Racial and Ethnic Differences in Diurnal Cortisol Rhythms: Are They Consistent Over Time?

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Background: Prior research indicates that blacks and Hispanics/Latinos have flatter diurnal cortisol declines across the day, a profile associated with poorer health. The stability of racial and ethnic differences in cortisol levels over time is not well understood, and additional research is needed to establish racial and ethnic differences in psychosocial stress levels as related to changes in cortisol levels. **Methods:** With data from a community-based study of 152 adults (mean age = 58 years; 53% women; 34% black, 26% Hispanic/Latino), we examined the magnitude of racial and ethnic differences over a 5-year period. Salivary cortisol samples were obtained 3 times per day for 3 days in Years 1, 3, 4, and 5. Life events and chronic stress were assessed by questionnaires in which participants reported on whether they had experienced specific types of events or stress within the past year. Depressive symptoms scales (Center for Epidemiologic Studies of Depression Scale) were also administered annually. Daily cortisol slopes were calculated by subtracting wakeup cortisol from bedtime levels and dividing by hours awake. **Results:** Increases in psychosocial stress were associated with flatter cortisol slopes among blacks ($\beta = 0.010$) and Hispanics/Latinos ($\beta = 0.014$), although including cardiovascular disease risk factors attenuates associations in blacks ($\beta = 0.007$; $p = .125$). Higher income predicts a steepening of cortisol rhythms across the study ($\beta = -0.003$; $p = .019$). **Conclusions:** Racial and ethnic differences in diurnal cortisol rhythms are stable over time. However, the magnitude of changes in cortisol levels associated with chronic stress levels may vary by racial and ethnic subgroups.
Key words: cortisol, HPA axis, race/ethnicity, health disparities.

HPA axis = hypothalamic-pituitary-adrenal axis; **SES** = socioeconomic status; **CVD** = cardiovascular disease; **BMI** = body mass index.

INTRODUCTION

Racial and ethnic minorities in the United States are at greater risk for experiencing numerous adverse health conditions, and African Americans have lower life expectancies than do their white counterparts on average (1). Minorities, on average, report higher levels of psychosocial stress, have lower levels of socioeconomic status (SES), and are exposed to more psychosocial stressors of various types, relative to whites (2–6). Thus, social-environmental influences are increasingly proposed as important contributors to racial and ethnic health disparities (7–10).

One mechanism through which social-environmental influences are hypothesized to influence health disparities is via stress-related alterations in activity of the body's biological stress systems. For example, activity of the hypothalamic-pituitary-adrenocortical (HPA) axis, one of the body's key stress systems, is strongly influenced by psychosocial stress, and alterations of the HPA axis are known to predict a variety of health outcomes and physiological processes relevant to health (11–15). As such, increased psychosocial stress among minorities and the consequent altered regulation of the body's stress systems represent important potential mechanisms through which social-environmental factors may contribute to health disparities.

Racial and Ethnic Differences in Stress Physiology

Much of the early research on racial and ethnic differences in stress biology focused on the sympathetic-adrenal-medullary system, the body's other major endocrine stress system. Racial and ethnic differences have been observed in high blood pressure, cardiovascular reactivity, and respiratory functioning (16–18). More recent research has begun to investigate racial and ethnic differences in the HPA axis (19–21), with a particular focus on differences in the diurnal rhythm of cortisol across the day. Individuals typically experience cortisol increases in response to negative emotion and stress in laboratory and naturalistic environments (22,23). In addition, the HPA system also follows a strong circadian rhythm. Cortisol levels are typically high upon waking, peak 30 to 40 minutes after awakening, then gradually decline throughout the remainder of the day, reaching a nadir around midnight (24,25).

Although several factors influence individual differences in the rates of cortisol decline across the day, flatter diurnal rhythms (attenuated declines across the day) are found among individuals with greater difficulties in interpersonal relationships, material hardships, poorer marital satisfaction, and exposure to stressful life events and trauma (26–32). Moreover, although periodic activations of the HPA system help to cope with acute, time-limited stressors, frequent or chronic activation of this system may adversely influence cognitive, metabolic, and immune functioning (11–13,15,33). Flatter cortisol rhythms have been associated with earlier mortality among breast cancer patients, higher evening blood pressure, coronary calcification, and predisease risk factors for cardiovascular disease (CVD) and Type 2 diabetes (34–37), suggesting that flatter cortisol rhythms may serve as one possible mechanism through which social-environmental stressors may operate to influence health disparities.

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Prior studies have found that African American adults (ages, 33–45 and 45–84 years) and African American and Hispanic/Latino adolescents (age, 16–18 years) have flatter diurnal cortisol slopes from wakeup to bedtime than their same-age white counterparts, with differences attributable to both lower wakeup (19–21) and higher bedtime cortisol levels (19,20), after adjustment for a broad range of psychosocial factors, including, chronic and episodic stress levels, SES, and other psychosocial influences.

Limitations of Past Studies and Study Objectives

Although past research has identified significant racial and ethnic differences in cortisol profiles, prior studies have analyzed these associations cross sectionally, making it impossible to determine whether racial and ethnic differences are consistent over time, or whether changes in psychosocial stress levels predict changes in cortisol rhythms. Answers to these questions are important for understanding the origins and meaning of racial and ethnic differences in cortisol diurnal rhythms. The current study aims to address these questions.

