. We hypothesized that participants living in tracts that experienced greater redlining would report higher stress as measured by HCC, and our findings supported this hypothesis. As expected, we found that tracts categorized with the highest historic redlining scores by the HOLC had statistically significantly higher cortisol levels compared to those living in ungraded tracts. We observed these findings among the full sample as well in a sub-sample of non-Hispanic Black participants and those who lived in Detroit at baseline. Hair cortisol is a useful measure of chronic stress, where elevated cortisol levels have been found to be associated with body mass index and cardiovascular disease risk factors such as high blood pressure and diabetes.[41] Our findings provide an understanding of how historic policies can impact stress outcomes, which may contribute to subsequent health disparities.

We identified tracts that were not provided with a grade by the HOLC or tracts that had <20% of their area assessed as “ungraded” and utilized these regions as the reference group for regression analyses. These areas served as a useful comparison group, as they were mainly undeveloped during the HOLC assessments and were not subjected or minimally exposed to redlining policies or practices. Despite being rated more favorably by the HOLC (e.g., “Best” or “Still Desirable”), individuals living in “low

redlining" census tracts were still found to have statistically significantly higher cortisol levels than those living in ungraded regions in the full sample. As seen in Figure 3.2, all three cities report the highest rates of redlining in the central portion of the city, with lower rates in the periphery of the city boundaries. Our findings may indicate differences in health outcomes among adolescents living in "urban" vs. "suburban" areas. Many participants living in ungraded regions were located outside urban areas within suburban neighborhoods, where they reported better health outcomes than their peers located within the larger metropolitan areas of Chicago, Detroit, and Toledo. These findings are consistent with previous literature, which identified that adolescents living in more densely populated areas had significantly higher HCC.[6]

We did not observe an association between low redlining and cortisol levels among sub-samples of non-Hispanic Black participants as well as those who lived in Detroit at baseline. We theorize that this is due to the distribution of sample participants by race/ethnicity. For example, the majority of non-Hispanic Black participants (51.9%) lived in high redlining areas, while less than one-quarter (22.5%) lived in ungraded areas. Therefore, when examining the full sample, we may have detected a significant effect of redlining on HCC because the majority (82.4%) of non-Hispanic white participants resided in ungraded regions.

We hypothesized that the association between historic redlining and adolescent hair cortisol concentration would be partially mediated by present-day census tract characteristics because redlining has shaped the distribution of people, resources, and investment over time.[11,22-24] Our findings supported this hypothesis, with 47.5% and 30.6% of the total effect between historic redlining and hair cortisol concentration

mediated by the proportion of the population identified as non-Hispanic Black and the proportion of the population below the poverty level, respectively. From previous literature we know that the present-day make-up of neighborhood demographics and resources is not randomly distributed, but rather is the legacy of racist policies and practices enacted over time.[12,31] Therefore, these findings are important because it provides evidence that historic policies continue to drive health outcomes in present-day independently, as well as indirectly through the composition of present-day neighborhood characteristics and resources.

Few studies have examined structural racism as a driver of adolescent stress. At the individual level, recent research has estimated the impact of racial discrimination on cortisol levels, a common biomarker of stress exposure, in adolescents and young adults. Ford et al. (2021) found that Black/African American adolescents had higher hair and salivary levels compared to their white counterparts in the Adolescent Health and Development Context study. They theorized that this finding may be due to inequitable exposure to chronic daily stressors, including racism and additional adversities such as violence and limited economic opportunities.[48] Similar findings were reported by DeSantis et al. (2007) who found that African-American and Hispanic adolescents reported flatter diurnal cortisol slopes (an indicator for potential subsequent adverse health outcomes) compared to their white peers.[49] These results are consistent with our findings and support our hypothesis that individual experiences of everyday discrimination from historic processes driven by structural racism impact health outcomes among adolescents.

Overall, our findings are consistent with ecosocial theory's [50] conceptualization of embodiment, which posits that social and environmental exposures get "under the skin" or are biologically embedded resulting in health differences, for example, through stress pathways.[51] Structural racism, and policies driven by structural racism, can lead to discrimination resulting in higher stress and "biological expressions of racism".[51] Another important element of ecosocial theory is identifying the governmental and non-governmental actors within differing levels of society that reinforce racism and using this information to hold institutions accountable.[51] Therefore, focusing on current neighborhood features and health alone ignores the policies and processes enacted over time that produced the present-day distribution of people and resources. For example, Robertson et al. (2023) found that neighborhoods that were graded the worst by the HOLC have received more place-based funding from 1990 – 2015 compared to more favorably graded tracts; however, investment impacts have not been equally distributed, particularly among homeownership opportunities with a decline in the share of Black homeowners.[52] Without additional insight into the historic policies and practices driven by structural racism that have shaped present-day neighborhoods, contemporary policies may not employ equitable solutions, which then reinforce harms among marginalized populations that were unjustly targeted by these policies in the first place. Equipped with a multi-level and historical perspective, we can begin to understand how neighborhood social, economic, and physical environment get "under the skin" to drive differences in stress biomarkers in adolescents in the present study and health disparities more broadly; we can also use this information to hold institutions accountable for enacting real change.[51]

Strengths and limitations

There are a few potential limitations to consider. First, the SAND sub-study of the FFCWS is comprised of a sample of 237 U.S. adolescents; the relatively small sample size may have limited our ability to detect statistically significant differences. Furthermore, 30.8% (n = 73) of SAND participants did not provide hair cortisol samples, which further reduced our sample. However, it is important to note that we did not find statistically significant differences on any key characteristics of interest when comparing those who provided hair cortisol samples compared to those who did not provide a sample (Table S3.1). Second, SAND only included participants from or near Chicago, Detroit, and Toledo. These midwestern cities may not be representative of other urban cities or regions throughout the United States that faced discriminatory lending practices from federal policies such as HOLC. Moreover, the generalizability of our sample may be further limited because the majority (68.9%) of SAND participants were from Detroit at baseline. Third, we examined the impact of historic redlining on health outcomes using one timepoint for exposure. This may not capture the full impact of historic redlining as we do not include a measure for duration of time in a redlined area, rather we measured redlining based on the participant's address during wave 6 (age 15) of the FFCWS data collection. However, hair cortisol concentration can capture three to four months of stress reactivity, thus using the wave 6 address provided an accurate representation of neighborhood exposure.[41] Finally, the residential security maps produced by the HOLC represent just one form of structural racism and discriminatory housing policies that took place during the 20th century.

Despite these limitations, we identified an association between structural determinants and cortisol levels in adolescents. Our study findings provide a novel

investigation of how historic redlining impacts health outcomes at the individual-level. Despite being a growing area of interest in public health, the majority of studies examining historic redlining rely on health outcomes at neighborhood or county level, with limited studies examining individual-level outcomes.[12,28-30,32] Our study fills a crucial gap in understanding the impacts of policies driven by structural racism on individual biological stress outcomes. We also identified using structural equation modeling how historic redlining practices have impacted the composition of present-day census tract characteristics such as percent of the population below the poverty level and racial/ethnic distributions. Finally, we identified the unique impact that tracts ungraded by the HOLC have on health outcomes among adolescents.

3.5 Conclusion

Future research may consider examining the relationship between redlining and cortisol using a sample of adolescents from diverse backgrounds including those residing in regions outside the Midwest to see if these relationships persist. Additional indicators of present-day neighborhood characteristics that could be examined include neighborhood safety or educational outcomes, as these have been found to be associated with cortisol levels in adolescents and children and may act as potential modifiers or mediators of this relationship.[7,53] Finally, future research may consider the impact of sensitive or critical periods of development during childhood and adolescents, and how exposure to structural factors such as historic redlining may impact outcomes based on the timing in which exposure occurs. Additional measures could include examining the impact of redlining at different timepoints (for example, in early childhood) or by utilizing a measure of cumulative exposure to historic redlining throughout

childhood and adolescence. The findings from this research support that historic structural racism is an upstream determinant of present-day health inequalities, and these disparities in health outcomes are likely to persist until structural racism is addressed.

3.6 Tables and figures

Table 3.1. Descriptive statistics for SAND participant and census tract characteristics by cortisol tertile (low vs. moderate vs. high)

	Low Cortisol (< 0.20) (N=51; 31.1%)		**Moderate (0.20 - < 3.21)** (N=56; 34.1%)		**High Cortisol (≥ 3.21)** (N=57; 34.8%)		**Overall** (N=164)		**p-value[1]**
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Cortisol (pg/mg)									**< 0.001**
Mean (SD)	1.55	(0.360)	2.62	(0.337)	4.92	(1.55)	3.08	(1.68)	
Historic redlining score									**0.010**
Low redlining	10	(19.6%)	12	(21.4%)	15	(26.3%)	37	(22.6%)	
High redlining	17	(33.3%)	31	(55.4%)	32	(56.1%)	80	(48.8%)	
Ungraded	24	(47.1%)	13	(23.2%)	10	(17.5%)	47	(28.7%)	
Race/ethnicity									**< 0.001**
Hispanic	2	(3.9%)	6	(10.7%)	0	(0%)	8	(4.9%)	
Non-Hispanic Black	31	(60.8%)	43	(76.8%)	55	(96.5%)	129	(78.7%)	
Non-Hispanic white	14	(27.5%)	3	(5.4%)	0	(0%)	17	(10.4%)	
other[2]	3	(5.9%)	3	(5.4%)	2	(3.5%)	8	(4.9%)	
Missing	1	(2.0%)	1	(1.8%)	0	(0%)	2	(1.2%)	
Sex at birth									0.617
Female	29	(56.9%)	32	(57.1%)	37	(64.9%)	98	(59.8%)	
Male	22	(43.1%)	24	(42.9%)	20	(35.1%)	66	(40.2%)	
Age									0.208
Mean (SD)	15.2	(0.367)	15.1	(0.334)	15.3	(0.552)	15.2	(0.433)	
City at birth									0.178

	Low Cortisol (< 0.20)		Moderate (0.20 - < 3.21)		High Cortisol (≥ 3.21)		Overall		p-value[1]
	(N=51; 31.1%)		(N=56; 34.1%)		(N=57; 34.8%)		(N=164)		
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Chicago	5	(9.8%)	11	(19.6%)	9	(15.8%)	25	(15.2%)	
Detroit	34	(66.7%)	37	(66.1%)	42	(73.7%)	113	(68.9%)	
Toledo	11	(21.6%)	7	(12.5%)	4	(7.0%)	22	(13.4%)	
Other	1	(2.0%)	1	(1.8%)	2	(3.5%)	4	(2.4%)	
Mother's age at baseline									0.382
Mean (SD)	26.8	(6.12)	25.7	(6.11)	25.3	(5.31)	25.9	(5.84)	
Missing	0	(0%)	1	(1.8%)	0	(0%)	1	(0.6%)	
Baseline relationship with father									0.189
Married	17	(33.3%)	11	(19.6%)	8	(14.0%)	36	(22.0%)	
Romantically Involved, Steady	26	(51.0%)	35	(62.5%)	38	(66.7%)	99	(60.4%)	
Other[3]	8	(15.7%)	10	(17.9%)	11	(19.3%)	29	(17.7%)	
Baseline maternal educational attainment									**0.044**
Less than high school	14	(27.5%)	26	(46.4%)	16	(28.1%)	56	(34.1%)	
High school or equivalent	10	(19.6%)	16	(28.6%)	18	(31.6%)	44	(26.8%)	
Some college or technical school	16	(31.4%)	10	(17.9%)	17	(29.8%)	43	(26.2%)	
College grad	11	(21.6%)	4	(7.1%)	5	(8.8%)	20	(12.2%)	
Missing	0	(0%)	0	(0%)	1	(1.8%)	1	(0.6%)	
Household income at 15 ($)									**0.006**

	Low Cortisol (< 0.20) (N=51; 31.1%)		Moderate (0.20 - < 3.21) (N=56; 34.1%)		High Cortisol (≥ 3.21) (N=57; 34.8%)		Overall (N=164)		p-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Mean (SD)	71200	(81300)	40500	(42600)	38100	(36700)	49200	(57600)	
Median [Min, Max]	49800	[2620, 500000]	29000	[2600, 240000]	27000	[700, 200000]	35000	[700, 500000]	
% Tract non-Hispanic Black									**0.001**
Mean (SD)	49	(39.8)	59.7	(38.1)	75.1	(29.2)	61.7	(37.2)	
% Poverty									**0.005**
Mean (SD)	21.8	(14.3)	26	(16.4)	31.3	(13.5)	26.5	(15.2)	

