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Early Social Origins of Biological Risks for Men and Women in Later Life

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Abstract

We investigate whether childhood exposures influence adult chronic inflammation and mortality risk via adult health characteristics and socioeconomic status (SES) and whether gender moderates these relationships. Analyzing a longitudinal national sample of 9,310 men and women over age 50, we found that childhood SES, parental behaviors, and adolescent behaviors were associated with adult chronic inflammation via health characteristics and SES in adulthood. The process of disadvantage initiated by low childhood SES (i.e., adult health risk factors, socioeconomic disadvantage, and chronic inflammation) subsequently raised mortality risk. In addition, gender moderated the mediating influence of childhood SES via unhealthy behaviors and parental behaviors via adult SES. Demonstrating how social forces shape biological health through multiple mechanisms informs health policies by identifying multiple points of intervention in an effort to reduce the lasting consequences of childhood disadvantage.

Keywords

childhood adversity; cumulative inequality; gender; health; life course; mortality

Across sociology, psychology, medicine, epidemiology, and gerontology, scholars have shifted the analytic frame of health by incorporating a life course perspective into studies of health inequality. Instead of a focus on proximal risks, a growing number of life course studies demonstrate the importance of distal influences on when and how inequalities develop. In many ways, the proliferation of life course analyses marks a return to a key element of the sociological imagination: studying the intersection of biography and history within society (Mills 1959). History sets the stage for how health risks and resources influence the life chances of individuals over time. By splicing early-life experiences with outcomes in later life, accumulating evidence suggests that the consequences of early-life

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SUPPLEMENTAL MATERIAL

Appendices A through C are available in the online version of the article.

disadvantage endure for long periods and shape health decades later (Ferraro, Schafer, and Wilkinson 2016; Yang et al. 2020).

Despite several breakthrough discoveries of the early origins of adult health, most studies are limited in two important ways. First, many health outcomes are self-reported. Although self-reports are useful for prognostic purposes, self-reported disease may be underrepresented among some people due to differential access to and bias within the health care system. Most surveys pose the disease question as whether “a doctor told you that you have” selected conditions, meaning that diseases may go undetected, especially among persons with fewer socioeconomic resources. Ideally, we need early signals of health risk before medical treatments are implemented, and a growing number of studies have incorporated biomarkers to identify “preclinical risk” (Baumeister et al. 2016). We build on those studies to examine how social biographies influence biological risk.

Second, although the literature has identified that early negative exposures are related to a host of adult health conditions, ranging from cancer to heart disease (Kemp et al. 2018; Morton, Mustillo, and Ferraro 2014), conceptual models call for greater attention to how these early risks lead to compromised health (Berkman 2009). Some studies point to “biological programming” during an early *critical period*, suggesting that the health consequences are largely determined by the timing and type of exposure. If early insults are programmed, are they indelible? Or are there intermediary mechanisms that explain how childhood insults set the stage for poor health in later life? Whereas the focus of many previous studies has been to identify the direct health consequences of early risks, there has not been commensurate attention to explore the multifaceted, intermediary processes (Hallqvist et al. 2004; Turner, Thomas, and Brown 2016). If, however, there are intermediary—perhaps modifiable—pathways of early negative exposures, this would be evidence that biological programming is not deterministic, paving the way for interventions to interrupt the chain of risks at various life stages.

This study is designed to address these limitations of prior research. Using a large national sample of older adults, we examine biological risk via two outcomes that are not self-reported: One is an “upstream” biomarker of chronic inflammation, and the other is the ultimate “downstream” marker, death. Distinctive from many prior studies, we examine a wide range of early negative exposures as well as multiple mechanisms that may mediate biological risk. We ask whether negative childhood exposures elevate biological risk decades later and whether midlife resources and risks mediate the potential consequences of early insults. We also give priority to gender differences in these processes. Although women generally outlive men, women experience poorer health (Read and Gorman 2010). Perhaps this pattern also exists on a biological level: Women experience more chronic inflammation but lower mortality risk than men. We begin with a consideration of the literature on the early origins of adult health, highlighting the role of chronic inflammation.

BACKGROUND

Social Determinants of Biological Health Risks

Disadvantageous childhood experiences, such as maltreatment, poor health, and low socioeconomic status (SES), have been linked to cancer (Kemp et al. 2018), cardiovascular disease (CVD; Morton et al. 2014), comorbidity (Ferraro et al. 2016), poor self-rated health (Haas 2006), and mortality in adulthood (Hayward and Gorman 2004). Although previous research has advanced our understanding of how early-life exposures can hasten disease onset and mortality, three attributes of the literature limit our understanding of the mechanisms involved.

First, many studies rely on samples that underrepresent black and Hispanic Americans (e.g., Midlife in the United States) and/or are geographically limited (e.g., Adverse Childhood Experiences Study; Wisconsin Longitudinal Study). Second, many studies analyze morbidity data predicated on a physician diagnosis, which may underrepresent disease prevalence among persons with limited socioeconomic resources (Ferraro and Farmer 1999). Relying on physician diagnoses, moreover, means that biological risk is assessed after the condition has escalated to a medical evaluation. Third, many studies examine biological risk due to childhood SES (Carroll, Cohen, and Marsland 2011; Stringhini et al. 2013; Yang et al. 2020) or abuse (Danese et al. 2007; Matthews et al. 2014), but comparatively few studies examine those in tandem with other exposures such as childhood health conditions and adolescent behaviors. The broader research on the childhood origins of adult health has shown that other facets of childhood, such as health and impairments, also influence adult health (Kemp et al. 2018). Examining multiple childhood exposures can determine which exposures are most consequential to adult health. Therefore, we examine whether multiple childhood exposures influence objectively assessed biological risk in a national sample of adults.

The use of biomarkers in social epidemiology is desirable for several reasons. First, biomarkers that tap into physiology have high predictive validity for disease onset and mortality and are recommended for clinical use (Emerging Risk Factors Collaboration 2010; McDade, Burhop, and Dohnal 2004). Biomarkers can identify at-risk persons before disease onset, enabling an earlier point of intervention. Second, advances in biomarker collection and analysis have led to reliable, quick, and relatively inexpensive procedures to gather and analyze biomarkers (McDade et al. 2004). Third, recognizing the utility of these measures, national U.S. health surveys have incorporated biological markers of health. The high validity and reliability of biomarkers coupled with their integration into national surveys provide a unique opportunity to examine health inequality on a biological level regardless of one's use and access to medical services. To do so, we focus on chronic inflammation as a potential biological mechanism of health inequality.