First, longitudinal data are analyzed to assess the temporal stability of racial differences over a 5-year period. Second, the extent to which racial differences are explained by average levels of psychosocial stress across the 5 years is investigated. Third, linear changes in cortisol slopes over time are examined among the study population as a whole and among specific subgroups. Next, associations between yearly changes in psychosocial stress and yearly changes in cortisol are analyzed, again in the whole sample and in subgroups. Finally, the robustness of these findings to adjustment for CVD risk factors is tested by entering body mass index (BMI) and diabetes at baseline into the model at Level 3. It was hypothesized that there would be moderate variability in cortisol rhythms over time across the four waves of the study, but that the racial gaps would remain fairly stable over time. In addition, yearly increases in psychosocial stress are expected to be associated with yearly flattening of cortisol slopes.

METHODS

The data for these analyses come from the Chicago Health, Aging, and Social Relations Study, a longitudinal study begun in 2002 that was designed to assess associations among social relationships, health, and aging in adults older than 50 years. The data on psychosocial stressors and social relationships were collected annually for 5 years, but salivary cortisol was collected during Years 1, 3, 4, and 5 only.

Participants were drawn from a community-based sample of adults born between 1935 and 1952, living in Cook County, IL. A multistage probability sampling design was used to identify households most likely to include a person likely to be eligible and to include equal numbers of white, non-Hispanic African American, and Hispanic/Latino American adults and equal numbers of men and women in each racial-ethnic group. Comparisons with national statistics indicate that this sample represents the urban population of this age group quite well (38).

Analytical Sample

The first wave of data was collected from 229 individuals. Participants included in these analyses were required to have valid cortisol data (i.e., a wakeup and bedtime sample and information on the timing of those samples) for at least 1 day (of the 3 days requested) per year, after exclusions for corticosteroid use and highly unusual sleep patterns, for at least 3 years of the study. For the 4 years of the study for which cortisol data were collected, the number of participants providing valid cortisol, sleep, and demographic data, in conjunction with complete information on psychosocial stress measures, for at least three of the four waves, ranged from 125 (at Wave 1) to 146 (Wave 3), 147 (Wave 4), and 157 (Wave 5).

Of the 229 participants who completed some portion of the study for at least 1 of the 4 years during which cortisol data were collected, 36 person-years of data (from 16 participants) were eliminated due to corticosteroid medication use and 10 person-years of data (from three people) were eliminated for having highly unusual sleep patterns (wakeup times before 3 AM or after 3 PM, or bedtimes before 4 PM or after 4 AM). An additional 58 people failed to provide valid cortisol data and/or information on psychosocial stressors. In total, 152 participants provided valid cortisol data for at least 3 years of the study, and 99 participants (61 female) provided valid cortisol data that constituted 514 person-years and 1272 person-days of data across the four waves of the study.

The study participants consisted of an ethnically diverse sample in which African Americans, whites, and Hispanics/Latinos constituted 34%, 41%, and 26% of the final sample, respectively, and 47% were male. Participants ranged in age from 50 to 68 years (mean [standard deviation] = 58 [4.5] years) at Wave 1. The 152 participants included in the final cortisol analyses did not differ from the larger sample of 229 who completed the interview and questionnaire portions of the study in terms of age, sex, household income, or psychosocial stress levels. The proportion of blacks and Hispanics/Latinos in the final analyses of the longitudinal cortisol study was slightly lower than that in the portion of the sample who did not complete the cortisol assessment at Wave 1. The cortisol measures available for those who completed less than 3 years of cortisol data collection did not differ significantly from those in the analytical sample.

Measures

The measures include the following: a questionnaire on eight domains of chronic stress (51 items) (39), Life Events Questionnaire (67 items) (40), Center for Epidemiologic Studies of Depression Scale (CES-D) (41), demographic questionnaires, and a health questionnaire and medications list developed by study investigators. The scores for all scales were standardized within each year before being analyzed.

Demographic and Health Questionnaires

On the demographic questionnaires, participants reported on their race/ethnicity, age, sex, and household income. Racial and ethnic identification choices included black/African American, white/Caucasian, and Hispanic/Latino. The original 12-category income variable was converted into dollar values representing the middle income level within each category, and then logarithmically transformed for each year. Because income varied little across the study period, each participant's average income across the study was analyzed as a person-level variable, and average income was logarithmically transformed and included in all models.

Typical levels of daily nicotine use and waketimes were included as covariates in all analyses (42,43). Only use of corticosteroid medications and extreme sleep patterns were considered grounds for exclusion.

Chronic Stress

Participants were asked to report on whether, over the past year, they had experienced stress due to a variety of objective circumstances in eight different domains, including general, money, work related, romantic, family, social relationships, residential, and caregiving (for others) stress, each of which was considered as a separate stressor in models (39). The general chronic stress domain scores ranged from 0 to 3, with a reliability of 0.78.

Life Event Questionnaire

The Life Event Questionnaire (LEQ) is a 51-item checklist based on the Revised Social Readjustment Rating Scale (40), modified slightly so as to provide more age-appropriate response choices for the advanced age of the current sample. Participants reported whether and how often an event had occurred during the last year. The final life events variable represents the total number of event occurrences from the Life Event Questionnaire, counting each occurrence as a separate event (range, 0–20).

Center for Epidemiologic Studies of Depression Scale

As a measure of depressive symptoms, all participants completed the CES-D during the interview protocol. This instrument is frequently utilized in population-based studies of nonclinical samples and has strong internal consistency (α = .90) (41). Because levels of depression have been known to influence basal cortisol regulation, CES-D scores were investigated as potential confounders in these analyses. Cronbach α values range from .88 to .89 across the 5-year study period (mean = .89). Item responses were recorded using a 4-point Likert scale ranging from 0 (*rarely or none of the time*) to 3 (*most or all of the time*).