[1] P-value based on ANOVA test (continuous variables) or chi-squared/Fishers exact test (categorical variables) comparing low vs. moderate vs. high cortisol

[2] Race/ethnicity = "other" includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = "Other" includes participants where mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child's father at baseline

Table 3.2 Descriptive statistics for SAND participant and census tract characteristics by historic redlining categories (ungraded vs. low redlining vs. high redlining)

	Ungraded (N=47; 28.7%)		**Low Redlining** (N=37; 22.6%)		**High Redlining** (N=80; 48.8%)		**P-value[1]**
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Cortisol tertile							**0.010**
Low Cortisol	24	47.1%	10	19.6%	17	33.3%	
Moderate Cortisol	13	23.2%	12	21.4%	31	55.4%	
High Cortisol	10	17.5%	15	26.3%	32	56.1%	
Cortisol (pg/mg)							**0.001**
Mean (SD)	2.32	(1.23)	3.24	(1.58)	3.45	(1.82)	
Race/Ethnicity							**< 0.001**
Hispanic	1	12.5%	1	12.5%	6	75.0%	
Non-Hispanic Black	29	22.5%	33	25.6%	67	51.9%	
Non-Hispanic white	14	82.4%	0	0.0%	3	17.6%	
other[2]	2	25.0%	3	37.5%	3	37.5%	
Missing	1	50.0%	0	0.0%	1	50.0%	
Sex at birth							0.404
Female	31	31.6%	18	18.4%	49	50.0%	
Male	16	24.2%	19	28.8%	31	47.0%	
Age							0.151
Mean (SD)	15.1	(0.247)	15.2	(0.435)	15.2	(0.503)	
City at birth							**0.018**
Chicago	7	28.0%	3	12.0%	15	60.0%	
Detroit	25	22.1%	29	25.7%	59	52.2%	
Toledo	14	63.6%	4	18.2%	4	18.2%	
Other	1	25.0%	1	25.0%	2	50.0%	

	Ungraded (N=47; 28.7%)		Low Redlining (N=37; 22.6%)		High Redlining (N=80; 48.8%)		P-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Mother's age at baseline							**0.040**
Mean (SD)	27.3	(6.01)	26.2	(6.18)	24.8	(5.44)	
Missing	0	0%	0	0%	1	1.3%	
Baseline relationship with father							**0.013**
Married	17	47.2%	9	25.0%	10	27.8%	
Romantically Involved, Steady	25	25.3%	21	21.2%	53	53.5%	
Other[3]	5	17.2%	7	24.1%	17	58.6%	
Baseline maternal educational attainment							**< 0.001**
Less than high school	12	21.4%	10	17.9%	34	60.7%	
High school or equivalent	7	15.9%	12	27.3%	25	56.8%	
Some college or technical school	13	30.2%	12	27.9%	18	41.9%	
College grad	15	75.0%	2	10.0%	3	15.0%	
Missing	0	0.0%	1	100.0%	0	0.0%	
Household Income at 15 ($)							**0.013**
Mean (SD)	79800	(90000)	39300	(29000)	35800	(31000)	
Median [Min, Max]	55200	[1800, 500000]	33200	[2620, 130000]	27200	[700, 144000]	
% Non-Hispanic Black							**< 0.001**
Mean (SD)	22.9	(26.4)	86.8	(17.3)	72.8	(31.6)	
% Tract below poverty							**< 0.001**
Mean (SD)	12.7	(10.6)	32.9	(11.2)	31.7	(14.0)	

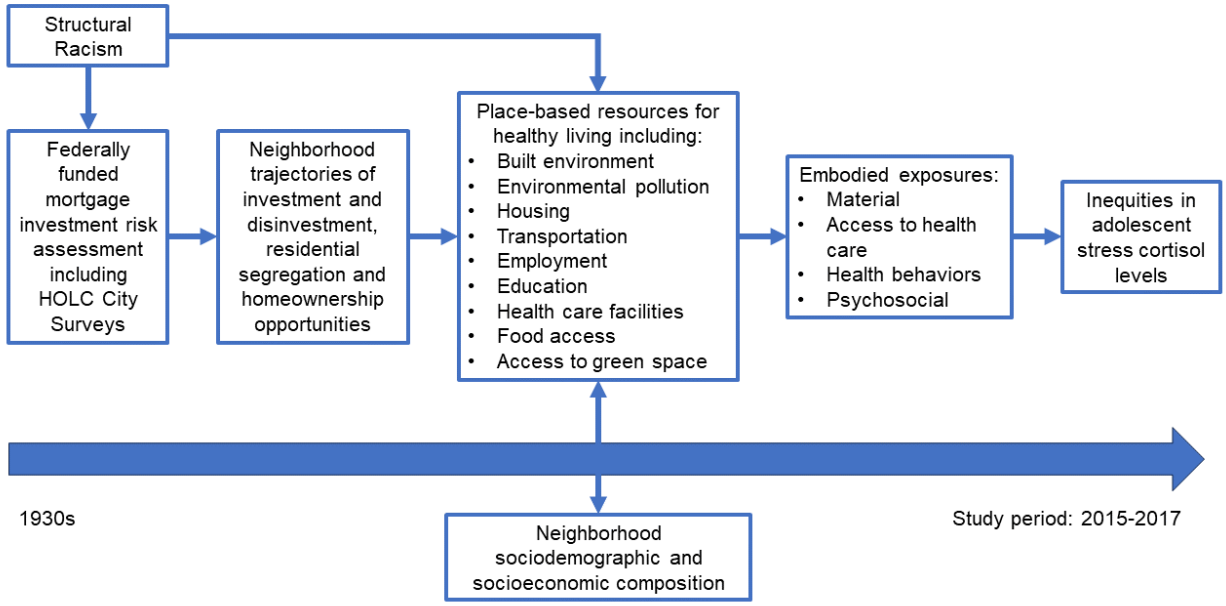
[1] P-value based on ANOVA test (continuous variables) or chi-squared/Fisher's exact test (categorical variables) comparing participants in low redlining vs. high redlining vs. ungraded census tracts
[2] Race/ethnicity = "other" includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander
[3] Baseline relationship with father = "Other" includes participants where mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child's father at baseline

Table 3.3 Association between log-transformed hair cortisol concentration (pg/mg) and historic redlining score (low redlining vs. high redlining vs. ungraded) among SAND participants

	Model 1: unadjusted			Model 2: adjusted for baseline city of residence			Model 3: adjusted for mother's age at birth			Model 4: full model [2]		
Full Sample (n = 163) [1]	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*
Low redlining	0.92	(0.22, 1.63)	**0.010**	0.81	(0.08, 1.53)	**0.029**	0.88	(0.18, 1.58)	**0.014**	0.76	(0.04, 1.48)	**0.039**
High redlining	1.13	(0.55, 1.72)	**<0.001**	0.99	(0.37, 1.61)	**0.002**	1.05	(0.45, 1.65)	**0.001**	0.88	(0.25, 1.51)	**0.006**
Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
	Model 1			**Model 2**			**Model 3**			**Model 4**		
Non-Hispanic Black Sample (n = 128) [1]	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*
Low redlining	0.47	(-0.38, 1.33)	0.277	0.48	(-0.39, 1.35)	0.278	0.48	(-0.38, 1.33)	0.275	0.49	(-0.38, 1.37)	0.268
High redlining	0.84	(0.09, 1.58)	**0.028**	0.82	(0.06, 1.58)	**0.034**	0.79	(0.03, 1.56)	**0.041**	0.78	(0.01, 1.55)	**0.049**
Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
	Model 1			**Model 2**			**Model 3**			**Model 4**		
Detroit at Baseline Sample (n = 113)	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*	*β*	*95% CI*	*p-value*
Low redlining	0.79	(-0.14, 1.73)	0.095	-	-	-	0.75	(-0.18, 1.68)	0.115	-	-	-
High redlining	1.03	(0.21, 1.85)	**0.014**	-	-	-	0.89	(0.05, 1.73)	**0.037**	-	-	-
Ungraded	[ref]	[ref]	[ref]	-	-	-	[ref]	[ref]	[ref]	-	-	-

[1] One participant missing mother's age at birth removed from sample
[2] Full model adjusted for both baseline city of residence and mother's age at birth

Figure 3.1 Theorized pathway linking historic redlining practices and policies to present-day chronic stress outcomes in adolescents*



* Figure adapted from Krieger et al. (2020)[12]

Figure 3.2 Original HOLC grading (left) and 2010 census tract historic redlining scores (right) for Study of Adolescent to Adult Development (SAND) cities (A: Chicago, IL; B: Detroit, MI; and C: Toledo, OH)

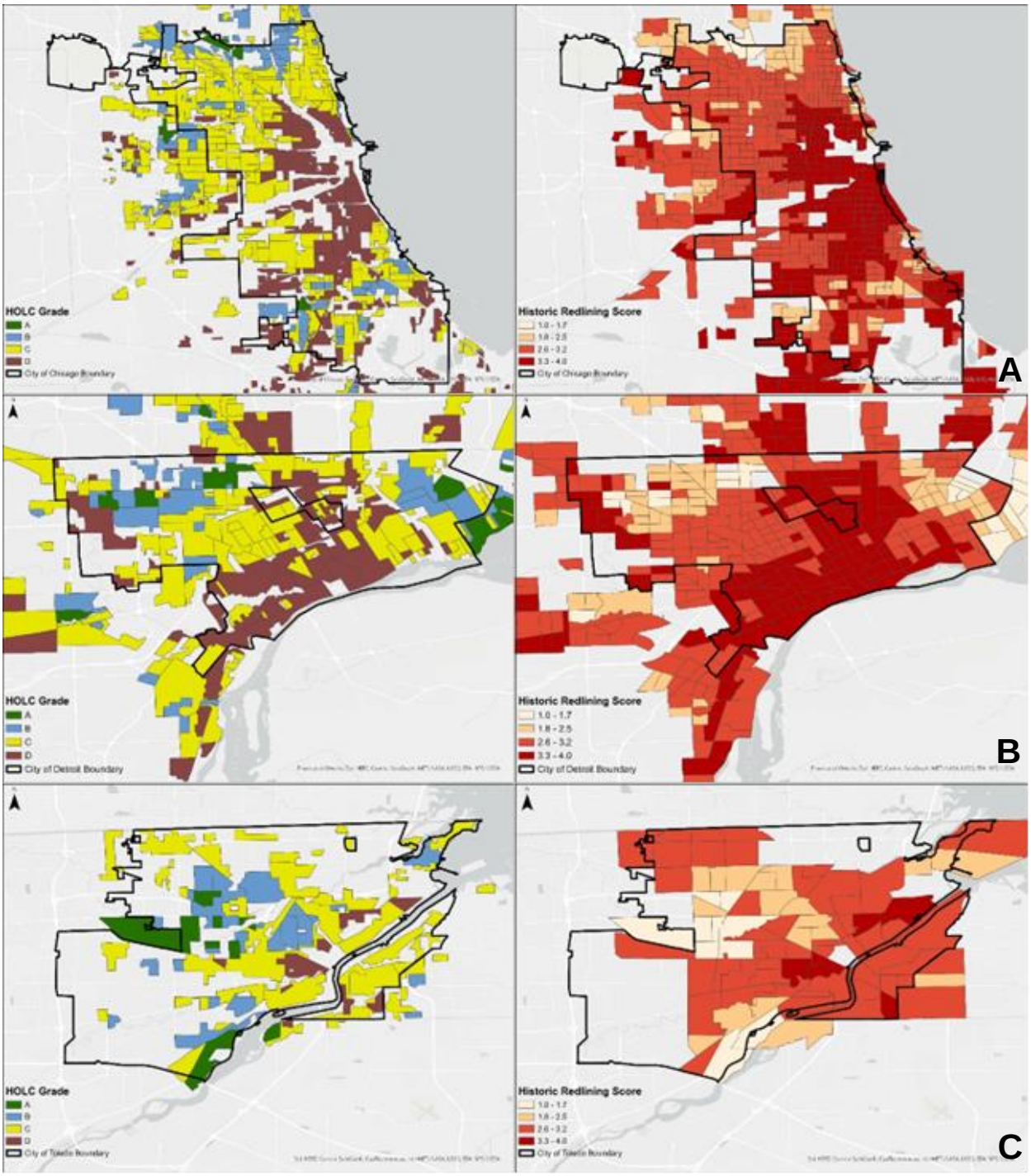
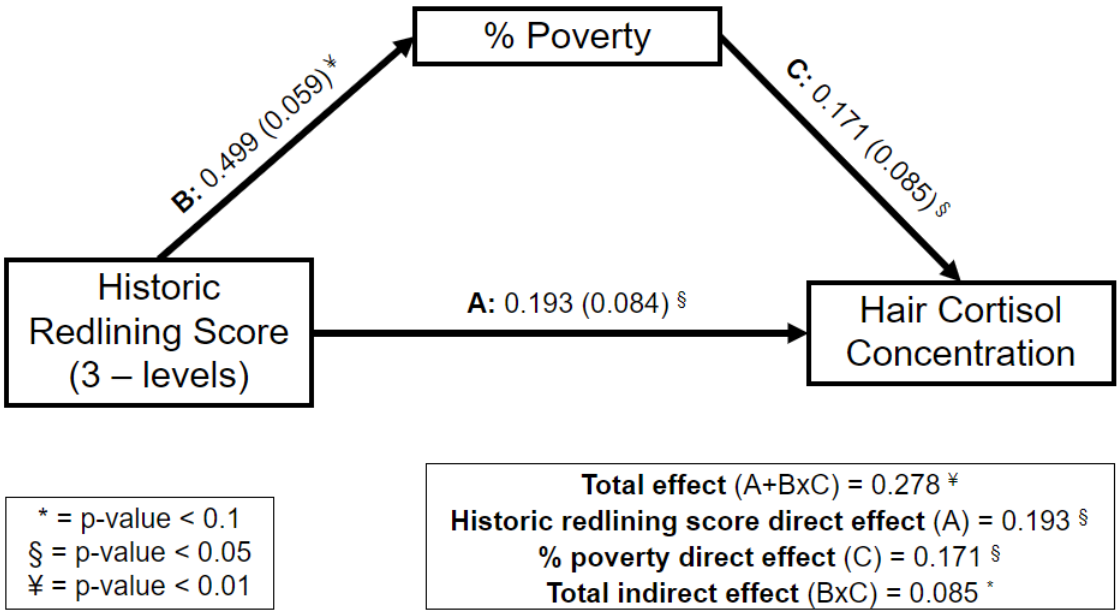