Whereas acute inflammation is a natural immune response to illness and injury, chronically elevated levels of inflammation can signal immune dysregulation and lead to Alzheimer's disease, cancer, CVD, disability, and premature mortality (Fagundes and Way 2014). Chronic inflammation has been observed in young (Taylor et al. 2006), midlife (Matthews et al. 2014), and older adults (Yang et al. 2017, 2020) who experienced childhood disadvantage. Some studies have linked childhood conditions to chronic inflammation more

than eight decades later, revealing the far-reaching influence of early-life exposures (Surtees et al. 2003).

Psychosocial pathways.—Given mounting evidence linking negative early-life experiences to late-life immune dysregulation, it is important to explicate the mechanisms for this link. Sociologists have identified several intermediary social processes connecting childhood experiences to adult health, especially adult health factors and SES, each of which is related to chronic inflammation (Yang et al. 2017, 2020). Negative childhood exposures have been linked to health factors such as smoking (Ferraro et al. 2016), body mass index (BMI; Matthews et al. 2014), and physical activity (Felitti et al. 1998), which elevate chronic inflammation (Herd, Karraker, and Friedman 2012). Childhood exposures also are associated with adult SES, including educational attainment and wealth (Haas 2006), which are associated with chronic inflammation (Pollitt et al. 2007). Thus, it may be that chronic inflammation is not the direct result of childhood exposures but that intermediary mechanisms are at play. To advance this line of inquiry, we investigate multiple health-related and socioeconomic pathways through which childhood exposures may influence immune functioning.¹

In designing this study, we couple an “upstream” health outcome, chronic inflammation, with the final life outcome—mortality. Both are measured by others, not the survey respondent, and capture early- or late-stage biological risk. Several exemplary studies have demonstrated a relationship between childhood exposures, adult SES, health lifestyles, and mortality (Hayward and Gorman 2004; Morton et al. 2014; Pudrovska and Anikputa 2014). However, we are unaware of any studies of these relationships that integrate chronic inflammation despite the fact that chronic inflammation markers have high predictive validity for mortality. We first examine whether childhood exposures influence adult SES, health characteristics, and chronic inflammation, then turn to mortality risk as our ultimate outcome of biological risk. We illustrate these relationships in Figure 1, anticipating mediation through midlife socioeconomic and health-related processes.

Gender.—Gender differences in life chances, longevity, and health are well established (Read and Gorman 2010; Yang and Kozloski 2011). Many studies of health, particularly those examining biomarkers, consider gender as a control variable only (Danese et al. 2007) or test gender interactions (Brummett et al. 2013). Each are plausible approaches, but we draw from sociology’s conceptualization of gender as social structure to explicate how gender influences health throughout the life course (Homan 2019; Risman 2004) and hypothesize *moderated mediation* (i.e., conditional indirect effects).

As social structure, gender stratifies individual behavior and social conditions, producing observable differences throughout the life course (Homan 2019). This study assesses multiple life domains at various life stages, each of which is intertwined with gender. Based

¹Some evidence suggests that body mass index (BMI) and smoking mediate the influence of early-life conditions on adult inflammation levels (Brummett et al. 2013; Matthews et al. 2014), whereas support for the mediational effect of adult socioeconomic status (SES) has been inconsistent (Surtees et al. 2003; Yang et al. 2017). It also remains unclear whether these mechanisms fully explain the relationship between childhood exposures and adult chronic inflammation (Matthews et al. 2014) or partially account for the association (Surtees et al. 2003).

on prior studies, we posit that the risk of childhood exposures on health outcomes is distinct for men and women (Herd et al. 2012; Kemp et al. 2018; Read and Gorman 2010; Yang and Kozloski 2011). In particular, previous research reveals that women suffer more health consequences than men due to childhood socioeconomic disadvantage (Hamil-Luker and O'Rand 2007; Pudrovska et al. 2014) and child abuse (MacMillan et al. 2001). A possible explanation is that gender socially patterns how individuals respond to childhood conditions: Women have reported similar childhood events as more upsetting and requiring a longer recovery period than men (Surtees and Wainwright 2007). Gendered responses to childhood exposures also likely influence health by moderating the effect of early-life conditions on adult health risks and SES, both of which are distributed among the population according to gender (Read and Gorman 2010). Empirical evidence has shown that adult health characteristics and SES exert differential health effects for men and women, including mortality (Pudrovska and Anikputa 2014; Pudrovska et al. 2014).

Although relatively few studies have actually tested for conditional indirect effects, Brummett et al. (2013) provided compelling evidence that BMI and smoking mediate the relationship between childhood conditions and adult chronic inflammation among men and that BMI is the sole mediator among women. Given emerging evidence indicating gender may influence the relationship between childhood exposures and adult chronic inflammation, as well as long-standing gender differences in health and mortality (Homan 2019; Read and Gorman 2010), we investigate whether moderated mediation operates for men and women facing life stressors.

Theoretical Framework

Cumulative inequality theory.—We draw primarily from cumulative inequality (CI) theory, a middle-range formulation elucidating how social inequality unfolds over the life course (Ferraro and Shippee 2009). CI theory is particularly useful for the current line of research because it brings the past into relational context with the present, piecing together life histories to explain how biological risk develops and differentiates over time.

Sociologists have highlighted life course accumulation processes, as manifest in Weber's ([1922] 1978) conceptualization of life chances, Merton's (1968) Matthew effect, Elder's (1974) life course perspective, and Pearlin's (2009) stress process. CI theory builds on these prior works but emphasizes the family context of child and human development. It also challenges the assumption that advantage and disadvantage are opposite ends of a spectrum because the consequences of each are typically so distinct; disadvantage increases exposure to risk, whereas advantage increases exposure to opportunity.

With respect to childhood as a sensitive period, CI theory posits that childhood conditions exert a lasting impact because they provide different opportunities and constraints, differentiating individuals early in life. Across generations, these initial differences can compound, channeling available choices, to perpetuate and perhaps amplify inequality. Unlike many studies that focus on one life stressor such as poverty, we consider multiple childhood exposures ranging from SES and parental behaviors to health conditions. In doing so, we hypothesize that negative early-life conditions initiate a lifelong process of unequal

opportunity structures and stress responses, which leads to chronic inflammation and, in turn, higher mortality risk (Taylor et al. 2006).

Our theoretical specification includes both the long-term influence of early exposures and the intermediary influences via adult risks, resources, and human agency. Some frameworks such as biological programming (Barker 1995) specify indelible influence perhaps through altering the phenotype (critical period). Others such as “strict” cumulative dis/advantage are premised on mathematical models using a single domain and “illustrated most simply by the process of wealth accumulation through the mechanism of compound interest” (DiPrete and Eirich 2006:272). Some expressions of strict cumulative advantage are even more determined because values cannot decrease (e.g., publication citation counts). By contrast, CI theory specifies a probability model based on social systems and incorporates human agency as well as the onset, duration, and gravity of exposures.