Cortisol Sampling/Assay Procedure

Participants were asked to provide three saliva samples per day for 3 days: upon awakening, 30 minutes postawakening, and at bedtime. They were instructed not to eat, smoke, brush their teeth, or drink beverages other than water for 30 minutes before providing these samples. Absorbent cotton rolls (Salivette: SARSTEDT, Nümbrecht, Germany) were used to collect saliva.

Samples were returned to the university laboratory via courier (44) and were refrigerated at −80°C until being shipped to the Laboratory for Stress Monitoring at the University of Göttingen, Germany, where they were assayed (45). Intra-assay coefficients of variation ranged from 2.8% to 8.4% (mean = 4.6%), and the interassay coefficient of variation was 3.4%. All cortisol values, which were originally measured in nmol/L, were logarithmically transformed in accordance with standard procedure to correct for a positive skew. The rate of cortisol decline for each day was calculated by subtracting wakeup cortisol levels from bedtime levels and dividing by hours awake, based on self-reported wakeup and bedtimes. It should be noted that because there were only two data points collected per day, with the exception of the excluded cortisol awakening response sample, the dependent variable does not represent a daily "slope," but rather the average hourly rate of decline across the waking day. Regardless, for the sake of efficiency, it is heretofore referred to as the slope. Thus, the slope in this case represents the average hourly cortisol decline.

Analytical Plan

One-way analyses of variance were first conducted to investigate whether there are racial and ethnic differences in levels of psychosocial stressors and depressive symptoms. Hierarchical linear modeling techniques were then used to simultaneously analyze within- and between-person factors that predict daily cortisol rhythms as the following research questions were investigated: a) the existence and stability of racial and ethnic differences in cortisol rhythms, b) the extent to which differences are attributable to average levels of psychosocial stress, c) linear changes in cortisol rhythms across the 5 years of the study, and d) changes in cortisol slopes in relation to changes in psychosocial stress levels. The final two questions are examined among the population as a whole, as well as among specific racial/ethnic, sex, and socioeconomic subgroups to determine whether certain subgroups are more vulnerable to the biological impact of psychosocial stress. All decisions regarding how the series of models would be built and which covariates and potential mediators and moderators would be entered at which level and which point in the sequence were made *apriori* based on the questions of primary interest and understanding of prior research (i.e., waketime and nicotine were always included as key behavioral covariates) (43,46). Race, age, and sex were included as key variables of interest in all models (Model 1). Next, linear changes in slopes across the 5 years were examined in relation to these key baseline sociodemographic covariates; individual stressors were included from the third model onward, and because of restrictions that result from the degrees of freedom available, only those stressors that were statistically significant were retained such that the number of significant predictors did not exceed the degrees of freedom (which it did not). Then, interactions between sociodemographic factors and stressors were tested and retained in the final model. Finally, the robustness of these associations to adjustment for CVD risk factors was tested, focusing on risks that have been found to be associated with cortisol activity (36). Ultimately, decisions regarding the specific variables and order of models were based on researchers' interest in the specific question regarding the stability of race/ethnicity and SES and cortisol activity, as well as the potential modifying role of psychosocial stress.

Multilevel Analyses

In the first set of analyses, mean-level differences in cortisol slopes across the waking day were analyzed, with key health and demographic variables, including race/ethnicity, entered in the model. The data consist of three levels: the day-level cortisol slopes, year-level psychosocial stress influences, and person-level demographic factors that remained constant across the period of the study. The day-level cortisol slopes were calculated by subtracting the logarithmically transformed bedtime cortisol levels from the wakeup cortisol levels and dividing by hours awake for each day. The day-level slope then serves as the dependent variable, and as the day-level slopes were not averaged, each person could have a up to 3 days/rows of data per year for a maximum of 12 days/rows of data across the 4 waves of the study, with a minimum of 1 day per year and a minimum of 3 of the 4 years. As such, each person was required to have between 3 and 12 days of data in total. Control variables included day-level time of waking and nicotine use. Multilevel modeling techniques are used to address the nested nature of the data (days within years within people), as they permit adjustment for the fact that within-person error terms are correlated over time (47). Analyses were conducted using HLM 7 (47). All models include random intercepts. Models 3 through 5 also include a random slope for psychosocial stress variables. Similar results were found analyzing data with the more conventional compound symmetry covariance structure, but this model is in accordance with theoretical model regarding these associations developed a priori before conducting analyses.

Model 1. Average Associations Between Race and Cortisol

Race/ethnicity was entered in the model at Level 3 (along with sex and age at baseline, and nicotine use and wakeup time for each day at Level 1) to determine whether significant racial and ethnic differences in cortisol rhythms were present on average across the 5 years of the study, controlling for age and sex and day-specific wakeup time and nicotine use. Whites served as the reference group. For each model, let t denote day of data collection; i, year of data collection; and j, person (the highest level at which data were measured). The model is represented in the following equation:

$$\text{Level 1}: \ \text{Cortisol slope}\,(\text{Day})_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 1.1$$

$$\text{Level 2}: \ \begin{aligned} \pi_{0ij} &= \beta_{00j} + \rho_{0ij} \\ \pi_{1ij} &= \beta_{10j} \\ \pi_{2ij} &= \beta_{20j} \end{aligned} \quad 1.2$$

$$\text{Level 3}: \ \beta_{00j} = \gamma_{000} + \gamma_{001j}\text{Black}_j + \gamma_{002j}\text{Hispanic/Latino}_j + \gamma_{003j}\text{AgeW1}_j + \gamma_{004j}\text{Male}_j + \upsilon_{00j} \quad 1.3$$

$$\begin{aligned} \beta_{10j} &= \gamma_{100} \\ \beta_{20j} &= \gamma_{200} \end{aligned}$$

The coefficients for black and Hispanic/Latino represent average group-level differences in cortisol rhythms between these groups and whites across the 5 years, controlling for age and sex, before adjustment for year-level psychosocial characteristics.