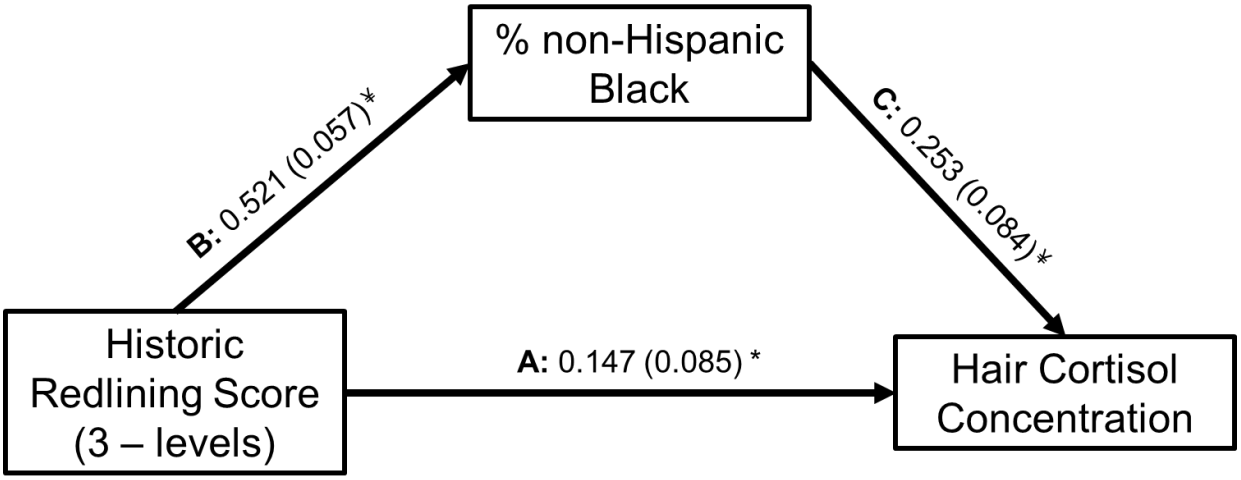
Figure 3.3 Pathway between historic redlining and log-transformed hair cortisol concentration, mediated via percent of census tract below poverty level using ACS 5-year estimates (2014 – 2018)



* = p-value < 0.1
§ = p-value < 0.05
¥ = p-value < 0.01

Total effect (A+BxC) = 0.278 ¥
Historic redlining score direct effect (A) = 0.193 §
% poverty direct effect (C) = 0.171 §
Total indirect effect (BxC) = 0.085 *

Figure 3.4 Pathway between historic redlining and log-transformed hair cortisol concentration, mediated via percent of census tract population identified as non-Hispanic Black using ACS 5-year estimates (2014 – 2018)



* = p-value < 0.1
§ = p-value < 0.05
¥ = p-value < 0.01

Total effect (A+BxC) = 0.278 ¥
Historic redlining score direct effect (A) = 0.147 *
% non-Hispanic Black direct effect (C) = 0.253 ¥
Total indirect effect (BxC) = 0.132 ¥

3.7 Supplemental Materials

Supplemental Table 3.1 Distribution of SAND participant characteristics and census tract characteristics by availability of hair cortisol samples (missing hair cortisol sample vs. not missing hair cortisol sample)

	Missing Cortisol (N=62; 26.2%) N (%)	**Not Missing Cortisol** (N=175; 73.8%) N (%)	**Overall** (N=237) N (%)	**p-value[1]**
Historic Redlining Score				0.537
Low redlining	10 (16.1%)	37 (21.1%)	47 (19.8%)	
High redlining	34 (54.8%)	80 (45.7%)	114 (48.1%)	
Ungraded	17 (27.4%)	47 (26.9%)	64 (27.0%)	
Missing	1 (1.6%)	11 (6.3%)	12 (5.1%)	
Race/Ethnicity				0.622
Hispanic	5 (8.1%)	8 (4.6%)	13 (5.5%)	
Non-Hispanic Black	42 (67.7%)	133 (76.0%)	175 (73.8%)	
Non-Hispanic white	6 (9.7%)	24 (13.7%)	30 (12.7%)	
other[2]	3 (4.8%)	8 (4.6%)	11 (4.6%)	
Missing	6 (9.7%)	2 (1.1%)	8 (3.4%)	
Sex at Birth				**< 0.001**
Female	18 (29.0%)	105 (60.0%)	123 (51.9%)	
Male	44 (71.0%)	70 (40.0%)	114 (48.1%)	
Age				**0.038**
Mean (SD)	15.3 (0.542)	15.2 (0.421)	15.2 (0.459)	
Missing	2 (3.2%)	0 (0%)	2 (0.8%)	
City at Birth				0.082
Chicago	8 (12.9%)	25 (14.3%)	33 (13.9%)	
Detroit	35 (56.5%)	119 (68.0%)	154 (65.0%)	
Toledo	17 (27.4%)	26 (14.9%)	43 (18.1%)	
Other	2 (3.2%)	5 (2.9%)	7 (3.0%)	
Mother's Age at Baseline				**0.028**

	Missing Cortisol (N=62; 26.2%) N (%)	**Not Missing Cortisol** (N=175; 73.8%) N (%)	**Overall** (N=237) N (%)	**p-value[1]**
Mean (SD)	24.3 (5.44)	26.2 (6.06)	25.7 (5.95)	
Missing	0 (0%)	1 (0.6%)	1 (0.4%)	
Baseline Relationship with Father				**0.040**
Married	9 (14.5%)	42 (24.0%)	51 (21.5%)	
Romantically Involved, Steady	32 (51.6%)	103 (58.9%)	135 (57.0%)	
other[3]	19 (30.6%)	30 (17.1%)	49 (20.7%)	
Missing	2 (3.2%)	0 (0%)	2 (0.8%)	
Baseline Maternal Educational Attainment				0.789
Less than high school	22 (35.5%)	58 (33.1%)	80 (33.8%)	
High school or equivalent	19 (30.6%)	45 (25.7%)	64 (27.0%)	
Some college or technical school	15 (24.2%)	49 (28.0%)	64 (27.0%)	
College grad	6 (9.7%)	22 (12.6%)	28 (11.8%)	
Missing	0 (0%)	1 (0.6%)	1 (0.4%)	
Household Income at 15 ($)				0.762
Mean (SD)	47800 (44100)	50000 (57600)	49400 (54400)	
Median [Min, Max]	40000 [1.00, 178000]	35000 [700, 500000]	36200 [1.00, 500000]	
Missing	1 (1.6%)	0 (0%)	1 (0.4%)	
% Census Tract non-Hispanic Black Residents				0.292
Mean (SD)	55.8 (36.8)	61.7 (37.2)	60.1 (37.1)	
Missing	1 (1.6%)	11 (6.3%)	12 (5.1%)	
% Census Tract Below Poverty				0.286
Mean (SD)	29.3 (17.9)	26.5 (15.2)	27.3 (16.0)	
Missing	1 (1.6%)	11 (6.3%)	12 (5.1%)	

[1] P-value based on ANOVA test (continuous variables) or chi-squared/Fisher's exact test (categorical variables) comparing participants missing hair cortisol samples vs. not missing hair cortisol samples

[2] Race/ethnicity = “other” includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = “other” includes participants where mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child’s father at baseline

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Chapter 4

Historic redlining and accelerated biological aging in urban adolescents

4.1 Background

During adolescence, psychosocial stressors can impact health outcomes when external stressors "get under the skin" impacting biological processes.[1] One biological response that may be impacted by these stressors is DNA methylation (DNAm). DNAm occurs in regions of the genome where there are clusters of cytosine-phosphate-guanine (CpG) dinucleotides, known as CpG islands.[2] These CpG islands are the main location for DNA modification, and DNAm refers to the process through which a methyl group (CH_3) is transferred to a cytosine nucleobase through DNA methyltransferase.[3] DNAm can act as either an amplifier or a suppressor of gene expression.[2,3]

DNAm can be used to assess epigenetic signatures of accelerated aging at the cellular level. Rather than relying on an imperfect measure of the aging process such as chronological age (or age in years), these DNAm signatures estimate epigenetic clocks that capture biological or physiological age.[4] Alteration in DNAm functioning may impact later life health outcomes as epigenetic age acceleration has been found to be associated with physical and cognitive functioning, chronic disease, and mortality.[4,5] Given that alterations to DNAm functioning can lead to subsequent adverse health outcomes, it is important to identify all possible pathways through which individuals may be at risk of greater DNAm age acceleration (DNAmAA).

Experiences from early life can become biologically embedded and may impact DNAm functioning because DNAm is modifiable by social and environmental factors.[6-8]

Harmful exposure during adolescence can lead to lifelong health implications; therefore, it is particularly crucial to identify exposures that may place adolescents at an increased risk of DNAmAA because this may have a serious impact on later life health outcomes. A few studies have examined this association, specifically investigating the impacts of household or individual-level socioeconomic characteristics and adversity on epigenetic signature outcomes in adolescents.[7,9,10] These studies found that early life adverse environments or experiences can lead to an increase in DNAmAA, and subsequent later health outcomes; however, the results did vary based on the methods used to measure epigenetic age. These findings provide a useful understanding of how social exposures can get "under the skin" resulting in health inequities among a population where adverse exposures may result in health complications later in life.