CI theory also moves beyond the strict cumulative dis/advantage notion of focusing on accumulation within a single domain. Building on Pearlin’s (2009) concept of stress proliferation, CI theory specifies that inequality diffuses across multiple life domains, as illustrated by the well-documented relationship between wealth and health. Indeed, processes of inequality often spill over into other life domains, creating a cascade of differential experiences based on social structures and personal choices. Consistent with the life course perspective, agency is a fundamental component of human experience, but available choices are constrained by social location and biography (Elder 1974; Mills 1959).

The gendered life course perspective.—Although CI theory provides insight into how early-life social exposures influence late-life health, the theory does not give explicit attention to the role of gender. Instead, gender is viewed mostly as a status and component of social structure. We contend that the gendered life course calls for more systematic integration, especially because of our focus on moderated mediation. A gendered life course perspective elucidates how biographical histories of men and women are constructed differently over time, giving priority to the structural disadvantages that women face (Moen 2001). Gendered processes are present in the earliest stages of life and persist. Early in the life course, gender socialization plays a fundamental role in how boys and girls are raised and treated. This differential treatment may explain why boys and girls experience different types of childhood exposures at different rates (Kemp et al. 2018; Mac-Millan et al. 2001). In addition, women’s lives are more likely to be shaped around other family members (Moen 2001). Thus, childhood exposures, which often occur within the context of the family, may become inextricably linked to women, exerting a stronger direct effect on health for women compared to men (Hamil-Luker and O’Rand 2007).

A gendered life course perspective also notes that gender norms and expectations of behaviors and lifestyles socially pattern mechanisms of health inequality. Empirical evidence has consistently shown that men engage in more risky health behaviors and lifestyles than women (Homan 2019). Given that prior research reveals that health characteristics (especially smoking and BMI) mediate the effect of childhood exposures on chronic inflammation for men but not women (Brummett et al. 2013), we hypothesize that midlife characteristics are more consequential for men than for women. In sum, we expect that the

direct effects of childhood exposures on adult chronic inflammation and mortality will be stronger for women, whereas the mediational effects will be stronger for men.

DATA AND METHODS

Sample

This study used six waves of data from the Health and Retirement Study (HRS), spanning 10 years. The HRS is a nationally representative, biennial panel study of American adults over age 50. We analyzed a sample of 9,310 adults who participated in the Enhanced Face-to-Face Interview and core surveys beginning in 2004, when the majority of childhood measures were added to the core surveys. Details of sample selection and composition are described in Appendix A in the online version of the article.

Measures

Chronic inflammation.—Adult chronic inflammation was assessed using dried blood spots of C-reactive protein (CRP), a reliable and valid marker of inflammation (McDade et al. 2004) and robust inflammatory outcome of childhood exposures (Baumeister et al. 2016).² CRP was a continuous variable measured in ug/mL. Because the focus was to assess chronic inflammation, ~10% of respondents who had CRP >10 ug/mL were removed from analyses because these cases likely indicate acute inflammatory disease or injurious stimuli—a practice consistent with prior research (Brummett et al. 2013). To adjust for skewness, CRP was log-transformed. Models included a flag indicating whether CRP was measured in 2006 (coded as 1) or 2008 (coded as 0).³

Mortality.—Mortality data were collected from proxies (usually a family member) and the National Death Index. Using this information, censor and duration variables were created to estimate survival models. The censor variable indicated whether the participant died during the six-year observation period from 2008 to 2014 (1 = died, 0 = otherwise). The observation period began in 2008 to maintain temporal ordering among the key variables, and respondents needed to survive until 2008 to collect CRP data. The duration variable was calculated as number of months alive since January 2008. For those who died during the observation period, duration was calculated as months until death since January 2008. For those who did not die (death not confirmed), duration was calculated as number of months from January 2008 until latest survey. The duration variable ranged from 3 to 84 months.

Childhood exposures.—Childhood exposures were measured using 28 self-reported, retrospective indicators of childhood experiences. These 28 indicators comprised five domains based on prior empirical and conceptual literature (Felitti et al. 1998; Kemp et al. 2018; Morton et al. 2014) and tetrachoric factor analysis. The five domains were childhood socioeconomic disadvantage, risky parent behaviors, chronic disease, impairment, and risky adolescent behaviors and mental health (hereafter, *adolescent behaviors*). Because the

²Following recommendation of the Health and Retirement Study (HRS) biomarker documentation report, the National Health and Nutrition Examination Survey (NHANES)-equivalent C-reactive protein (CRP) values were used (Crimmins et al. 2013).

³The CRP measurement flag also accounts for potential measurement error due to within- and between-assay imprecision and a small set of CRP assays done at Biosafe instead of the University of Vermont (Crimmins et al. 2013).

majority of indicators (22/28) had binary response categories, each indicator was initially dichotomized (1 = exposure occurred, 0 otherwise). Next, the indicators were summed within each domain and top-coded. Childhood SES, risky parental behaviors, chronic disease, and childhood impairment were top-coded at 2, with 2 indicating two or more exposures within that domain (few respondents experienced more than two exposures in each domain). Risky adolescent behaviors were top-coded at 1 (few respondents reported more than one). Details of the indicators and domains are provided in Appendix B in the online version of the article.

Health characteristics.—Health characteristics included smoking, BMI, and exercise assessed in 2004. Smoking was a continuous variable measured as pack-years. Among smokers, respondents reported when they began smoking, when they quit (if applicable), and how much they smoked daily, on average. From this information, we calculated total years smoked (year stopped minus year started for former smokers; 2004 minus year started for current smokers). Next, we multiplied total years smoked by average number of cigarettes smoked daily and divided by 20 (cigarettes per pack) to calculate pack-years smoked. Respondents who never smoked were coded as 0. To adjust for skewness, a constant of 1 was added, and then pack-years was log-transformed.

BMI was calculated from self-reported weight and height. BMI was measured in kg/m^2 and top-coded at $61.3 \text{ kg}/\text{m}^2$. For mortality analyses, we used grand-mean centered constituent and squared terms due to the nonlinear relationship between BMI and mortality among older adults. Exercise was a continuous variable. Respondents were asked how often they took part in vigorous exercise or activities such as running/jogging, swimming, cycling, aerobics/gym workouts, tennis, or digging with spade/shovel. Response categories of daily, >1 time per week, 1 time per week, 1 to 3 times per month, and never were reverse-coded so that higher values indicate more frequent exercise.