Model 2: Do Average Psychosocial Stress Levels Mediate Associations Between Race and Cortisol?

Next, average levels of psychosocial stress were examined to explain average differences in cortisol rhythms by analyzing average levels of psychosocial stress from across the study period as potential mediators of racial and ethnic differences in cortisol (2.3).

$$\text{Level 1}: \ \text{Cortisol slope (Day)}_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 2.1$$

$$\text{Level 2}: \ \begin{aligned} \pi_{0ij} &= \beta_{00j} + \rho_{0ij} \\ \pi_{1ij} &= \beta_{10j} \\ \pi_{2ij} &= \beta_{20j} \end{aligned} \quad 2.2$$

$$\begin{aligned} \text{Level 3}: \ \beta_{00j} = {} & \gamma_{000} + \gamma_{001j}\text{Black}_j + \gamma_{002j}\text{Hispanic/Latino}_j \\ & + \gamma_{003j}\text{AgeW1}_j + \gamma_{004j}\text{Male}_j \\ & + \gamma_{005j}\text{Average Psychosocial Stress Levels}_j \\ & + \upsilon_{00j} \end{aligned} \quad 2.3$$

$$\begin{aligned} \beta_{10j} &= \gamma_{100} \\ \beta_{20j} &= \gamma_{200} \end{aligned}$$

Model 3: General Trends in Cortisol Rhythms Over a 5-Year Period

Next, linear trends in cortisol rhythms across the 5 years of the study were investigated. A year growth term (baseline = year 0) was added at Level 2 (3.2). Race/ethnicity, sex, age, and SES were added as potential modifiers of the growth parameter at Level 3, to determine whether there were linear changes in cortisol slopes across the study among any particular subgroups, represented by the following equation:

$$\text{Level 1}: \ \text{Cortisol slope (Day)}_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 3.1$$

$$\text{Level 2}: \ \begin{aligned} \pi_{0ij} &= \beta_{00j} + \beta_{01}\text{Year of Study}_{0ij} + \rho_{0ij} \\ \pi_{1ij} &= \beta_{10j} \\ \pi_{2ij} &= \beta_{20j} \end{aligned} \quad 3.2$$

$$\begin{aligned} \text{Level 3}: \ \beta_{00j} = {} & \gamma_{000} + \gamma_{001}\text{Black}_j + \gamma_{002}\text{Hispanic/Latino}_j \\ & + \gamma_{003}\text{AgeW1}_j + \gamma_{004}\text{Male}_j + \gamma_{005}\text{Income}_j \\ & + \upsilon_{00j} \end{aligned} \quad 3.3a$$

$$\beta_{01j} = \gamma_{001} + \gamma_{01}\text{Black}_j + \gamma_{02}\text{Hispanic/Latino}_j + \gamma_{03}\text{AgeW1}_j + \gamma_{05}\text{Income}_j + \upsilon_{01j} \quad 3.3b$$

$$\begin{aligned} \beta_{10j} &= \gamma_{100} \\ \beta_{20j} &= \gamma_{200} \end{aligned}$$

Model 4: Yearly Changes in Psychosocial Stress and Changes in Cortisol Rhythms: Main Effects

Yearly changes in levels of psychosocial stress and depressive symptoms were analyzed in relation to yearly changes in cortisol by entering psychosocial stress variables from yearly interviews into the model at Level 2. Yearly data on general chronic stress, negative life events, and depressive symptoms were examined as potential contributors to year-to-year changes in cortisol rhythms. Each psychosocial stress variable was first analyzed individually, and those found to be significantly associated with yearly changes in cortisol, independently of the other psychosocial variables, were retained in the final model.

$$\text{Level 1}: \ \text{Cortisol slope (Day)}_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 4.1$$

$$\text{Level 2}: \ \begin{aligned} \pi_{0ij} &= \beta_{00j} + \beta_{01}\text{Year of Study}_{0ij} + \beta_{02}\text{Psychosocial Stressor}_{0ij} + \rho_{0ij} \\ \pi_{10j} &= \beta_{10j} \\ \pi_{20j} &= \beta_{20j} \end{aligned} \quad 4.2$$

$$\begin{aligned} \text{Level 3}: \ \beta_{00j} = {} & \gamma_{000} + \gamma_{001}\text{Black}_j + \gamma_{002}\text{Hispanic/Latino}_j \\ & + \gamma_{003}\text{AgeW1}_j + \gamma_{004}\text{Male}_j + \gamma_{005}\text{Income}_j \\ & + \upsilon_{00j} \end{aligned} \quad 4.3$$

$$\begin{aligned} \beta_{01j} &= \gamma_{010} \\ \beta_{02j} &= \gamma_{020} \\ \beta_{10j} &= \gamma_{100} \\ \beta_{20j} &= \gamma_{200} \end{aligned}$$

Model 5: Do Yearly Changes in Psychosocial Stress Predict Yearly Changes in Cortisol Rhythms in Certain Subgroups?