Neighborhood-level factors may also serve as an important determinant for DNAm functioning in adolescents. A large body of literature has detailed the pathways through which neighborhood-level exposures may impact health outcomes. Neighborhood-level factors such as pollution, violence, socioeconomic deprivation, lack of access to health promoting resources, poor housing quality, and racial residential segregation have been found to be associated with adverse health outcomes.[11-13] These harmful factors can then become embodied, driving inequities in health.[14] For example, neighborhood disadvantage has been found to be associated with DNAmAA in adults and adolescents.[15-18] The impacts of discriminatory neighborhood-level exposures, such as segregation, can be particularly harmful resulting in "biological expressions of racism" where environmental exposures impact health outcomes at the cellular level.[14,19]

One potential neighborhood-level factor that may impact DNAmAA is exposure to structural racism. Structural racism refers to the ideologies and practices that reinforce racial discrimination and can be seen through various interconnected institutional systems such as education, housing, healthcare, public health, and criminal legal systems, labor markets, etc.[20] The impacts of structural racism have altered the distribution of present-day resources and opportunities, which limit opportunities for minoritized racial groups while simultaneously improving outcomes for white populations.[20,21]

Historic redlining serves as a useful proxy for historic structural racism, as it has impacted disparities in housing and wealth accumulation. Historic redlining refers to the systematic way in which federal agencies and private institutions denied mortgages and lending services in regions of the United States that were deemed "risky for investment".[22] One well-documented example of historic redlining comes from the Home Owners' Loan Corporation (HOLC) maps, which were created in 1933 by the federal government and examined over 200 urban cities throughout the United States.[22] In these maps, regions that were identified as "risky for investment" were outlined in red, thus, this process became known as redlining. The HOLC surveyors used racially motivated language and assessment methods, specifically targeting Black Americans and immigrant neighborhoods with less favorable grades.[22-24] The impacts of the HOLC maps can been seen through the distribution of present-day neighborhood resources and demographic distributions. Neighborhoods that were redlined by the HOLC have suffered worse neighborhood conditions including limited access to health promoting resources, segregation, and neighborhood disinvestment.[25-27] As a result, individuals

living in these neighborhoods may be at an increased risk of adverse health outcomes, including accelerated biologic aging due to living under worse material conditions.

To our knowledge, no previous study has evaluated the relationship between structural racism, measured via historic redlining, on DNAmAA in adolescents. This study addressed this gap by examining the association between historic redlining and DNAmAA, measured using epigenetic clocks, in adolescents. We hypothesized that adolescents living in historically redlined neighborhoods would have greater DNAmAA compared to their peers who lived in urban neighborhoods not subjected or minimally exposed to redlining policies. Further, we hypothesized that Black and Hispanic adolescents would report greater DNAmAA as these populations continue to be inequitably harmed by the impacts of historic redlining policies.[28] The findings from this study can be used to demonstrate how past policies continue to impact health outcomes in present-day.

4.2 Methods

Study population

Data come from the Future of Families and Child Wellbeing Study (FFCWS). FFCWS is a longitudinal birth cohort study with a baseline sample of 4,898 U.S. children and caregivers who were followed over six waves: 1) birth (1998 – 2000), 2) age 1 (1999 – 2001), 3) age 3 (2001 – 2003), 4) age 5 (2003 – 2006), 5) age 9 (2007 – 2010), and 6) age 15 (2014 – 2017).[29] Participants of FFCWS came from 20 large cities (population ≥ 200,000) throughout the U.S. FFCWS participants were over-sampled to include a large proportion of Black and Hispanic participants as well as low-income families.[30] Data for this study came from wave 6 of the FFCWS (n = 3,444). Participants

who did not provide a valid address and could not be linked to historic redlining data as well as those who did not provide a saliva sample were excluded from this study. Additionally, participants missing any covariates of interest were removed, resulting in a final analytic sample of 1,686.

DNA methylation accelerated aging

Saliva samples were collected among FFCWS participants using the Oragene DNA Self-Collection kit as part of the Year 15 follow-up wave. Approximately 500g of genomic DNA quantified using Quant-iT Picogreen ds DNA kit (ThermoFisher Scientific) was subjected to bisulfite conversion using the EZ-96 DNA Methylation kit (Zymo Research) and analyzed using the Illumina Infinium Human Methylation 450K and EPIC methylation arrays. DNAm quality control was performed using EWAStools.[31] Probes were removed if the detection value was >0.01 for the 450K array or >0.05 for the EPIC array. If the number of methylated or unmethylated bead count was fewer than four, or if probes were identified by the ENmix function QCinfo using default parameters.[32] Samples were excluded if ENmix identified outlier methylation or bisulfite conversion values, or if the DNAm predicted sex differed from survey recorded sex.

This study used eight epigenetic clocks, including Horvath Pan-Tissue Estimator,[33] Hannum,[34] Pediatric-Buccal-Epigenetic Clock,[35] Skin and Blood Clock,[36] DNAmPhenoAge,[37] DNAm GrimAge,[38] Dunedin Pace of Aging Methylation,[39] and DunedinPACE.[40] Additional information on these eight epigenetic clocks is available (Table S4.1). Epigenetic clocks were calculated by the FFCWS team and made publicly available. Details on the training dataset and which characteristic or phenotype (e.g., age, mortality) each epigenetic clock was trained on are detailed in FFCWS documentation and Table S4.1.[41] DNAmAA was generated by regressing chronological

age on each clock and obtaining the residual value. The residual values for each clock were used as dependent variables in the present study.

Historic redlining score

Historic redlining scores come from the HOLC "residential security" maps and were computed by Meier and Mitchell (2022).[42] In the early 20th century, the HOLC assigned one of four grades to each neighborhood evaluated: A – "Best", B – "Still Desirable", C – "Definitely Declining", or D – "Hazardous".[43] To calculate historic redlining scores, neighborhoods identified by the HOLC as "Best" were given an initial score of 1, while "Still Desirable", "Definitely Declining" and "Hazardous" were scored as 2, 3, and 4, respectively. Redlining scores were then multiplied by the total percentage of census tract area assessed by the HOLC. Tracts with <20% of their area assessed by HOLC were excluded. This procedure resulted in a continuous historic redlining. A lower score indicates "low redlining", whereas a higher score indicates "high redlining". Historic redlining scores based on 2010 census tract boundaries were linked to the FFCWS sample by FFCWS staff using participants' reported addresses during wave 6 (age 15) of the FFCWS data collection.

We examined historic redlining scores as a categorical variable. Meier and Mitchell (2022) previously divided historic redlining scores into four intervals based on the national distribution of redlining scores: 1.00–1.749 (level 1), 1.75–2.49 (level 2), 2.5–3.249 (level 3), and 3.25–4.00 (level 4). Areas not assessed by the HOLC, or with <20% of their area scored, were identified as "ungraded". We combined levels 1 and 2 historic redlining score categories, which were more favorably graded by HOLC appraisers, to create a three-level exposure variable: "Low redlining" (levels 1 and 2,

historic redlining score range: 1.00–2.49), “High redlining” (levels 3 and 4, range: 2.5–4.00), and “ungraded”.

Covariates

For descriptive purposes, we examined a variety of covariates. In wave 6 of FFCWS, participants were asked to self-identify their race/ethnicity by responding to the question: “What is your race and ethnicity?” Interviewers entered participant’s responses as an open-ended question and aggregated responses for race and ethnicity. In this study, race and ethnicity was then examined as four categories: Hispanic; non-Hispanic Black; non-Hispanic white; and other. The category “other” includes participants who identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander.

Additional participant demographics examined included sex at birth (male or female, with no nonbinary response options available in FFCWS at baseline), participant age in years at FFCWS wave 6, and city of residence at birth (Chicago, Detroit, Toledo, or Other). City of residence at baseline was also included to account for potential differences in SAND sampling for each city. Maternal characteristics included maternal relationship with child’s father at baseline (married, romantically involved/steady, or other, which includes on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another), and smoking status during pregnancy (ever smoked vs. never smoked). Smoking status during pregnancy was included as a covariate because previous literature has identified that smoke exposure is associated with DNAm in adolescents.[44] We also examined indicators of socioeconomic position, measured using maternal educational attainment at baseline (less than high school, high school or equivalent, some college or technical school, or

college graduate), and household poverty ratio at age 15 (0 – 49%, 50 – 99%, 100 – 199%, 200 – 299%, 300%+). Assay type (Illumina EPIC or 450K methylation) was included as a covariate to account for any potential differences in measurement based on the assay used to measure DNAm. Finally, sample cell proportions derived from DNAm data (epithelial cells and fibroblasts) were included as covariates in the analysis.

Statistical analysis

Descriptive statistics examined participant characteristics of the study sample. We used linear regression to examine the association between the 3-level exposure of historic redlining scores (low redlining, high redlining, and ungraded [reference category]) and DNAmAA for each of the eight epigenetic clocks. We first adjusted for age, baseline city of residence, assay type, cell proportions, and mother's smoking during pregnancy. We then additionally adjusted for household poverty ratio. Participants missing any covariates of interest were removed from the sample resulting in an analytic sample size of 1,686. Finally, we re-ran these two models stratified by race/ethnicity (non-Hispanic Black participants (n = 811); Hispanic participants (n = 364)) to examine differences in the association between historic redlining and DNAmAA across racialized groups. We hypothesized that Black and Hispanic populations would have a significant association between historic redlining and DNAmAA due to embodiment of racism. All analyses were conducted using R version 4.2.1.[45]

4.3 Results

Table 4.1 reports summary statistics for each of the eight epigenetic clocks used in the analysis. The Horvath and Hannum clocks are 1st generation clocks and use chronological age as the outcome measure, while the remaining six clocks are 2nd or 3rd

generation and are used to predict age-related phenotypes. The values reported for each clock are in years, except the Dunedin POAM 38 and POAM 45, which are measured in changes in accelerated aging (a value of 1 is referent).

Among the 1,692 FFCWS participants who provided samples to estimate DNAm, 52.1% lived in census tracts that were not assessed by HOLC City surveyors (ungraded tracts), while 11.4% lived in low redlining census tracts, and 36.5% lived in high redlining tracts (Table 4.2). There was a statistically significant association between historic redlining category and participant race/ethnicity ($p < 0.001$). Among Hispanic participants, the majority lived in ungraded tracts (57.0%), compared to low (8.0%) and high redlining tracts (35.1%). Among non-Hispanic Black participants, 45.3% lived in high redlining tracts, while 40.0% lived in ungraded tracts, and a small proportion lived in low redlining tracts (14.7%). Among non-Hispanic white participants, almost all (80.3%) lived in ungraded tracts. The majority (53.0%) of participants who were categorized as a race/ethnicity of "other" lived in ungraded regions, while 13.6% lived in low redlining tracts, and 33.3% lived in high redlining tracts.

The sample was evenly split between males (n = 852) and females (n = 840), and the mean age of participants was 15.6 years (standard deviation [SD]: 0.67). Over half (54.5%) of participants' parents were unmarried but romantically involved at baseline. Parent's baseline relationship status was statistically significantly associated with historic redlining categories ($p < 0.001$). Participants with parents who were married at baseline more often lived in ungraded tracts compared to high redlining tracts, whereas participants with parents who reported being unmarried but romantically involved or "other" more often lived in high redlining tracts. Most mothers of participants

reported never smoking during pregnancy (81.1%); however, mother's smoking during pregnancy was still significantly associated with historic redlining category ($p = 0.009$).

Mother's baseline educational attainment was strongly associated with historic redlining categories ($p < 0.001$). As maternal educational attainment increased, there was an increase in the proportion of participants living in ungraded regions. For example, among participants with mothers who reported a high school education or lower, about 47% lived in ungraded tracts compared with 54.5% among participants whose mothers had some college or technical training, and 73.4% among participants whose mothers had a college or a graduate degree. Adolescents who lived in a high redlining tract more often had mothers with lower levels educational attainment, for example, comparing those whose mother reported less than high school (43.5%) to those with a college or graduate degree (13.5%).