Socioeconomic status.—Adult SES variables included 2004 measures of education and wealth. Education was a continuous measure in years (highest level completed). Wealth was a continuous variable measured in dollars and calculated as total household assets minus all debt.⁴ Wealth is a more reliable indicator of finances than income for older adults; many are retired and, therefore, not receiving an annual salary. Wealth also taps into the accumulated assets and debts older individuals have incurred over their lifetime. Given that wealth ranged from approximately $-\$2.25$ million to $\$31.5$ million, a cube root transformation of wealth was used to adjust for skewness and reduce error variability. Unlike a square root or log-transformation, a cube root transformation can be applied to zero and negative values.

Gender.—Gender was self-reported and assessed at baseline. A dummy variable for female was created (1 = female, 0 = male).

The measurement of all other variables is described in Appendix A in the online version of the article.

⁴The wealth variable came from the publicly available RAND data set. RAND used 15 indicators of wealth from HRS data, imputing missing values utilizing several imputation methods.

Analysis

We used Mplus 8 to estimate a series of regression and Cox proportional hazards models. The first set of analyses examined the relationship between childhood exposures and adult chronic inflammation. Models were first estimated without mediators to establish a baseline relationship between childhood exposures and adult chronic inflammation. Next, adult health characteristics and SES mediators were simultaneously introduced into the models. Statistical tests of mediation were conducted using Monte Carlo integration and a maximum likelihood robust estimator to produce standard errors for direct and indirect effects via the delta method (Muthén 2011). Paths were created to establish a direct relationship between (a) childhood exposures and each mediator and (b) each mediator and CRP; indirect effects were calculated as the product of the two paths ($a \times b$).

The second set of analyses examined mortality risk, again initially estimating models without mediators to establish a baseline relationship between childhood exposures and adult mortality. Next, adult health characteristics, SES, and chronic inflammation were simultaneously introduced into the models. Statistical tests of mediation were conducted following the steps outlined previously but with an additional path (c) from chronic inflammation to mortality. Hence, indirect effects were calculated as a product of three paths ($a \times b \times c$).

Descriptive and inferential statistics were weighted and adjusted for the complex survey design (stratification and clustering). Full-information maximum likelihood was used for item-missing data on the independent variables.

Sensitivity analyses.—Several supplementary analyses were conducted to verify the robustness of the results. First, preliminary analyses were conducted to determine whether the form and measurement of the overall models varied by gender. Overall model fit did not improve substantially when stratified by gender (statistical evidence for measurement invariance). Therefore, we utilized a single, pooled sample, estimating a series of gender interactions for each of the significant key variables. Moderated mediation was examined by calculating conditional indirect effects for men and women and using a Wald test to compare coefficients. Statistically significant moderating effects are presented.

Second, we investigated three alternative coding schema for each domain: (1) total count domains (total count of indicators not top-coded), (2) standardized domains (dividing total counts by number of indicators in each domain), and (3) dichotomous domains (1 = experienced at least one indicator in that domain, 0 = otherwise). These analyses revealed that top-coding was appropriate and reduced Type II error.

Third, we reestimated models using a more conservative CRP cutoff of 8.6 ug/mL for chronic inflammation (Herd et al. 2012). Overall, conclusions were similar except that risky parental behaviors were nonsignificant and gender moderated the effect of childhood SES on BMI.

RESULTS

Table 1 displays descriptive statistics for the total sample and by gender. The means of logged CRP were .406 and .601 for men and women, respectively. Approximately 14.1% of men and 11.9% of women died during the six-year observation period from 2008 to 2014. For men and women, the most common childhood exposure was socioeconomic disadvantage, whereas the least common was risky adolescent behaviors. Overall, the sample is pre-dominantly white, married, and born in the 1940s. Approximately half of the sample is taking a hypertensive or psychiatric medication.

Most variables varied by gender. On average, women lived longer than men despite having higher levels of inflammation. Women experienced more childhood socioeconomic disadvantage and chronic diseases than men. Men reported more risky parental and adolescent behaviors and impairments during childhood than women. Men were more likely to have a higher BMI and smoked more pack-years than women but exercised more. On average, men had more education and wealth than women.

Chronic Inflammation

Table 2 displays results from regressing chronic inflammation on the independent variables. Model 1 includes each childhood domain and adult chronic inflammation without the mediators. Low childhood SES, risky parental behaviors, and risky adolescent behaviors predicted CRP net of all covariates. Each additional indicator of socioeconomic disadvantage during childhood increased adult CRP by .065 units ($p < .01$). Each additional risky parental behavior in childhood increased adult CRP by .035 units ($p < .05$). Respondents who reported at least one risky adolescent behavior had higher CRP by .078 units on average compared to those who did not report any risky adolescent behaviors ($p < .05$). Gender did not moderate any childhood effects but exerted a direct effect on CRP. Women, on average, had higher CRP than men ($p < .001$). Birth cohort, race-ethnicity, prescription medications, and measurement year also predicted CRP. Compared to those born in the 1950s, people born before 1920 ($p < .01$) or in the 1920s ($p < .05$) had lower CRP on average. Compared to white respondents, black and Hispanic respondents had higher CRP ($p < .01$). Respondents taking prescription medication had higher CRP ($p < .001$). Respondents whose CRP was collected in 2006 had lower CRP than respondents whose CRP was collected in 2008 ($p < .001$).

When adult health characteristics and SES mediators were introduced in Model 2, the effects of childhood SES, risky parental behaviors, and risky adolescent behaviors became nonsignificant. The effect of gender remained significant ($p < .001$), but gender did not moderate any of the effects of adult health characteristics or SES on CRP. Each adult health-related and socioeconomic variable had a significant effect on CRP net of childhood exposures and adult risk factors. Each additional unit of pack-year smoked increased CRP by .051 units ($p < .001$). A one-unit increase in BMI was associated with an increase of .047 units of CRP ($p < .001$). Respondents who exercised more frequently had lower CRP ($p < .05$). Each additional year of education decreased CRP by .019 units ($p < .001$), whereas higher levels of wealth predicted lower CRP ($p < .001$). The effects of medication and measurement year remained significant, whereas racial-ethnic differences were no longer

significant. The effects of birth cohort differed. Whereas CRP for the 1910 and 1920 cohorts no longer differed from the 1950 cohort, the 1940 cohort had higher CRP than the 1950 cohort ($p < .05$).