Demographic variables were added at Level 3 as potential moderators of year-level psychosocial stressors significantly associated with cortisol, to test whether associations between yearly changes in psychosocial stress and cortisol rhythms differed according to race/ethnicity, sex, age, or SES. Average income was also included both as a potential independent predictor of cortisol rhythms, as well as a potential moderator of associations between race/ethnicity and cortisol.

$$\text{Level 1}: \ \text{Cortisol slope (Day)}_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 5.1$$

$$\text{Level 2}: \ \begin{aligned} \pi_{0ij} &= \beta_{00j} + \beta_{01}\text{Year of Study}_{0ij} + \beta_{02}\text{Psychosocial Stressor}_{0ij} + \rho_{0ij} \\ \pi_{1ij} &= \beta_{10j} \\ \pi_{2ij} &= \beta_{20j} \end{aligned} \quad 5.2$$

$$\begin{aligned} \text{Level 3}: \ \beta_{00j} = {} & \gamma_{000} + \gamma_{001}\text{Black}_j + \gamma_{002}\text{Hispanic/Latino}_j \\ & + \gamma_{003}\text{AgeW1}_j + \gamma_{004}\text{Male}_j + \gamma_{005}\text{Income}_j \\ & + \upsilon_{00j} \end{aligned} \quad 5.3a$$

$$\begin{aligned} \beta_{10j} &= \gamma_{100} \\ \beta_{20j} &= \gamma_{200} \end{aligned}$$

$$\beta_{01j} = \gamma_{010} + \gamma_{011}\text{Black}_j + \gamma_{012}\text{Hispanic/Latino}_j + \gamma_{013}\text{AgeW1}_j + \gamma_{014}\text{Male}_j + \gamma_{015}\text{Income}_j + \upsilon_{01j} \quad 5.3b$$

(5.3c) $\beta_{02j} = \gamma_{020} + \gamma_{021}\text{Black}_j + \gamma_{022}\text{Hispanic/Latino}_j + \gamma_{023}\text{AgeW1}_j + \gamma_{024}\text{Male}_j + \gamma_{025}\text{Income}_j + \upsilon_{02j}$

Model 6: Are Findings Robust to Adjustment for CVD Risk Factors?

Information on CVD risk factors was added at Level 3 to test whether associations between race/ethnicity, SES, psychosocial stress, and cortisol rhythms were independent predictor of these risk factors. However, because of participants' advanced ages, as well as the fact that these CVD risk factors

could either serve as the cause or reflect the consequences of cortisol activity, thereby potentially serving as potential mediators as well as potential confounds of any observed associations between race/ethnicity and cortisol, results with and without CVD risk covariates were included.

Finally, as a robustness check, CVD risk factors were entered into the model at Level 3. BMI and diabetes status at baseline were included in the model to assess the extent to which associations of race/ethnicity with cortisol were independent of CVD risk factors.

$$\text{Level 1}: \ \text{Cortisol slope}\,(\text{Day})_{tij} = \pi_{0ij} + \pi_{1ij}\text{Waketime}_{tij} + \pi_{2ij}\text{Nicotine}_{tij} + \epsilon_{tij} \quad 6.1$$

$$\text{Level 2}: \ \pi_{0ij} = \beta_{00j} + \beta_{01}\text{Year of Study}_{0ij} + \beta_{02}\text{Psychosocial Stressor}_{0ij} + \rho_{0ij} \quad 6.2$$

$$\pi_{1ij} = \beta_{10j}$$
$$\pi_{2ij} = \beta_{20j}$$

(6.3a) Level 3: $\beta_{00j} = \gamma_{000} + \gamma_{01j}\text{Black}_j + \gamma_{02j}\text{Hispanic/Latino}_j + \gamma_{03j}\text{AgeW1}_j + \gamma_{04j}\text{Male}_j + \gamma_{05j}\text{Income}_j + \gamma_{06j}\text{BMI}_j + \gamma_{05j}\text{Diabetes}_j + \upsilon_{00j}$.

$$\beta_{10j} = \gamma_{100}$$
$$\beta_{20j} = \gamma_{200}$$

$$\beta_{01j} = \gamma_{010} + \gamma_{011}\text{Black}_j + \gamma_{012}\text{Hispanic/Latino}_j + \gamma_{013}\text{AgeW1}_j + \gamma_{014}\text{Male}_j + \gamma_{015}\text{Income}_j + \gamma_{016}\text{BMI}_j + \gamma_{015}\text{Diabetes}_j + \upsilon_{01j}. \quad 6.3b$$

$$\beta_{02j} = \gamma_{020} + \gamma_{021}\text{Black}_j + \gamma_{022}\text{Hispanic/Latino}_j + \gamma_{023}\text{AgeW1}_j + \gamma_{024}\text{Male}_j + \gamma_{025}\text{Income}_j + \gamma_{026}\text{BMI}_j + \gamma_{025}\text{Diabetes}_j + \upsilon_{02j}. \quad 6.3c$$

After completing analyses of all six models in the series, the functional forms of all key predictors (psychosocial stress measures) were examined in relation to cortisol and believe that the functional forms used are appropriate. The distributions of raw residuals were all normal and homoskedastic.

This study was conducted with the approval of the Institutional Review Board of the University of Chicago. All participants provided informed consent before participating in the study.