Socioeconomic position measured via household poverty ratio was strongly associated with historic redlining categories ($p < 0.001$). Similar to previous characteristics, adolescents living in low redlining tracts did not markedly differ by household poverty ratio category. However, adolescents living below the poverty line (0 – 49% and 50 – 99%) were more likely to live in high redlining tracts (51.8% and 48.3%, respectively) as opposed to ungraded tracts (34.1% and 38.7%, respectively). In comparison, those living at 300%+ the poverty level were more likely to report living in ungraded tracts (69.9%) compared to high (18.5%) or low redlining tracts (11.6%).

Table 4.3 reports estimates from linear regression analyses examining the association between historic redlining and the eight epigenetic clocks for the full sample. Model 1 shows the association after adjusting for age, baseline city of residence, assay

type, cell proportions, and mother's smoking during pregnancy (n = 1,686). Relative to living in ungraded tract, living in a high redlining tract was statistically significantly associated with GrimAge ($p < 0.001$), Horvath ($p = 0.009$), PhenoAge ($p = 0.006$), POAM 45 ($p = 0.001$), and Skin/Blood ($p = 0.017$) DNAmAA. GrimAge and POAM 45 were also associated with living in low redlining tract ($p = 0.046$ and $p = 0.037$, respectively) relative to ungraded tracts. Hannum was the only clock to have a significant association for living in a low redlining tract but not high redlining tract ($\beta = -0.157$; 95% CI: -0.269, -0.045).

After additionally adjusting for household poverty ratio, findings were similar to Model 1; however, there was no longer a statistically significant association for low redlining relative to ungraded in GrimAge and there was no longer an association with POAM 45 for low redlining or high redlining. In analyses restricted to non-Hispanic Black participants (n = 811), there was only a significant association for high redlining in the Horvath fully adjusted model (Table S4.3). In Hispanic participants (n = 364), there was no significant association for any epigenetic clock (Table S4.4).

4.4 Discussion

This study was the first to investigate the impact of historic structural racism, measured via historic redlining, on DNAmAA among a sample of adolescents residing in urban areas of the United States. We hypothesized that neighborhoods less favorably graded by the HOLC would be associated with accelerated biological aging. We found that in four of the eight epigenetic clocks examined, individuals living in high redlining tracts had statistically significantly greater accelerated aging compared to those living in

ungraded tracts not subjected or minimally exposed to discriminatory lending practices captured in the HOLC maps.

Our findings are consistent with previous literature showing that neighborhood disadvantage is associated with biological accelerated aging.[6,15-17] Mrug et al. (2023) investigated the impacts of neighborhood disadvantage during adolescence on biologic aging at age 27 using four epigenetic clocks (Hannum, Horvath, PhenoAge, and GrimAge).[16] They found that participants who had experienced neighborhood disadvantage and harsh parenting in adolescence had accelerated epigenetic aging in adulthood. We observed a similar association: adolescents living in high redlining tracts reported greater DNAmAA compared to those living in ungraded tracts, and high redlining tracts were found to correlate with lower socioeconomic position including lower maternal educational attainment at baseline, and higher rates of adolescents living households with income below the federal poverty level.

Overall, our findings are consistent with the concept of embodiment from ecosocial theory, which posits that social and environmental factors become biologically embedded and, in turn, drive health inequities.[14,46] Exposure to chronic stressors, such as discrimination and adversity, have been previously documented as risk factors for DNAmAA.[7,47] However, it is not well understood how structural factors, such as structural racism and the legacy of discriminatory government and business practices, drive health disparities in biologic aging outcomes. Embodiment helps to understand how chronic exposure to discriminatory policies and practices can become biologically embedded or get “under the skin” as the body is under a constant state of stress, resulting in alterations at the cellular level.

Our study extends studies of concurrent neighborhood poverty and DNAmAA by showing that high redlining, a structural driver of present-day neighborhood conditions, was associated with accelerated biological aging for half of the epigenetic clocks examined, even after adjusting for key covariates of interest, including present-day socioeconomic position. Other research on historic redlining and health outcomes in adults found that living in formerly redlined neighborhoods may only be detrimental for people of color.[28] We did not find this to be the case in the present study. We observed a statistically significant association between high redlining and DNAmAA in the full sample, but not among non-Hispanic Black or Hispanic participants alone, which does not support our initial hypothesis. We found that the majority of adolescents living in high redlining tracts in this study self-identified as Black or Hispanic. Therefore, these results are particularly surprising given that high redlining was associated with DNAmAA in the full sample. These findings may be the result of limited age variation among the non-Hispanic Black and Hispanic participants in our sample. Future studies may wish to further examine these associations in more diverse populations to evaluate the potential pathways impacting biologic aging outcomes among marginalized populations.

Strengths and limitations

Our study was the first to examine the impact of historic redlining on DNAmAA using epigenetic clocks in adolescents. Our findings provide a novel understanding of how historic structural racism may become biologically embedded in adolescents living in urban areas in the U.S. We utilized “ungraded” census tracts as the reference group, which served as a useful comparison because these regions were not subject to historic redlining practices. Another strength of our analysis was the use of multiple epigenetic clocks to examine the impact of redlining on DNAmAA. We were able to examine not

only 1st generation clocks (e.g., Horvath and Hannum) that measure chronological age, we were also able to incorporate 2nd generation clocks that predict age-related phenotypes (e.g., GrimAge, PhenoAge). The inclusion of multiple clocks in our analysis provided a more robust understanding of how structural racism impacts DNAmAA.[16] Despite seven of the eight epigenetic clocks being trained on adult samples, previous literature has found that saliva samples from children can still serve as valid measures of aging from clocks derived from adult blood samples.[10]

A final strength of our analysis was our sample characteristics. The majority of studies examining DNAmAA have utilized participant samples with European origins of descent.[48] The FFCWS is a representative study of urban US births, providing a diverse, majority Black and Hispanic sample with exposure to historic redlining.[30] Our diverse sample allowed us to investigate the potential differing impact of historic redlining across race/ethnicity groups via sub-sample analyses. Future work should continue to investigate potential inequitable impacts of structural racism on biological aging outcomes among minoritized racial and ethnic groups.

Despite the strengths of our study, there are a few limitations to consider. First, only approximately half (56.9%) of the FFCWS sample at wave 6 provided a saliva sample for DNA methylation assays. Individuals missing epigenetic clock information were more likely to be non-Hispanic Black (45.7% missing vs. 54.3% not missing) (Table S4.2). Individuals missing historic redlining scores were more likely to be Hispanic (26.5% missing vs. 73.6% not missing) or non-Hispanic white (18.8% missing vs. 81.2% not missing). However, after examining a sub-sample of non-Hispanic Black participants, we found that adolescents who were missing saliva samples did not

significantly differ from those not missing saliva samples on any key characteristics. Therefore, we assessed that the non-Hispanic Black population included in the current study was representative of the FFCWS non-Hispanic Black population overall. Another limitation is that historic redlining exposure was examined at one time point. Because we did not measure the total time an individual spent living in a formerly redlined area, this measure may not fully capture the impact of redlining. Finally, misclassification of historic redlining scores may have occurred as present-day census tracts do not align with historic HOLC graded regions. The use of a census tract-level measure to assign exposure levels may not meet the gold standard practice of utilizing participant addresses to assign redlining scores.[49]

4.5 Conclusion

We identified that adolescents living in neighborhoods that were historically redlined had greater DNAm age acceleration in four of the eight epigenetic clocks examined. These findings suggest that historic structural racism continues to drive health inequities in the present-day. It is crucial for future policies to acknowledge and hold accountable the institutions responsible for driving the inequities observed in the present-day. Potential policy options include investment in historically redlined areas, which could address socioeconomic disparities created by redlining by revitalizing housing, providing access to jobs, or improving neighborhood infrastructure. Future research should consider the longitudinal impacts of other measures of structural racism on health outcomes related to biologic aging.

4.6 Tables and Figures

Table 4.1 Descriptive measures of DNA methylation epigenetic clocks from the Future of Families and Child Wellbeing Study at wave 6 (n = 1692)

	Mean (SD)	Median [Min, Max]
Horvath	15.5 (4.28)	15.0 [4.76, 37.8]
Hannum	25.1 (7.23)	24.0 [7.67, 58.0]
Horvath Revised (Skin/Blood)	12.7 (3.14)	12.4 [5.61, 24.9]
PedBE	12.6 (2.47)	12.1 [5.93, 23.6]
PhenoAge	5.33 (6.45)	5.39 [-16.9, 28.9]
POAM 38	1.09 (0.101)	1.09 [0.579, 1.40]
POAM 45	1.27 (0.179)	1.26 [0.780, 1.91]
GrimAge	22.7 (6.19)	22.7 [5.27, 46.2]

Table 4.2 Descriptive statistics of Future of Families and Child Wellbeing participant and census tract characteristics by historic redlining categories at wave 6 (n = 1692)

	Ungraded (N=881; 52.1%)		**Low Redlining** (N=193; 11.4%)		**High Redlining** (N=618; 36.5%)		**Overall** (N=1692)		**p-value[1]**
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Race/Ethnicity[2]									**< 0.001**
Hispanic	208	56.99	29	7.95	128	35.07	365	100.00	
Non-Hispanic Black	325	40.02	119	14.66	368	45.32	812	100.00	
Non-Hispanic white	241	80.33	21	7.00	38	12.67	300	100.00	
other	70	53.03	18	13.64	44	33.33	132	100.00	
Missing	37	44.58	6	7.23	40	48.19	83	100.00	
Sex at birth									0.769
Female	430	51.19	97	11.55	313	37.26	840	100.00	
Male	451	52.93	96	11.27	305	35.80	852	100.00	
Age									**0.041**
Mean (SD)	15.5	(0.670)	15.6	(0.639)	15.6	(0.678)	15.6	(0.670)	
Parent's Baseline Relationship Status[3]									**< 0.001**
Married	276	66.99	45	10.92	91	22.09	412	100.00	
Romantically Involved, Steady	433	46.96	109	11.82	380	41.21	922	100.00	
other	165	47.97	37	10.76	142	41.28	344	100.00	
Missing	7	50.00	2	14.29	5	35.71	14	100.00	
Mother's Smoking During Pregnancy									**0.009**
None	738	53.79	155	11.30	479	34.91	1372	100.00	
Smoked during pregnancy	142	44.65	38	11.95	138	43.40	318	100.00	
Missing	1	50.00	0	0.00	1	50.00	2	100.00	
Mother's Baseline Educational Attainment									**< 0.001**
Less than high school	257	46.81	53	9.65	239	43.53	549	100.00	

	Ungraded (N=881; 52.1%)		Low Redlining (N=193; 11.4%)		High Redlining (N=618; 36.5%)		Overall (N=1692)		p-value[1]
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
High school or equivalent	241	47.91	62	12.33	200	39.76	503	100.00	
Some college or technical school	242	54.50	50	11.26	152	34.23	444	100.00	
College grad	141	73.44	25	13.02	26	13.54	192	100.00	
Missing	0	0.00	3	75.00	1	25.00	4	100.00	
Household Poverty Ratio									**< 0.001**
0-49%	85	34.14	35	14.06	129	51.81	249	100.00	
50-99%	113	38.70	38	13.01	141	48.29	292	100.00	
100-199%	246	52.01	49	10.36	178	37.63	473	100.00	
200-299%	132	54.55	21	8.68	89	36.78	242	100.00	
300%+	302	69.91	50	11.57	80	18.52	432	100.00	
Missing	3	75.00	0	0.00	1	25.00	4	100.00	

[1] P-value based on ANOVA test (continuous variables) or chi-squared test (categorical variables) comparing participants in low redlining vs. high redlining vs. ungraded census tracts

[2] Race/ethnicity = "other" includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = "other" includes participants whose mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child's father at baseline

Table 4.3 Associations between historic redlining categories and DNA methylation age acceleration in the Future of Families and Child Wellbeing Study at wave 6 (n = 1,686)