Mediation results.—Figures 2 to 4 illustrate the significant mediational results for Table 2, Model 2. Figure 2 displays mediation results for childhood SES (for complete mediational effects, see Appendix C, Table S2 in the online version of the article). Indirect effects revealed that the relationship between childhood SES and adult CRP was mediated by BMI ($b = .035, p < .001$), exercise ($b = .003, p < .05$), education ($b = .017, p < .001$), and wealth ($b = .015, p < .001$). For men and women, childhood socioeconomic disadvantage led to higher BMI ($b = .732, p < .001$), less frequent exercise ($b = -.137, p < .001$), fewer years of education ($b = -.866, p < .001$), and less wealth ($b = -6.762, p < .001$), each of which led to higher CRP. Statistical comparison of indirect effects revealed that smoking mediated the effect of childhood SES on adult CRP for men but not women (Wald test: difference = .009, $p < .01$). For men, the effect of low childhood SES on chronic inflammation was transmitted via higher pack-years (indirect effect: $b = .009, p < .01$). Gender did not moderate any other pathways.

Figure 3 displays mediation results for risky parental behaviors (for complete mediational effects, see Appendix C, Table S3 in the online version of the article). Indirect effects revealed that the relationship between parental behaviors and adult CRP was mediated by smoking ($b = .014, p < .001$) via more pack-years smoked ($b = .280, p < .001$) for men and women. Statistical comparison of indirect effects revealed that adult SES mediated the effect of parental behaviors on adult CRP for men but not women (education Wald test, $p < .01$; wealth Wald test, $p < .05$). For men, the effect of risky parental behaviors on chronic inflammation was transmitted via fewer years of education (indirect effect: $b = .003, p < .05$) and less wealth (indirect effect: $b = .005, p < .05$). Gender did not moderate any other pathways.

Figure 4 displays mediation results for risky adolescent behaviors (for complete mediational effects, see Appendix C, Table S4 in the online version of the article). Indirect effects revealed that the relationship between adolescent behaviors and adult CRP was mediated by smoking ($b = .017, p < .01$), BMI ($b = .029, p < .05$), exercise ($b = .004, p < .05$), and wealth ($b = .009, p < .05$) for men and women. Risky adolescent behaviors led to more pack-years smoked ($b = .324, p < .001$), higher BMI ($b = .607, p < .05$), less frequent exercise ($b = -.161, p < .01$), and less wealth ($b = -4.048, p < .01$), each of which led to higher CRP. Gender did not moderate any pathways.

Mortality

Our second aim treats chronic inflammation as endogenous, but the ultimate outcome is mortality, testing the full pathway model in Figure 1. The results of the survival models are displayed in Table 3, with Model 1 specifying a baseline relationship between each childhood domain and adult mortality. Only childhood SES predicted mortality net of all covariates. Each additional experience of socioeconomic disadvantage during childhood increased mortality risk by 16.6% ($p < .01$). Gender had a direct effect on mortality but did

not moderate the effect of childhood SES. Compared to men, women had a 38.3% ($p < .001$) lower mortality risk. Birth cohort, marital status, and prescription medication also were associated with mortality risk. Compared to the 1950 cohort, the 1910, 1920, and 1930 cohorts had higher mortality risks ($p < .001$). Being married lowered mortality risk ($p < .001$). Respondents taking a prescription medication had higher mortality risk ($p < .01$).

When the health-related, socioeconomic, and biological mediators were introduced in Model 2, the effect of childhood SES became nonsignificant. Each mediator had a direct effect on mortality. The more pack-years smoked, the higher the mortality risk ($p < .001$). BMI had a nonlinear, reverse-J shaped effect. Higher BMI was protective against mortality until the inflection point (27.5 kg/m^2) at which higher BMI raised mortality risk ($p < .001$). Respondents who exercised more frequently had lower mortality risk ($p < .01$). More education ($p < .05$) and greater wealth ($p < .001$) reduced mortality risk. Each additional unit of CRP increased mortality risk by 22% ($p < .001$). Although gender did not moderate any direct effects of the mediators, women continued to have a lower risk of mortality than men ($p < .001$). The effects of birth cohort and prescription medication remained significant, whereas the effects of marital status and race-ethnicity changed. Marital status became nonsignificant. Compared to white respondents, Hispanic respondents had lower mortality risk ($p < .01$).

Mediation results.—Figure 5 illustrates the mediational pathways from childhood SES to adult mortality from Table 3, Model 2 (for complete mediational effects, see Appendix C, Table S5 in the online version of the article). Indirect effects for the paths from childhood SES to adult mortality via BMI and CRP ($b = .007$, $p < .001$), exercise and CRP ($b = .001$, $p < .05$), education and CRP ($b = .003$, $p < .01$), and wealth and CRP ($b = .003$, $p < .01$) indicated statistical support for mediation for men and women. For BMI, childhood socioeconomic disadvantage led to higher BMI ($b = .733$, $p < .001$), which led to higher CRP ($b = .047$, $p < .001$), thereby raising mortality risk ($b = .199$, $p < .001$). For exercise, childhood socioeconomic disadvantage led to less frequent exercise ($b = -.137$, $p < .001$), less frequent exercise led to higher CRP ($b = -.026$, $p < .05$), and higher CRP subsequently raised mortality risk ($b = .199$, $p < .001$). Similarly, childhood socioeconomic disadvantage led to fewer years of education ($b = -.865$, $p < .001$) and less wealth ($b = -6.757$, $p < .001$), lower adult education and wealth led to higher CRP (respectively, $b = -.019$, $p < .001$; $b = -.002$, $p < .001$), and higher CRP subsequently increased mortality risk ($b = .199$, $p < .001$). The indirect effect from childhood SES to mortality via smoking and CRP was significant for men only ($b = .002$, $p < .01$) and differed from the indirect effect for women (Wald test: difference = .002, $p < .01$). For men, childhood socioeconomic disadvantage led to more pack-years smoked ($b = .177$, $p < .001$), which led to higher CRP ($b = .052$, $p < .001$), subsequently raising mortality risk ($b = .199$, $p < .001$).

DISCUSSION

Life course scholars have made great strides to advance our understanding of the early social origins of adult health by identifying links between negative childhood exposures and a wide range of health problems. The present study focused on the intersection of sociology and biology by examining how social factors influence a core biological process of responding to

insults. The inflammatory response is essential for the body's recognition of and defense against insults, but this research reveals that early negative exposures lead to adult health risk factors and socioeconomic disadvantage that incur additional bodily insults, culminating in important biological risks in later life. This is the first study, to our knowledge, that investigates the links between multiple domains of childhood exposures (e.g., SES, disease, parental behavior), adult inflammation, and mortality in a national sample. Many prior studies examine the link between childhood SES or abuse and chronic inflammation in nonrepresentative samples but stop short of integrating additional domains of early exposures, investigating mortality as an outcome, and testing for mediation and moderation. We elaborate on the substantive and theoretical implications of this study.