RESULTS

Racial and Ethnic Differences in Psychosocial Stress Levels

One-way analyses of variance of psychosocial characteristics, followed with Tukey HSD post hoc analyses, revealed that whites had significantly lower levels of general chronic stress ($F(2,153) = 6.68$, $p < .003$), relative to both blacks and Hispanics/Latinos in this sample (Tukey HSD post hoc tests: $p = .003$ and $p = .005$, respectively). Whites also had significantly higher levels of income than did both minority groups ($F(2,153) = 43.3$, $p = .021$) (Tukey HSD post hoc tests: both p values = .02) and had lower levels of depressive symptoms, as determined by the CES-D ($F(2,153) = 29.48$, $p = .011$) than did blacks ($p = .02$) and Hispanics/Latinos ($p = .007$). Finally, whites also had significantly fewer negative life events ($F(2,153) = 101.2$, $p = .092$) than did blacks (Tukey HSD: $p = .032$), but not Hispanics/Latinos ($p = .21$). Blacks and Hispanics/Latinos did not differ significantly from one another with respect to any of these variables, and the three racial and ethnic groups did not differ significantly from one another

TABLE 1. Demographic and Health Characteristics of the Analytical Sample Stratified by Race and Ethnicity: CHASRS

	Total (n = 152)	White (n = 62)	Black (n = 51)	Hispanic/Latino (n = 39)
Demographics				
Male, %	47%	48%	45%	49%
Age at Wave 1, y	57.5 (4.5)	58.2 (4.1)	58.2 (4.9)	55.67 (3.9)
Household income, $	68,111 (58,057)	80,020 (57, 635)	62, 478 (51.659)	54,994 (33,104)
Behavioral covariates				
Wake-up time	6:40 AM (1 h 34 min)	6:36 AM (1 h 00 min)	6:40 AM (1 h 13 min)	7:01 AM (1 h 23 min)
Bedtime	11:04 PM (1 h 06 min)	10:59 PM (1 h 16 min)	11:04 PM (1 h 45 min)	11:13 (1 h 30 min)
Nicotine (packs/d)	0.18 (0.64)	0.13 (0.43)	0.20 (0.55)	0.26 (0.67)
Psychosocial stressors				
General chronic stress	1.31 (0.99)	1.05 (0.66)	1.47 (0.78)	1.48 (0.81)
No. stress domains	5.56 (1.81)	5.17 (1.48)	5.88 (1.41)	5.67 (1.69)
Life events	3.95 (3.14)	3.41 (2.25)	4.43 (2.98)	4.06 (2.08)
CES-D	9.05 (8.26)	7.00 (5.18)	10.33 (6.73)	11.03 (10.22)
CVD risk factors				
Diabetes, % (n)	12.5 (19)	4.8 (3)	15.7 (8)	20.5 (8)
BMI, kg/m^2	31.56 (6.62)	30.6 (6.02)	33.05 (7.65)	31.16 (5.87)
Cortisol				
Wake-up level[a]	15.79 (6.87)	17.8 (7.37)	14.60 (7.02)	14.27 (4.94)
Bedtime level[a]	5.27 (5.34)	5.20 (5.54)	6.65 (6.41)	3.69 (2.31)
Slope (% hourly decline)[b]	−0.09 (0.05)	−0.10 (0.04)	−0.07 (0.03)	−0.10 (0.03)

CHASRS = Chicago Health, Aging, and Social Relations Study; CES-D = Center for Epidemiologic Studies of Depression Scale; CVD = cardiovascular disease; BMI = body mass index.

Values are presented as mean (standard deviation), unless otherwise indicated.

[a] Cortisol values indicated are raw scores in nmol/L; those used in the regression analyses were natural logarithmically transformed.

[b] Cortisol slopes indicate the percent decline per hour across the waking day [Day-Level Slope = (Bedtime Cortisol Levels − Wake-up Cortisol Levels)/Hours Awake].

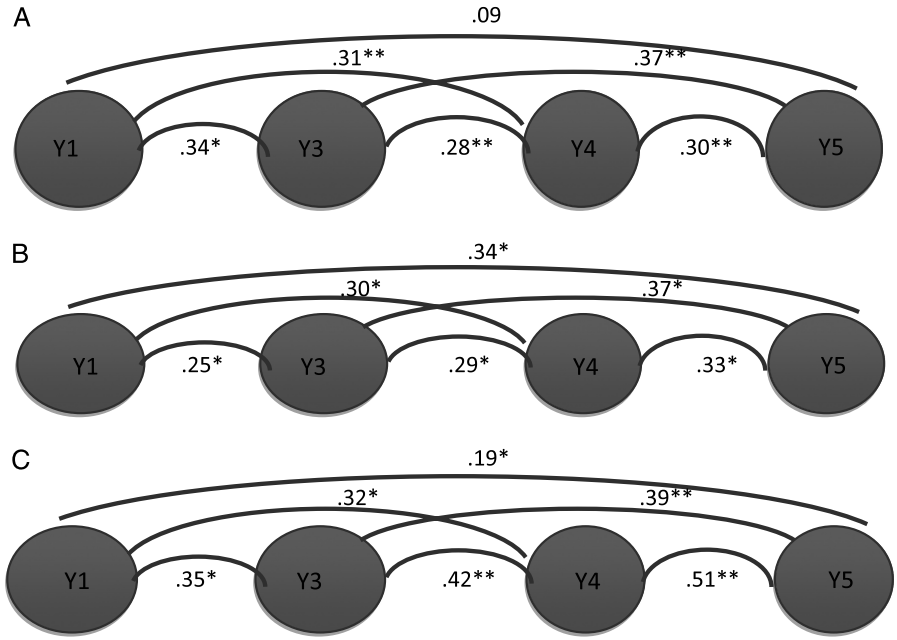

Figure 1. Correlations between cortisol slopes and wakeup and bedtime levels over time. A, Diurnal cortisol rhythms across the waking day. B, Wakeup cortisol levels. C, Bedtime cortisol levels.

on specific subdomains of chronic stress (Tukey HSD: all p values > .10). Specific information regarding the levels of psychosocial stress and covariates, stratified by race/ethnicity, is presented in Table 1.