		Model 1 [1]				Model 2 [2]			
Clock		*Est.*	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
GrimAge	*Low Redlining*	0.091	0.002	0.181	**0.046**	0.074	-0.015	0.164	0.104
	High Redlining	0.150	0.090	0.211	**< 0.001**	0.117	0.055	0.179	**< 0.001**
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Hannum	*Low Redlining*	-0.157	-0.269	-0.045	**0.006**	-0.150	-0.262	-0.037	**0.009**
	High Redlining	0.017	-0.058	0.093	0.652	0.035	-0.043	0.112	0.383
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath	*Low Redlining*	0.033	-0.107	0.172	0.646	0.040	-0.100	0.179	0.578
	High Redlining	0.125	0.031	0.219	**0.009**	0.130	0.033	0.227	**0.008**
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PedBE	*Low Redlining*	0.047	-0.100	0.193	0.533	0.040	-0.108	0.187	0.599
	High Redlining	0.041	-0.058	0.140	0.419	0.035	-0.067	0.137	0.502
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PhenoAge	*Low Redlining*	-0.074	-0.227	0.079	0.344	-0.078	-0.231	0.076	0.321
	High Redlining	0.144	0.041	0.248	**0.006**	0.127	0.021	0.233	**0.019**
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Dunedin Pace of Aging (38)	*Low Redlining*	0.032	-0.104	0.167	0.647	0.011	-0.124	0.147	0.872

Clock		Model 1 [1]				Model 2 [2]			
		Est.	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
	High Redlining	0.075	-0.016	0.167	0.107	0.039	-0.055	0.133	0.418
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Dunedin Pace of Aging (45)	*Low Redlining*	0.175	0.011	0.339	**0.037**	0.125	-0.038	0.287	0.132
	High Redlining	0.188	0.077	0.299	**0.001**	0.092	-0.020	0.205	0.108
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath Revised (Skin/Blood)	*Low Redlining*	0.044	-0.061	0.149	0.410	0.043	-0.063	0.149	0.423
	High Redlining	0.087	0.016	0.158	**0.017**	0.085	0.012	0.159	**0.022**
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

[1] Model 1: adjusted for age, baseline city of residence, assay type, cell proportion, and mother's smoking during pregnancy
[2] Model 2: model 1 covariates and household poverty ratio

4.7 Supplementary materials

Table S4.1 Description of eight epigenetic clocks used to measure DNA methylation accelerated aging in Future of Families and Child Wellbeing Study

Epigenetic Clock	Sample/Population	Outcome	Tissue
Hannum	N = 656 adults aged 19 – 101 years old	Chronological age	Whole blood
Horvath	N = 8,000 samples from 82 DNA methylation array datasets	Chronological age	Multi-tissue (51 healthy tissues and cell types)
Pheno Age	N = 456 participants from Invecchiare in Chianti (InCHIANTI) study aged 21 – 100 years old	Phenotypic age	Whole blood
Horvath Revised (Skin/Blood)	N = 2,222 across 26 datasets	Chronological age	Blood, skin, saliva, and fibroblast
Grim Age	N = 2,356 from Framingham Heart Study	Mortality risk estimator	Whole blood
PedBE	N = 1,721 samples from 11 pediatric cohorts	Chronological age	Buccal
Dunedin Pace of Aging (38)	N = 954 from Dunedin Study 1972 – 1973 birth cohort	Changes in 18 biomarkers	Whole blood
Dunedin Pace of Aging (45)	N = 1037 from Dunedin Study 1972 – 1973 birth cohort	Changes in 19 biomarkers	Whole blood

Table S4.2 Descriptive statistics of Future of Families and Child Wellbeing Study participant characteristics by epigenetic clock data availability for full sample at wave 6 (n = 3,444)

	Missing Clocks (N=1483; 43.1%)	**Not Missing Clocks** (N=1961; 56.9%)	**Overall** (N=3444)	**P-value [1]**
Historic Redlining Score				0.824
Ungraded	639 (43.1%)	877 (44.7%)	1516 (44.0%)	
Low Redlining	151 (10.2%)	193 (9.8%)	344 (10.0%)	
High Redlining	448 (30.2%)	616 (31.4%)	1064 (30.9%)	
Missing	245 (16.5%)	275 (14.0%)	520 (15.1%)	
Race/Ethnicity [2]				**0.011**
Hispanic	320 (21.6%)	493 (25.1%)	813 (23.6%)	
Non-Hispanic Black	732 (49.4%)	869 (44.3%)	1601 (46.5%)	
Non-Hispanic white	237 (16.0%)	353 (18.0%)	590 (17.1%)	
other	112 (7.6%)	149 (7.6%)	261 (7.6%)	
Missing	82 (5.5%)	97 (4.9%)	179 (5.2%)	
Sex at Birth				0.117
Female	695 (46.9%)	973 (49.6%)	1668 (48.4%)	
Male	788 (53.1%)	988 (50.4%)	1776 (51.6%)	
Parent's Baseline Relationship Status [3]				0.359
Married	349 (23.5%)	481 (24.5%)	830 (24.1%)	
Romantically Involved, Steady	788 (53.1%)	1054 (53.7%)	1842 (53.5%)	
other	340 (22.9%)	409 (20.9%)	749 (21.7%)	
Missing	6 (0.4%)	17 (0.9%)	23 (0.7%)	
Mother's Smoking During Pregnancy				0.797
None	1195 (80.6%)	1590 (81.1%)	2785 (80.9%)	
Smoked during pregnancy	284 (19.2%)	368 (18.8%)	652 (18.9%)	

	Missing Clocks (N=1483; 43.1%)	Not Missing Clocks (N=1961; 56.9%)	Overall (N=3444)	P-value [1]
Missing	4 (0.3%)	3 (0.2%)	7 (0.2%)	
Mother's Baseline Educational Attainment				**0.041**
Less than high school	474 (32.0%)	621 (31.7%)	1095 (31.8%)	
High school or equivalent	505 (34.1%)	590 (30.1%)	1095 (31.8%)	
Some college or technical training	347 (23.4%)	521 (26.6%)	868 (25.2%)	
College grad	156 (10.5%)	225 (11.5%)	381 (11.1%)	
Missing	1 (0.1%)	4 (0.2%)	5 (0.1%)	
Household Poverty Ratio				0.464
0-49%	183 (12.3%)	281 (14.3%)	464 (13.5%)	
50-99%	254 (17.1%)	331 (16.9%)	585 (17.0%)	
100-199%	414 (27.9%)	560 (28.6%)	974 (28.3%)	
200-299%	226 (15.2%)	273 (13.9%)	499 (14.5%)	
300%+	389 (26.2%)	511 (26.1%)	900 (26.1%)	
Missing	17 (1.1%)	5 (0.3%)	22 (0.6%)	

[1] P-value based on chi-squared test comparing participants with DNAm saliva samples vs. those missing DNAm saliva samples

[2] Race/ethnicity = “other” includes participants who self-identified as non-Hispanic from more than one racial category; American Indian or Alaska Native; Asian; or Native Hawaiian or Pacific Islander

[3] Baseline relationship with father = “Other” includes participants whose mother indicated a relationship status of on-again/off-again, just friends, hardly ever speak to one another, or never speak to one another with child’s father at baseline

Table S4.3 Associations between historic redlining categories and DNA methylation age acceleration among non-Hispanic Black FFCWS participants at wave 6 (n = 811)

		Model 1 [1]				Model 2 [2]			
Clock		*Est.*	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
GrimAge	*Low Redlining*	0.037	-0.095	0.170	0.580	0.035	-0.098	0.168	0.605
	High Redlining	0.068	-0.025	0.170	0.151	0.058	-0.036	0.153	0.227
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Hannum	*Low Redlining*	-0.129	-0.286	0.027	0.105	-0.135	-0.291	0.022	0.092
	High Redlining	0.044	-0.066	0.155	0.430	0.048	-0.064	0.160	0.402
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath	*Low Redlining*	0.027	-0.166	0.220	0.785	0.027	-0.166	0.221	0.781
	High Redlining	0.135	-0.002	0.271	0.053	0.141	0.002	0.279	**0.046**
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PedBE	*Low Redlining*	0.123	-0.082	0.327	0.241	0.117	-0.088	0.323	0.262
	High Redlining	0.035	-0.110	0.180	0.636	0.035	-0.112	0.182	0.640
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PhenoAge	*Low Redlining*	-0.078	-0.301	0.145	0.493	-0.079	-0.303	0.144	0.485
	High Redlining	0.125	-0.033	0.282	0.120	0.121	-0.038	0.281	0.137
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

Clock		Model 1 [1]				Model 2 [2]			
		Est.	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
Dunedin Pace of Aging (38)	*Low Redlining*	0.029	-0.159	0.217	0.765	0.025	-0.163	0.212	0.796
	High Redlining	0.019	-0.113	0.152	0.774	-0.008	-0.141	0.126	0.911
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Dunedin Pace of Aging (45)	*Low Redlining*	-0.009	-0.244	0.226	0.940	-0.017	-0.253	0.218	0.885
	High Redlining	0.024	-0.142	0.190	0.777	0.007	-0.161	0.175	0.935
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath Revised (Skin/Blood)	*Low Redlining*	0.030	-0.120	0.181	0.694	0.030	-0.121	0.181	0.697
	High Redlining	0.048	-0.058	0.155	0.375	0.054	-0.054	0.162	0.324
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

[1] Model 1: adjusted for age, baseline city of residence, assay type, cell proportion, and mother's smoking during pregnancy

[2] Model 2: model 1 covariates and household poverty ratio

Table S4.4 Associations between historic redlining categories and DNA methylation age acceleration among Hispanic FFCWS participants at wave 6 (n = 364)

		Model 1 [1]				Model 2 [2]			
Clock		*Est.*	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
GrimAge	*Low Redlining*	-0.017	-0.219	0.184	0.865	-0.023	-0.225	0.180	0.827
	High Redlining	0.075	-0.051	0.201	0.242	0.081	-0.047	0.209	0.216
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Hannum	*Low Redlining*	-0.255	-0.535	0.026	0.075	-0.271	-0.554	0.012	0.060
	High Redlining	0.112	-0.063	0.287	0.211	0.096	-0.083	0.275	0.293
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath	*Low Redlining*	0.004	-0.376	0.385	0.983	-0.011	-0.396	0.374	0.954
	High Redlining	0.065	-0.173	0.302	0.593	0.074	-0.170	0.317	0.553
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PedBE	*Low Redlining*	-0.300	-0.665	0.065	0.107	-0.310	-0.674	0.054	0.095
	High Redlining	-0.054	-0.281	0.174	0.643	-0.083	-0.313	0.148	0.480
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
PhenoAge	*Low Redlining*	-0.117	-0.488	0.253	0.534	-0.117	-0.490	0.257	0.538
	High Redlining	0.092	-0.139	0.323	0.433	0.101	-0.135	0.337	0.402
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

Clock		Model 1 [1]				Model 2 [2]			
		Est.	*Lower CI*	*Upper CI*	*P-value*	*Est.*	*Lower CI*	*Upper CI*	*P-value*
Dunedin Pace of Aging (38)	*Low Redlining*	-0.245	-0.601	0.110	0.175	-0.276	-0.635	0.083	0.131
	High Redlining	-0.006	-0.228	0.215	0.955	-0.056	-0.283	0.171	0.627
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Dunedin Pace of Aging (45)	*Low Redlining*	-0.036	-0.422	0.351	0.856	-0.102	-0.490	0.286	0.607
	High Redlining	0.036	-0.205	0.278	0.768	-0.043	-0.288	0.203	0.731
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
Horvath Revised (Skin/Blood)	*Low Redlining*	-0.001	-0.270	0.268	0.993	-0.021	-0.292	0.251	0.881
	High Redlining	0.097	-0.071	0.265	0.257	0.088	-0.084	0.260	0.315
	Ungraded	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]

[1] Model 1: adjusted for age, baseline city of residence, assay type, cell proportion, and mother's smoking during pregnancy

[2] Model 2: model 1 covariates and household poverty ratio

4.8 References

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Chapter 5

Conclusion

5.1 Conclusion

The findings from this dissertation provide a novel investigation of the relationship between structural racism, measured via historic redlining, on stress outcomes in adolescents. This dissertation examined the impacts of historic redlining on stress outcomes in adolescents from the Future of Families and Child Wellbeing Study (FFCWS) and a sub-sample of FFCWS participants from the Study of Adolescent to Adult Neurodevelopment (SAND). Overall, this dissertation provided evidence that historic redlining was associated with several indicators of stress in present-day adolescents living in Midwestern cities. Mediation analyses showed no direct effect of historic redlining on perceived stress, but we found a statistically significant indirect effect of redlining on perceived stress through neighborhood poverty. There was a significant direct effect of historic redlining on hair cortisol concentration, as well as a significant indirect effect of redlining on cortisol through neighborhood poverty and the proportion of neighborhood identified as non-Hispanic Black. These results provide evidence that historic structural racism is related to present-day health outcomes and that these associations may be mediated by present-day neighborhood conditions.