First, the findings herein underscore the importance of considering multiple childhood exposures. In our investigation of the early social origins of biological risks, we found that childhood SES, risky parental behaviors, and adolescent behaviors were associated with biological risk more than four decades later. These results demonstrate that childhood exposures beyond childhood SES (Pollitt et al. 2007) and abuse (Danese et al. 2007) can have lasting biological consequences, giving strong evidence to chronic inflammation as an under-the-skin marker of the early social origins of biological risk. Moreover, linking childhood SES to adult chronic inflammation not only supports previous research (Brummett et al. 2013; Yang et al. 2017) but also strengthens the evidence by adjusting for other childhood exposures and elucidating the life course process of how this relationship carries through to mortality. Indeed, the salience of childhood SES was observed in the mortality analyses, but health policymakers and practitioners should be cognizant of other childhood exposures associated with biological risks. We urge future research to consider multiple domains of childhood exposures to identify which exposures influence adult biological risks.

Second, our investigation of the long-term direct effects found no evidence of indelible effects. Instead, we uncovered considerable evidence of mediation across multiple domains in a national survey of U.S. adults. Although the link between childhood conditions and adult health is frequently observed, there have been repeated calls for understanding the actual mechanisms instead of relying on a black-box model of epidemiology (Kelly-Irving and Delpierre 2019; Turner et al. 2016). As Yang et al. (2020:614) argued, the "interrelated life-course processes underlying the associations between early-life SES and health risk" are complex. Making use of a longitudinal national survey with social, behavioral, and biological data, we found that the effects of childhood exposures *diffused* across multiple health-related and socioeconomic domains, subsequently influencing physiology. Late-life health inequality indeed has early origins, but it is not a matter of indelible effects or simple cumulative disadvantage within a single domain. Rather, the effect of childhood social conditions on biological risk was carried through into late life by a multidimensional process consisting of health characteristics and social statuses (Ferraro and Morton 2018; Ferraro and Shippee 2009).

Whereas prior research has demonstrated that health characteristics mediate the effect of childhood exposures on adult inflammation levels (Brummett et al. 2013; Matthews et al. 2014), the mediating role of adult SES has been inconsistent. Perhaps the intergenerational

transmission of socioeconomic disadvantage and its physiological consequences are not detected unless indirect effects are assessed (Yang et al. 2017). Surtees et al. (2003) reported that childhood exposures were related to education and lymphocyte count but did not test for whether education mediates the relationship between early exposures and lymphocyte count. Alternatively, the type of childhood exposures and socioeconomic indicators examined may uncover context-specific mediating effects. Indeed, we found that different childhood exposures entailed distinct mediational processes. Empirically, this highlights the importance of model specification to study pathways to enhance our understanding of life course health processes. Substantively, it clarifies that biological risks can be modified by social structures, which in turn can reduce risks and activate resources to advance health.

Many biologically based theories of health focus on the direct biological consequences of early-life experiences but do not account for other important life course processes that may mediate such risks (Barker 1995; Hertzman and Boyce 2010). In contrast, this study demonstrates that adult socioeconomic and health-related factors fully attenuated the relationship between childhood exposures and adult chronic inflammation and mortality. Perhaps stress-regulatory mechanisms that are chronically activated due to noxious childhood conditions become weakened and subsequent threats, like adult socioeconomic disadvantage and unhealthy behaviors, push people past a biological threshold, triggering physiological dysregulation. Whatever the case, it is imperative to underscore how fields like sociology can inform other disciplines in the social, behavioral, and physical sciences by explicating how early-life social conditions structure life course processes that influence health. Failing to do so may inadvertently give rise to biological determinism or at least an ontogenetic depiction of biological processes.

Third, the long arm of childhood experiences is distinctive for men and women (Hayward and Gorman 2004). Consistent with our moderated-mediation expectations and prior research (Brummett et al. 2013), the effect of childhood SES on smoking was stronger for men, setting off a cascade of risks extending to chronic inflammation and mortality for men only. This finding is consistent with gendered norms of smoking and the historical context of when many of the HRS respondents were adolescents and young adults. Similarly, the effect of risky parental behaviors on education and wealth was stronger for men, and their mediational effects on chronic inflammation were significant for men only. Considering historical context, there was a structural lag of women entering college and the labor force. Compared to women, men in the HRS likely entered the economy earlier in the life course, closer to childhood, and experienced a greater economic impact due to the proximity of these childhood exposures.

Conversely, some of our gender expectations were not supported, notably that the direct effects of childhood exposures on biological risks would be stronger for women. Perhaps this is due to our biological outcomes, unlike prior life course studies that utilized outcomes such as cancer (Kemp et al. 2018), heart attack (Hamil-Luker and O'Rand 2007), and psychopathology (MacMillan et al. 2001). We also found few such instances of moderated mediation and offer two speculations as to why. First, the lack of moderated mediation reveals the gravity of childhood SES for men and women. Childhood SES had the most salient effects on adult biological risk, but only one of five mediators was moderated by

gender. Second, moderated mediation was present only for childhood exposures measuring parental characteristics (childhood SES and parental behaviors). Childhood exposures capturing respondent characteristics were not moderated by gender, suggesting the importance of a gendered family influence. Nonetheless, there is some evidence to suggest that a gendered life course perspective offers a fruitful lens of interpretation for health inequality. Beyond the moderated pathways, bivariate relationships indicate that gender structures the life course differentially for men and women: Childhood exposures, adult health characteristics, SES, inflammation levels, and mortality varied by gender in expected ways based on prior research (Herd et al. 2012; Read and Gorman 2010; Yang and Kozloski 2011). Notably, women generally had higher levels of inflammation but lower mortality risk.⁵

On the theoretical front, several elements of CI theory were supported by this research. Examples include (a) the role of family lineage leading to status attainment and health, (b) identification of childhood as a sensitive period for human development and social stratification, and (c) the contingent nature of accumulation processes across domains due to social context and human agency. The mortality analyses capture the essence of how social and biological processes intersect: Late-life mortality reflects a lifetime of differential experiences, traced to childhood—and hence prior generations—and socioeconomic resources are central to the mechanism of chronic inflammation driving survival chances.