Stability in Cortisol and Psychosocial Stress Over Time

There was moderate stability in cortisol slopes across years ranging from $r = 0.09$ ($p = .15$) to $r = 0.37$ ($p < .001$; average $r = 0.29$), as well as wakeup ($r = 0.32$ to $r = 0.36$, all p values < .001) and bedtime cortisol levels ($r = 0.20$, $p = .041$-.53 and $p < .001$) for periods ranging from 1 to 4 years (Fig. 1).

Among the entire study population, there were moderate to high levels of stability across the various types of stressors. Levels of depressive symptoms ($r = 0.61$-0.73, $p < .001$; average $r = .69$, $p < .001$) were fairly stable across the 5 years. The stability in number of negative life events ranged from $r = 0.34$ to 0.65 ($p < .001$), with an average of $r = 0.51$ ($p < .001$) across years. Correlations for general chronic stress across the years ranged from 0.36 to 0.56, ($p < .001$; average $r = 0.47$, $p < .001$). Household income was highly correlated across the four waves of the study ($r = 0.76$-0.89, $p < .001$) and was therefore averaged across the years and included as a person-level variable at Level 3.

Racial and Ethnic Differences in Cortisol Rhythms

Model 1

In the first model, average racial and ethnic differences in cortisol slopes across the study period were investigated. On average, African Americans had significantly flatter salivary diurnal cortisol rhythms ($\beta = 0.03$, $p < .001$), relative to their white counterparts, across the four waves of the study. Controlling for other demographic characteristics and health behaviors, they experienced less of a decline in cortisol across the day (Fig. 2). Hispanics/Latinos did not differ significantly from whites ($\beta = -0.001$, $p > .10$). In addition, participants who woke up later experienced slightly steeper declines in cortisol levels across the waking day ($\beta = -0.007$, $p < .001$), relative to those who woke up earlier. There were no significant differences in cortisol rhythms according to age or sex, before controlling for levels of psychosocial stress.

Model 2

Year-level psychosocial stress was aggregated to the person-level and entered them into the model at Level 3, and they failed to alter the significance of race/ethnicity-cortisol associations (not shown). African Americans continued to experience declines in cortisol levels that were 2.5% lower per hour (i.e., their slopes are 2.5% flatter), relative to their same-age white counterparts, after controlling for average psychosocial stress levels, comparable to the unadjusted model.

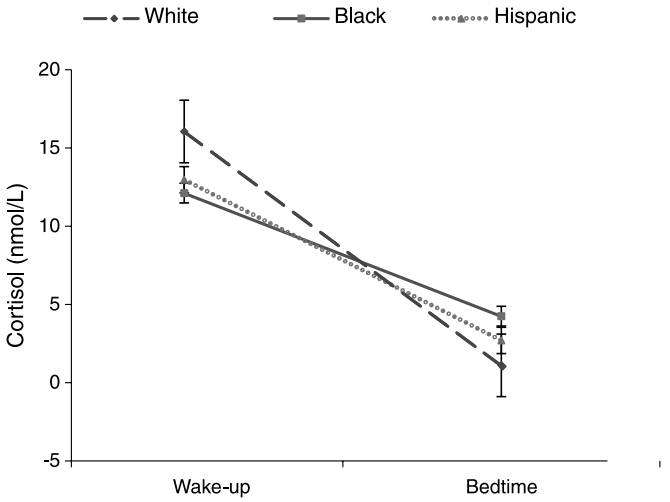

Figure 2. Average wake-up and bedtime cortisol levels by race.

Model 3

Controlling for health and demographic factors, there were no significant linear changes in cortisol rhythms across the study period among the sample as a whole ($\beta = 0.001$, $p > .10$; not shown). There were no significant linear trends in yearly changes in cortisol rhythms according to race or sex, but there was a significant relative steepening of the rhythm over the years among those of higher income, relative to their lower income peers ($\beta = -0.004$, $p = .020$).

Model 4

Each of the psychosocial stress variables was analyzed individually to identify whether any of them predicted changes in cortisol rhythms. The main effect for general chronic stress was not significant, indicating that changes in chronic stress levels were not significantly related to changes in cortisol rhythms among white females ($\beta = 0.001$, $p > .10$).

Model 5

Next, year-level psychosocial stressors that were significantly associated with cortisol rhythms were analyzed again with demographic variables added as potential moderators at Level 3, to test whether associations between yearly changes in psychosocial stress and cortisol rhythms differed according to demographic characteristics (Table 2). Yearly increases in chronic stress levels predicted flattening of the diurnal rhythm from 1 year to the next among blacks ($\beta = 0.010$, $p = .046$), Hispanics/Latinos ($\beta = 0.014$, $p = .004$), and males ($\beta = 0.009$, $p = .033$). In addition, higher average income continued to predict a relative steepening of the diurnal rhythm across the study period ($\beta = -0.004$, $p = .019$), independently of other psychosocial influences.

Finally, CVD risk factors (BMI and diabetes status) at baseline were entered as controls into the model at Level 3 to determine whether findings were robust to these potential confounds. Results for all models were similar, and none of the coefficients changed substantially (not shown). The only significant difference was that the interaction between black and general chronic stress predicting flatter cortisol slopes was attenuated from $\beta = 0.010$ to $\beta = 0.007$ and is no longer statistically significant ($p = .15$). Yearly increases in chronic stress levels still predicted flattening of the diurnal rhythm from 1 year to the next among Hispanics/Latinos ($\beta = 0.012$, $p = .010$) and males ($\beta = 0.009$, $p = .027$), after adjustment for CVD risk factors. Diabetes ($\beta = 0.016$, $p < .05$) and higher BMI ($\beta = 0.018$, $p = .016$) were also associated with cortisol slopes.