As seen in Figure 5.1, structural racism directly impacted federally funded mortgage risk assessment programs, including the Home Owners' Loan Corporation (HOLC) City Surveys conducted in the 1930s.[1] Many of these assessments were motivated by racist ideologies and practices as predominantly Black and immigrant neighborhoods were frequently cited as "risky for investment".[1] Redlining has resulted in

harmful impacts, including decreased residential investment as well as limited homeownership opportunities and racial residential segregation.[2,3] Structural racism has also directly contributed to intermediary determinants of health including the built environment, housing, access to quality education, and access to health-promoting resources including food access and green space.[4] These neighborhood-level factors are frequently cited as important determinants of health and have been found to be associated with a variety of chronic diseases and mental health outcomes.[5,6] Structural racism may also drive inequities in the distribution of present-day sociodemographic characteristics including racial/ethnic compositions of neighborhoods and socioeconomic composition, which are known determinants of health inequities.[4] These intermediary pathways may then contribute to individual-level circumstances including embodied exposures, which can ultimately lead to health disparities.[7] Using this conceptual framework, we are better able to understand the various pathways through which historic redlining has impacted present-day neighborhoods, which in turn, result in inequitable health outcomes.

5.2 Aim 1: Historic structural racism and perceived stress in adolescents

The first aim of this dissertation evaluated the impact of historic redlining on perceived stress outcomes using a sample of adolescents from the FFCWS SAND sub-study (n = 213). Perceived stress was measured using the 14-question Perceived Stress Scale (PSS-14).[9] Linear regression results showed that, compared with adolescents living in ungraded census tracts that were not subjected or minimally exposed to redlining practices, those living in high redlining census tracts had statistically significantly higher total PSS-14 scores, even after adjusting for covariates

including baseline city of residence and sex at birth. Similar findings were observed in a sub-sample of non-Hispanic Black adolescents. We used structural equation modeling (SEM) to examine the potential mediating effects of present-day neighborhood factors on total PSS-14 scores. We found that present-day neighborhood poverty, but not neighborhood racial composition, mediated the association between historic redlining and PSS score.

To our knowledge, this dissertation is the first study to examine the relationship between historic redlining and perceived stress among adolescents, filling a key gap in the literature. Corresponding with our hypothesis and conceptual framework, historic redlining was found to be associated with present-day socioeconomic characteristics. Although we did not observe a statistically significant indirect effect of neighborhood racial composition on perceived stress outcomes, these findings are still important for understand the potential mediating pathways that drive inequities in adolescent stress outcomes.

Our results indicate that present-day socioeconomic neighborhood conditions act as a mediator between historic redlining and perceived stress outcomes in adolescents. Our SEM analyses showed a statistically significant indirect effect of redlining on perceived stress through neighborhood poverty, but no significant indirect effect through neighborhood racial/ethnic composition. Previous literature has identified socioeconomic status to be an important factor contributing to perceived stress outcomes, where lower socioeconomic status is associated with higher perceived stress.[10,11] However, the majority of these studies focused on individual socioeconomic status, rather than neighborhood-level factors. Our findings help to illuminate additional

pathways through which adolescents may be at an increased risk of stress, including historic policies that have, in turn, impacted the makeup and distribution of resources in present-day neighborhoods.

We also examined the impact of historic redlining on perceived stress among a sub-sample of non-Hispanic Black adolescents. We hypothesized that redlining would be associated with perceived stress among non-Hispanic Black participants because redlining practices specifically discriminated against Black communities by grading predominantly Black neighborhoods as “Hazardous” for investment.[1] Our findings among the sub-sample corresponded with our findings in the full sample and supported our initial hypothesis: we found that high redlining, but not low redlining, was associated with higher perceived stress among non-Hispanic Black adolescents. The findings from our sub-sample indicate that non-Hispanic Black adolescents living in neighborhoods that experienced housing discrimination continue to experience the harmful effects of these policies and processes.

Historic redlining has shaped present-day neighborhood sociodemographic conditions via reinforcing institutions, which have shaped access to mortgage lending, (de)investment in housing, wealth accumulation opportunities, and employment opportunities.[2,12] These outcomes in turn can impact individual-level circumstances, including socioeconomic status, which has been found to be associated with perceived stress levels in adolescents.[10,11] Additionally, neighborhood factors that may be the result of historic redlining policies and practices, such as safety, and access to greenspace, and have been found to affect perceived stress levels.[13-17] Thus, our findings from Aim 1 are useful for understanding the various mechanisms that may be

driving disparities in adolescent health outcomes, including perceptions of stress, which may in turn impact later life health outcomes. We can also use these findings to hold institutions that reinforce racist ideologies and practices accountable, so that we can address adolescent health inequities.

5.3 Aim 2: Structural racism and hair cortisol levels in adolescents

The second aim of this dissertation examined whether historic redlining was associated with hair cortisol levels, a biomarker of stress, in a sub-sample of SAND adolescents (n = 163). Living in formerly redlined neighborhoods, including both high and low redlined neighborhoods, compared to ungraded neighborhoods was associated with greater hair cortisol concentrations in adolescents in multivariate analyses. In a sub-sample of non-Hispanic Black participants, we found that the association between high redlining and cortisol levels persisted while the association between low redlining exposure (v. ungraded) and cortisol levels was no longer statistically significant. Structural equation modeling was used to assess the potential mediating effects of neighborhood factors on biological stress outcomes in adolescents. The association between redlining and cortisol levels was mediated by present-day neighborhood racial composition, but not neighborhood poverty levels.

To our knowledge, no prior study has examined the impact of historic redlining on cortisol levels in adolescents. Previous studies have examined the impact of race/ethnicity as a potential driver of disparities in cortisol response in urban and suburban adolescents and found that non-Hispanic Black adolescents had higher cortisol levels compared to their non-Hispanic white peers.[18,19] These findings are consistent with our results from Aim 2 as the majority of non-Hispanic Black participants

from SAND lived in high redlining tracts, and exposure to high redlining significantly increased cortisol levels, compared to living in an ungraded tract, where the majority of non-Hispanic white participants lived. These findings also correspond with the proposed conceptual framework, as historic redlining has impacted the distribution of present-day sociodemographic characteristics, including racial and ethnic composition of neighborhoods.[20,21] Neighborhood characteristics then drive stress outcomes in adolescents as exposure to high redlining disproportionately places adolescents at risk of higher cortisol levels, and non-Hispanic Black adolescents were more likely to reside in high redlining tracts, compared to their non-Hispanic white peers who were more likely to live in ungraded tracts not exposed, or minimally exposed to HOLC redlining policies and practices.

Our findings from Aim 2 are consistent with ecosocial theory's conceptualization of embodiment, which argues that social and environmental factors get "under the skin" and lead to health inequities, such as differences in stress outcomes.[22,23] Similar to Aim 1, we found that present-day neighborhood characteristics are a mediator of the effects of historic structural racism as measured by redlining on present-day stress in adolescents. In Aim 1 we found that the percentage of the population below poverty was a significant mediator between redlining and perceived stress, while there were no statistically significant mediating effects observed via census tract racial/ethnic composition. In contrast, in Aim 2 we did not find a significant mediating pathway via census tract poverty, but we found that the proportion of the population identified as non-Hispanic Black was a significant mediating pathway between historic redlining and cortisol levels. The difference in findings of potential mediating pathways from Aim 1 to

Aim 2 may illuminate the ways in which structural racism drives health outcomes, particularly when examining subjective versus biological measures of stress. For example, subjective measures of stress, such as perceived stress, may be potentially mediated via neighborhood socioeconomic characteristics, while neighborhood racial/ethnic composition may be along the causal pathway linking historic redlining to biological measures of stress. Despite identifying different mediating pathways, Aim 1 and Aim 2 both provide evidence that historic redlining practices and policies, which were driven by structural racism, impact contemporary stress outcomes in adolescents. We theorize that this association is driven by inter-related institutions such as banking, housing, and education that have resulted in inequitable access to health promoting opportunities and resources at the neighborhood level, which in turn seem to drive disparities in mental health outcomes among adolescents in the present-day.

5.4 Aim 3: Historic redlining and accelerated biological aging in urban adolescents

The third aim of this dissertation evaluated the impact of historic redlining on DNA methylation accelerated aging (DNAmAA) using the full FFCWS wave 6 (age 15) sample (n = 1,686). DNAmAA was measured from participant saliva samples used to estimate eight epigenetic clocks. Regression findings showed that adolescents living in high redlining tracts had greater DNAmAA compared to those living in ungraded tracts. This association was observed for four of eight clocks (DNAm GrimAge, Horvath Pan-Tissue Estimator, DNAm PhenoAge, and Skin and Blood Clock), even after adjusting for age, baseline city of residence, assay type, cell proportions, mother's smoking status during pregnancy, and household poverty ratio. We also observed a significant association in the Hannum clock for low redlining exposure but not for not high redlining

exposure. We observed no significant association for the Pediatric-Buccal-Epigenetic Clock or either Dunedin Pace of Aging clocks. Examining these associations among non-Hispanic Black participants and Hispanic participants separately did not replicate findings observed in the full sample.

No previous study has examined the impact of historic redlining on DNAmAA in adolescents. These findings indicate that structural racism, which drove historic redlining assessments, influences present-day biomarkers of stress and aging in adolescents. DNAmAA has been previously found to be associated with a variety of health outcomes including chronic disease, BMI, physical and cognitive functioning.[24,25] Our findings from this aim identify potential structural determinants of DNAmAA.

Previous literature found that neighborhood conditions, including socioeconomic disadvantage, safety, access to health promoting resources, and social cohesion were associated with DNAm accelerated aging outcomes in adult and adolescent samples.[26-29] However, limited research has examined the impact of structural racism on age acceleration outcomes in adolescents. It is important to study biologic measures of stress such as DNAm age acceleration because they provide a measure of stress at the cellular level, which goes beyond individual perceptions of stress[30] and illustrates that stress can become embodied as a result of inequitable exposures driven by structural processes. DNAmAA is an extension of the impact cortisol can have on biologic health outcomes; chronic exposure to stressors may result in prolonged elevated cortisol levels or allostatic load, which in turn may result in increased cellular aging as the body becomes “weathered” by these chronic exposures.[31]

Similar to Aim 2, ecosocial theory helps to conceptualize how structural racism can become biologically embedded to result in present-day health disparities. As seen in the conceptual model, neighborhood trajectories of investment have contributed to place-based resources such as access to quality education, jobs, and health promoting services. Previous literature has identified that social determinants of health, including socioeconomic status, educational attainment, and household instability are associated with adverse DNAm trajectories and outcomes in adults and adolescents.[24,32-34] Furthermore, place-based factors may lead to embodied exposures such as health behaviors that have been previously linked to DNAmAA including tobacco and alcohol consumption, diet, and physical activity.[35] These factors may in turn impact adolescent stress outcomes, as observed in Aim 3 where adolescents living in historically redlined census tracts had accelerated aging outcomes for half of the epigenetic clocks examined.

5.5 Strengths and Limitations

This dissertation is the first to examine the impact of historic redlining on stress outcomes among adolescents. We used data from a diverse birth cohort of adolescents from U.S. urban areas. Because the FFCWS oversampled for Hispanic and Black populations as well as low-income populations,[36] we could examine the effects of historic redlining on populations that may be uniquely vulnerable to the effects of historic redlining, including non-Hispanic Black adolescents.[37] Most previous studies that examined factors associated with DNAmAA via epigenetic clocks utilized samples with European ancestry.[30] Utilizing the FFCWS sample allowed us to examine the effects of

structural racism on DNAmAA in a sample of predominantly Black and Hispanic adolescents.