Our research also seeks to address what we consider limitations of the theory. First, although the theory emphasizes the role of social systems and the dialectic of agency and social structures, this study demonstrates that seemingly agentic processes like health behaviors are structured by social systems, such as childhood SES or, in some cases, gender. By underscoring how health behaviors and physiology are not simply capturing individual choices and biology but rather socially patterned functions of broader social structures, it might be useful to situate the findings of this study into broader theoretical discussions of social stratification. Whereas CI theory contributes a life course focus on the role of childhood and diffusion of inequality across domains, classical approaches to the study of social inequality highlight the role of family lineage via social reproduction and embed individuals within the socially structured confines of parental social location (Bourdieu and Passeron 1977). From this perspective, parent's social location is not simply a starting point in the life course but also continues to structure how individuals traverse the life course from adult social status to health characteristics. Although agency and individual choice are important factors of health, theoretical applications of CI theory should not underestimate the role of social systems and stratification. Accordingly, we recommend vigilance when examining cumulative health inequality, emphasizing that social context and biography shape individual health processes.

Second, although the theory gives attention to moderation and mediation processes, the present research draws explicit attention to moderated mediation for how early exposures influence biological risk. Given the theory's emphasis on probabilistic effects, we contend

⁵.We focused on the social antecedents to biological health risks, emphasizing the role of gender. However, biological sex hormones also likely influence biological health risks, and future research should consider disentangling the effects of gender from sex.

that more attention should be given to moderated mediation to account for the complexity of life course processes. We discovered that gender plays an important role in shaping how indirect effects of childhood exposures on health operate. Future research should consider influences on health at the intersection of other social structures such as race, ethnicity, and nativity.

The findings presented herein also should be interpreted in light of this study's limitations. First, childhood data are retrospective and, therefore, subject to recall bias. We took precautions to minimize such bias (excluding respondents with low cognition scores) and controlled for variables that can bias retrospective recollection (Vuolo et al. 2014). Second, the HRS does not measure CRP earlier in the life course. We were unable to ascertain when CRP became elevated, nor did we examine trajectories of CRP. We did, however, focus on chronic inflammation, rather than acute inflammation, in an effort to capture persistent, long-term physiological wear and tear rather than an immediate inflammatory response. Third, the HRS does not assess hormonal drug therapy or statin use. Chronic inflammation may be masked (from statins) or heightened (from hormone drugs) for some HRS participants. Fourth, the age of the sample (>50) may underestimate the effects of childhood exposures on biological risks. Individuals who experienced the most severe early-life disadvantages are more likely to experience premature mortality or incarceration and, therefore, are less likely to be included in these analyses. Thus, parameter estimates of the mechanisms studied here may be a conservative assessment of the pathways. Fifth, bias due to systematic inequality in health care may be unaccounted for, especially given that adults do not enter the study until after age 50. Although we attempted to adjust for bias in the health care system by utilizing measures that do not require a physician diagnosis and continuous data rather than arbitrary clinical thresholds (CRP and BMI), bias likely exists and remains a critical point of consideration for future research. These limitations, however, provide an opportunity for future studies of the early origins of adult health.

CONCLUSION

American children have been experiencing increasingly unequal childhoods, including the widening of socioeconomic disparities, since the 1960s (Berkman 2009). Unlike some deterministic models of the early origins of adult health, this study's findings are consistent with the importance of specifying the life course processes linking childhood conditions to adult health. The evidence is clear that increasing childhood social inequality leads to increasing health inequality because childhood exposures stratify individuals on multiple life domains that affect health. Moreover, this study contributes to the literature by establishing chronic inflammation as both a valuable indicator of preclinical biological risk and a specific mechanism for how early insults raise the risk of premature mortality. We conclude that because the imprint of negative early exposures is not directly related to either biological risk, there is ample opportunity to interrupt the chain of health risks at various stages in the life course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Conceptual Model of Proposed Relationships among Childhood Exposures, Adult Health Characteristics, Adult SES, Chronic Inflammation, and Mortality for Men and Women.
Note: SES = socioeconomic status.

Figure 2.

Mediation Results from Childhood SES to Adult Chronic Inflammation for (a) Men and (b) Women.

Note: Paths from childhood SES to adult chronic inflammation are displayed if indirect effect is significant at the .05 level. Dashed line indicates significantly different indirect effect for men compared to women at the .05 level of significance. Coefficients are unstandardized and adjusted for variables in Table 2, Model 2. SES = socioeconomic status; BMI = body mass index.

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed tests).

Figure 3.

Mediation Results from Childhood Risky Parental Behaviors to Adult Chronic Inflammation for (a) Men and (b) Women.

Note: Paths from risky parental behavior to adult chronic inflammation are displayed if indirect effect is significant at the .05 level. Dashed line indicates significantly different indirect effect for men compared to women at the .05 level of significance. Coefficients are unstandardized and adjusted for variables in Table 2, Model 2.

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed tests).

Figure 4.

Mediation Results from Risky Adolescent Behaviors to Adult Chronic Inflammation for Men and Women.

Note: Paths from risky adolescent behavior to adult chronic inflammation are displayed if indirect effect is significant at the .05 level. Indirect effects did not differ for men and women. Coefficients are unstandardized and adjusted for variables in Table 2, Model 2. BMI = body mass index.

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed tests).

Figure 5.

Mediation Results from Childhood SES to Adult Mortality for (a) Men and (b) Women.

Note: Paths from childhood SES to adult mortality are displayed if indirect effect is significant at the .05 level. Dashed line indicates significantly different indirect effect for men compared to women at the .05 level of significance.

Coefficients are unstandardized and adjusted for variables in Table 3, Model 2. SES = socioeconomic status; BMI = body mass index.

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed tests).

Table 1.Descriptive Statistics of Variables, Health and Retirement Study (2004–2014; $N = 9,310$).

Variable	Range	Total Sample Mean (SD) ^a	Male Sample Mean (SD)	Female Sample Mean (SD)
<i>Chronic inflammation</i>				
CRP, logged	−3.912–2.303	.513 (1.007)	.406 (.991)	.601 (1.011)
<i>Mortality</i>				
2008–2014 mortality	0, 1	.129	.141	.119
Months until death ^b	3–84	78.694 (15.147)	78.192 (15.795)	79.105 (14.584)
<i>Childhood exposures</i>				
SES disadvantage	0–2	1.287 (.838)	1.222 (.857)	1.340 (.819)
Risky parent behaviors	0–2	.877 (.652)	.890 (.638)	.867 (.663)
Chronic disease	0–2	.455 (.698)	.400 (.650)	.500 (.731)
Impairment	0–2	.228 (.487)	.281 (.537)	.184 (.437)
Risky adolescent behaviors	0, 1	.090	.129	.059
<i>Adult health characteristics</i>				
Pack-years smoked, logged	0–5.994	1.510 (1.658)	1.854 (1.714)	1.230 (1.555)
BMI	9.6–61.3	27.614 (5.339)	27.949 (4.583)	27.335 (5.858)
Exercise	1–5	2.164 (1.356)	2.383 (1.374)	1.985 (1.314)
<i>Adult SES</i>				
Education	0–17	13.130 (2.889)	13.452 (2.990)	12.867 (2.776)
Wealth, cube root	−130.950–315.755	60.587 (36.143)	63.082 (36.217)	58.544 (35.958)
<i>Covariates</i>				
1910 cohort	0, 1	.027	.020	.033
1920 cohort	0, 1	.130	.110	.146
1930 cohort	0, 1	.222	.215	.228
1940 cohort	0, 1	.401	.423	.383
1950 cohort	0, 1	.220	.232	.210
White	0, 1	.835	.846	.825
Black	0, 1	.075	.067	.081
Hispanic	0, 1	.068	.064	.071

Variable	Range	Total Sample Mean (SD) ^a	Male Sample Mean (SD)	Female Sample Mean (SD)
Other race	0, 1	.023	.023	.023
Married	0, 1	.700	.811	.609
Prescription medications	0, 1	.520	.491	.543
CRP measurement in 2006	0, 1	.490	.498	.483

Note: Descriptive statistics are weighted. Italicized numbers indicate significant differences between male ($n = 3,747$) and female ($n = 5,563$) samples ($p < .05$). CRP = C-reactive protein; SES = socioeconomic status; BMI = body mass index.

^aStandard deviation (SD) of dichotomous variables is omitted because it is a function of the mean.

^bAmong respondents who died between 2008 and 2014.

Table 2.
Regression of Chronic Inflammation on Independent Variables (Health and Retirement Study: 2004–2008).

Independent Variables	Model 1 <i>b</i> (SE) ^a	Model 2 <i>b</i> (SE)
<i>Childhood exposures</i>		
SES disadvantage	.065 ** (.020)	-.003 (.020)
Risky parent behaviors	.035 * (.018)	.014 (.018)
Chronic disease	-.016 (.016)	-.012 (.015)
Impairment	.035 (.026)	-.006 (.024)
Risky adolescent behaviors	.078 * (.040)	.025 (.035)
<i>Gender</i>		
Female	.185 *** (.022)	.228 *** (.021)
<i>Covariates</i>		
1910 cohort ^b	-.220 ** (.076)	.015 (.077)
1920 cohort ^b	-.102 * (.040)	.039 (.041)
1930 cohort ^b	-.072 (.044)	.005 (.040)
1940 cohort ^b	.037 (.037)	.073 * (.032)
Black ^c	.137 ** (.048)	-.012 (.045)
Hispanic ^c	.107 ** (.041)	-.042 (.045)
Other race ^c	-.156 (.110)	-.172 (.104)
Married	-.036 (.031)	.022 (.031)
Prescription medications	.225 *** (.025)	.079 *** (.022)
CRP measurement in 2006	-.097 *** (.026)	-.109 *** (.025)
<i>Adult health characteristics</i>		
Pack-years smoked		.051 *** (.007)
BMI		.047 *** (.003)
Exercise		-.025 * (.010)

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Independent Variables	Model 1 <i>b</i> (SE) ^a	Model 2 <i>b</i> (SE)
<i>Adult SES</i>		
Education		-.019 *** (.005)
Wealth		-.002 *** (.000)
<i>R</i> ²	.037	.104
AIC	161,398	433,110
<i>N</i>	9,310	9,310

Note: SES = socioeconomic status; BMI = body mass index; AIC = Akaike information criterion; SE = standard error.

^a Unstandardized coefficient (standard error).

^b Reference group: 1950s cohort.

^c Reference group: white.

* *p* .05,

** *p* < .01,

*** *p* < .001 (two-tailed tests).

Table 3.

Cox Proportional Hazards Regression Models for Mortality (Health and Retirement Study: 2004–2014).

Independent Variables	Model 1 HR (CI)	Model 2 HR (CI)
<i>Childhood exposures</i>		
SES disadvantage	1.166 ^{**} (1.054, 1.290)	1.097 (.995, 1.210)
Risky parent behaviors	.999 (.905, 1.103)	.951 (.862, 1.050)
Chronic disease	.982 (.905, 1.066)	.974 (.903, 1.052)
Impairment	1.048 (.816, 1.116)	.954 (.817, 1.114)
Risky adolescent behaviors	.998 (.767, 1.300)	.911 (.702, 1.184)
<i>Gender</i>		
Female	.617 ^{***} (.547, .695)	.629 ^{***} (.563, .704)
<i>Covariates</i>		
1910 cohort ^a	21.434 ^{***} (14.382, 31.976)	23.012 ^{***} (15.441, 34.295)
1920 cohort ^a	9.318 ^{***} (6.469, 13.423)	9.356 ^{***} (6.544, 13.343)
1930 cohort ^a	3.432 ^{***} (2.309, 5.099)	3.360 ^{***} (2.264, 4.983)
1940 cohort ^a	1.319 (.876, 1.984)	1.297 (.867, 1.941)
Black ^b	1.143 (.912, 1.433)	.949 (.739, 1.220)
Hispanic ^b	.913 (.730, 1.141)	.710 ^{**} (.555, .908)
Other race ^b	.664 (.352, 1.250)	.627 (.329, 1.196)
Married	.803 ^{***} (.710, .907)	.981 (.857, 1.123)
Prescription medications	1.208 ^{**} (1.065, 1.370)	1.163 [*] (1.031, 1.311)
CRP measurement in 2006	.996 (.858, 1.088)	1.004 (.899, 1.122)
<i>Adult health characteristics</i>		
Pack-years smoked		1.191 ^{***} (1.153, 1.231)
BMI		.965 ^{***} (.950, .979)
BMI ²		1.002 ^{***} (1.001, 1.004)
Exercise		.908 ^{**} (.856, .966)

Independent Variables	Model 1 HR (CI)	Model 2 HR (CI)
<i>Adult SES</i>		
Education		.969* (.942, .997)
Wealth		.993*** (.991, .996)
<i>Adult chronic inflammation</i>		
CRP		1.220*** (1.120, 1.328)
Log likelihood	-75,482	-272,552
AIC	151,463	545,887
N	9,310	9,310

Note: SES = socioeconomic status; BMI = body mass index; CRP = C-reactive protein; AIC = Akaike information criterion; HR = hazard ratio; CI = confidence interval.

^aReference group: 1950s cohort.

^bReference group: white.

* $p < .05$;

** $p < .01$;

*** $p < .001$ (two-tailed tests).