Despite a growing body of literature examining the impacts of historic redlining on contemporary health outcomes, few prior studies utilized individual-level data to measure health outcomes. Rather, many previous studies depended on health outcome data measured at the census tract or ZIP code level. In contrast, this study examined the effects of historic redlining on three present-day stress outcomes among adolescents measured at the individual-level. Additionally, we utilized ungraded census tracts as our reference group when examining associations with high and low redlined census tracts. Ungraded tracts provide a comparison of tracts not subjected or minimally exposed to historic redlining practices and policies.

Another strength of this dissertation is that it examined historic redlining in relation to three well-established stress measures. The perceived stress scale is one of the most commonly used measures of subjective stress.[38] Hair cortisol concentration has been found to be a validated measure of longer-term cortisol levels.[39,40] DNAmAA assesses biologic aging at the cellular level and previous studies have validated the use of epigenetic clocks among child samples.[34] Utilizing both subjective and biological measures of stress allowed us to uncover potential relationships between historic redlining and stress that may otherwise have been unaccounted for if limited to only one measure. Furthermore, examining various stress outcome measures helps provide stronger evidence of a causal association between historic redlining practices and stress outcomes in adolescents because we observed a significant association between high redlining and stress outcomes among all three measures.

Lastly, adolescence is a critical period for growth and development, where adverse exposures can lead to lifelong health complications.[41-44] Adolescent mental health is a growing public health concern, with the distribution of mental health outcomes not equally distributed among the population. Without consideration of structural causes, interventions may not fully address root causes, which can then result in these structural determinants persisting and continuing to drive inequities in health outcomes. Identification of upstream determinants can help to target interventions that effectively alleviate health inequities.

Despite the strengths of this dissertation, there are several limitations to note. First, we examined associations between historic redlining and stress outcomes at one time point (age 15). We do not know the length of time each adolescent was exposed to that particular level of redlining. It is possible that their levels of exposure to redlining changed throughout childhood if their family moved during this time period. Another consideration is the potential for misclassification of historic redlining scores. Historic redlining scores were assigned to individuals based on the census tract they lived in at wave 6 (age 15) of the FFCWS. Present-day census tracts do not perfectly align with the geography of cities from the early 20th century, which was used to assess investment risk by the HOLC City surveyors. Utilizing census tract-level historic redlining score assignment may not provide as accurate an exposure assignment as the gold standard of using participant addresses to assign redlining scores.[45] We expect nondifferential misclassification of the outcome, as the exposure classification is not expected to be impacted by the measured outcomes. Therefore, we would expect the

direction of misclassification to be towards the null, resulting in a weaker detectable association.[45,46]

A final consideration for this analysis is the generalizability of the findings. For Aim 1 and Aim 2 we utilized a sub-sample of FFCWS participants who lived in or near three urban regions in the U.S. at baseline, including Chicago, Detroit, and Toledo. Redlining practices varied throughout the U.S. depending on the assessment methods utilized by HOLC City surveyors. By using a sample primarily limited to three cities in the Midwest, our findings may not be representative of redlining practices experienced by adolescents living in all urban areas nationally. Additionally, the majority of SAND participants were located in Detroit, so this may further limit the national generalizability of findings. However, redlining reinforced racial residential segregation, and both Chicago as well as Detroit are highly segregated cities where the impacts of redlining has been well documented.[47,48] Therefore, these cities are important to study when examining the impacts of redlining on present-day outcomes.

5.6 Policy Implications

Our conceptual model theorizes that historic redlining, which was driven by structural racism, has impacted present-day neighborhoods through various mediating pathways. One major way that historic redlining has altered present-day neighborhoods is through disinvestment of formerly redlined areas. The HOLC redlining maps specifically discriminated against Black neighborhoods, most often citing them as "Hazardous" for investment".[1] As a result, neighborhoods that were historically redlined have faced decreased investment, which has impacted homeownership opportunities and subsequent wealth accumulation among racially minoritized populations.[2] Utilizing

this understanding of how historic redlining has impacted the makeup and distribution of resources in present-day neighborhoods coupled with the findings from this dissertation, we can now identify potential policy solutions that can be implemented to address the impacts of policies driven by structural racism.

One specific policy that could be implemented to address the effects of structural racism from historic redlining practices would be to reform bank lending procedures to ensure fair mortgage lending opportunities, particularly among racially minoritized populations living in historically redlined areas. Although redlining was formally outlawed via the passage of the Fair Housing Act in 1968, private institutions have continued to discriminate against Black populations with subprime loans.[3,49] Previous literature has also identified that historically redlined neighborhoods were associated with greater current discriminatory lending, measured as low lending occurrence and high cost loans.[50] Because there is a well-documented relationship between historic redlining and neighborhood trajectories of investment that have impacted homeownership opportunities and wealth accumulation, intervening along this pathway may help to reduce racial wealth gaps and increase access to homeownership opportunities among racially minoritized populations that were discriminated against in historic lending risk assessment programs.

An important consideration for this potential policy is to ensure that mortgage lending opportunities are equitably distributed and not only benefiting populations who have profited from homeownership policies in the past. Robertson et al. (2023) found that neighborhoods graded as “D” (hazardous) by the HOLC received, on average, a greater share of federal funding compared to tracts graded as A (best), B (still

desirable), and C (definitely declining).[49] However, regions graded as D also saw lower rates of non-Hispanic Black homeownership, which may indicate racial disparities in who benefits from funding opportunities. If additional lending opportunities were to be supplied to historically redlined neighborhoods, equitable initiatives would need to be utilized to ensure that funding is supporting those who continue to be disproportionately harmed by policies driven by structural racism. This might require additional oversight by federal agencies such as the Fair Housing Finance Agency, to ensure lending institutions are not only equitably supplying loans, but unfavorable loan interest rates are not being disproportionately granted at higher rates among marginalized populations.

Another consideration for reforming bank lending procedures is the differential impact that homeownership opportunities may have among Black families. Taylor (2019) argues that becoming a homeowner for Black families does not guarantee economic stability or wealth accumulation because majority Black neighborhoods have been historically discriminated against with higher interest rates and property devaluation.[51] Additional policies such as homeowner retention programs, as well as renter assistance programs may also need to be implemented in conjunction to try to address potential adverse effects or to offer additional methods to ensure housing stability and alleviate economic strains among marginalized populations.[49,52] Overall, this proposed policy can help to address disparities in socioeconomic opportunities, which can help to intervene on the hypothesized pathway linking historic redlining and stress outcomes among adolescents.

5.7 Future Directions

This dissertation builds on the current body of literature that examines the impacts of historic redlining on contemporary health outcomes. Despite a growing number of publications investigating associations between historic redlining and present-day health, few studies have been conducted in adolescent samples, and limited studies examine individual-level outcomes. Future studies should attempt to replicate these findings to confirm the causality of this association in other diverse samples. Future research could further investigate the mediating pathways through which redlining is associated with present-day individual-level health indicators or examine structural determinants of contemporary adolescent health outcomes, as these findings can be used to make the greatest impacts on health disparities.

This dissertation examined the impact of historic redlining on stress outcomes in adolescents at one time point. Future studies should explore the impacts of historic redlining on stress using different lifecourse models, including sensitive periods, critical periods, or cumulative exposure across childhood and adolescence.[53] For example, a sensitive period lifecourse approach would investigate if the association between historic redlining and stress at various times to identify if the association was stronger at a specific timepoint. In comparison, a critical period lifecourse approach would examine if exposure was associated with a specific critical period in childhood/adolescence. Finally, an accumulation lifecourse approach would evaluate if the sum of exposure to redlining over time was associated with stress. One method that could be utilized to investigate lifecourse effects is the Structured Approach to Evaluating Life-Course Hypotheses (SLCMA). SLCMA allows for investigation of multiple life-course approaches simultaneously and can be used to determine which theory is the best fit.[54]

These methods may help to uncover potential timepoints in which exposure to redlining is particularly crucial to development and later-life wellbeing. Indeed, previous findings have indicated that ages 3 – 5 may be a sensitive period for exposure to adversity in childhood and DNAm outcomes in adolescence.[33] Identifying potentially sensitive periods for exposure can then help policy initiatives target populations that are at the highest risk and intervene when effects may be particularly harmful.

Taken together, the findings from this dissertation highlight the impacts of structural racism, measured using historic redlining as a proxy, on present-day health outcomes of adolescents. Adolescents living in historically redlined neighborhoods had significantly higher levels of subjective and biologic stress outcomes compared to their peers living in regions that were not subjected or minimally exposed to redlining policies and practices. These findings emphasize the need for policies to address the inequitable exposure to structural racism.

5.8 Dissertation Summary

This dissertation used data from the Future of Families and Child Wellbeing Study (FFCWS) as well as a sub-sample of FFCWS participants from the Study of Adolescent to Adult Neural Development (SAND) to assess associations between historic redlining, driven by structural racism, and stress outcomes in adolescents using three measures of stress: 1) perceived stress via the Perceived Stress Scale, 2) hair cortisol concentration, and 3) eight epigenetic clocks used to measure DNAmAA. We identified associations between high historic redlining and stress outcomes among both subjective and biologic measures of stress. Further, we found that present-day neighborhood characteristics act as potential mediators between historic redlining and

stress outcomes in adolescents. These findings support ecosocial theory of embodiment and provide evidence that structural racism can become biologically embedded in adolescents driving health disparities in the present-day. These findings point to the need for policies that provide access to equitable resources and opportunities within racially minoritized populations who were disproportionately harmed by the policies and practices of historic redlining in the early 20th century. Without consideration of these structural factors, we may not be fully addressing the root causes driving health inequities in present-day.

5.9 Figures

Figure 5.1 Conceptual framework linking historic redlining and present-day adolescent stress outcomes*

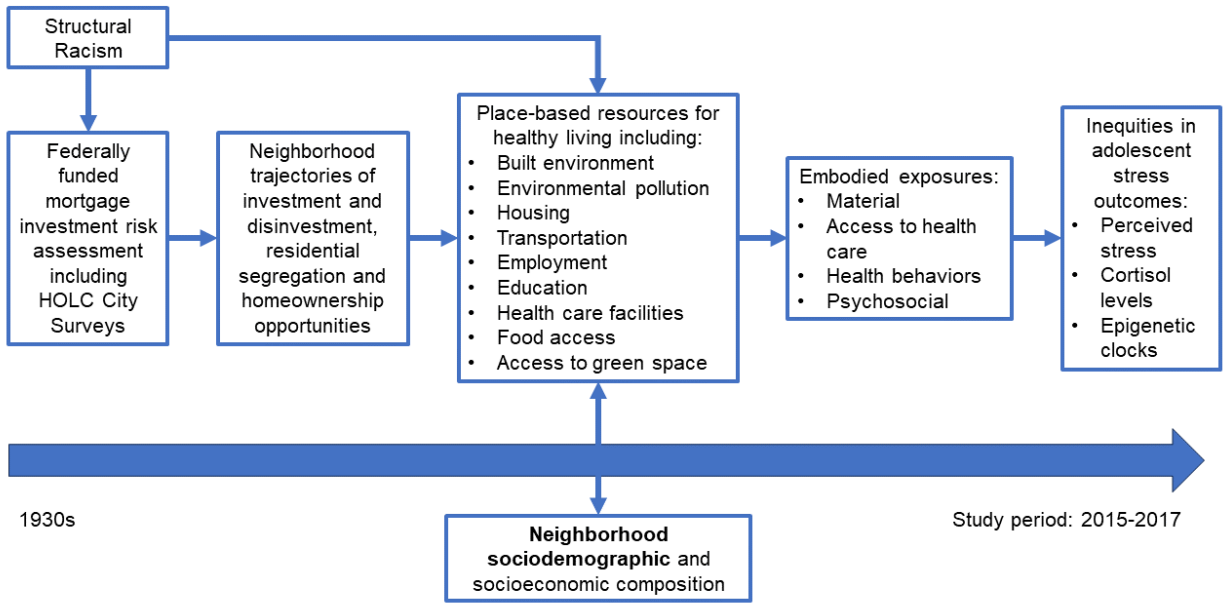

*Figure adapted from: Krieger et al. (2020)[8]

5.10 References

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