DISCUSSION

This study is the first to examine the stability of racial and ethnic differences in diurnal cortisol rhythms longitudinally. These analyses investigate whether racial and ethnic differences in HPA axis parameters are modified by changes in psychosocial stress levels over a 5-year period. Although there was significant variability in cortisol rhythms from year-to-year across the entire sample, the magnitude of the racial and ethnic differences remained consistent across the study period. Replicating prior cross-sectional research, average levels of psychosocial stress across the study period did not explain racial and ethnic differences in cortisol slopes.

Although average psychosocial stress levels did not explain racial and ethnic differences across the study period, within-person yearly changes in general chronic stress predicted significant changes in cortisol rhythms among blacks, Hispanics/Latinos, and males, indicating that these groups may be particularly vulnerable to increases in chronic stress. These findings were robust to adjustment for additional cardiovascular risk factors (BMI and diabetes), which serve as potential confounds and/or mediators of this association for Hispanics/Latinos and males. Associations between changes in chronic stress and cortisol rhythms were found despite the fact that minorities in this study experienced less variability in chronic stress levels from year-to-year and were more likely to experience consistently high levels of chronic stress. Because minorities reported experiencing higher levels of general chronic stress throughout the study, that they were more affected to year-to-year changes in stress may be due to the higher severity of the stressors experienced by minority groups, rather than a true racial and ethnic difference in stress vulnerability. Moreover, given the advanced ages of our participants, experiences before the study may have already influenced racial and ethnic differences by Wave 1, and the robust differences observed during the study period may be at least partially attributable to a lifetime of higher chronic stress levels among minorities.

Finally, although income differences did not explain racial and ethnic differences in cortisol, higher income, regardless of race/ethnicity, predicted a relative steepening of cortisol slopes across the 5-year period. This was the only factor that significantly predicted systematic linear trends in cortisol slopes with time and age across the study period. Lower SES was also associated with marginal increases in bedtime cortisol levels across the 5 years. This may have implications for socioeconomic disparities in health. In particular, income differences in basal cortisol activity may play a role in the increased likelihood of lower income adults developing adverse health outcomes at younger ages than their high SES counterparts.

This study is the first to focus on analyzing potential psychosocial explanations for racial and ethnic changes in cortisol rhythms in adults. The results replicate prior research indicating that significant racial and ethnic differences in cortisol diurnal rhythms exist among cohorts of various ages (19–21), and demonstrate that significant racial and ethnic differences in basal cortisol patterns extend into later adulthood. Similar to their younger counterparts, African American adults older than 50 years have flatter diurnal slopes across the waking day than their same-age white peers. In contrast with prior research on adolescents (19), the diurnal rhythms of Hispanics/Latinos in this sample did not differ significantly from those of whites.

Although slopes of males did not differ from those of females on average, sex modified associations between yearly increases in chronic stress and flatter cortisol rhythms. Similarly, African Americans and Hispanics/Latinos who experienced yearly increases in chronic stress also had flatter cortisol rhythms, although the black–chronic stress interaction was

TABLE 2. Psychosocial Predictors of Yearly Changes in Cortisol Rhythms

Variable	Coefficient	SE	*t* Statistic	*p*
Level 1 intercept, $\pi 0$				
Level 2, $\beta 00$				
Intercept3, $\gamma 000$	−0.087	0.003	−28.48	<.001
Black, $\gamma 001$	0.030	0.006	4.95	<.001
Hispanic/Latino, $\gamma 002$	−0.001	0.006	−0.10	.92
Age, $\gamma 003$	0.000	0.001	0.38	.71
Gender, $\gamma 004$	0.008	0.005	1.51	.13
Income, $\gamma 005$	−0.002	0.003	−0.49	.63
ChronicStress, $\gamma 006$	0.001	0.003	0.33	.75
Level 2, year of study, $\beta 01$				
Intercept3, $\gamma 010$	0.001	0.001	0.79	.43
Black, $\gamma 011$	0.003	0.003	0.81	.42
Hispanic/Latino, $\gamma 012$	−0.003	0.004	−0.63	.53
Age, $\gamma 013$	−0.001	0.000	−1.88	.061
Gender, $\gamma 014$	0.002	0.003	0.20	.85
Income, $\gamma 015$	−0.004	0.002	2.37	.019
ChronicStress, $\gamma 016$	−0.001	0.002	−0.34	.74
Level 2, general chronic stress, $\beta 03$				
Intercept3, $\gamma 020$	0.001	0.003	0.32	.75
Black, $\gamma 021$	0.010	0.005	2.01	.046
Hispanic/Latino, $\gamma 022$	0.014	0.005	2.94	.004
Male, $\gamma 023$	0.009	0.004	2.15	.033
Age, $\gamma 024$	0.000	0.001	0.63	.53
Income, $\gamma 025$	−0.003	0.003	−1.41	.16
ChronicStress, $\gamma 026$	−0.002	0.002	−1.11	.27
Waketime slope, $\pi 1$				
Level 2, $\beta 10$				
Intercept3, $\gamma 100$	−0.007	0.001	−4.63	<.001
Nicotine slope, $\pi 2$				
Intercept2, $\beta 20$				
Intercept3, $\gamma 200$	−0.000	0.003	−0.07	.95

Random Effect	**SD**	**Variance Component**	***df***	χ^2	***p***
Intercept1, $\rho 0$	0.025	0.001	172	387.18	<.001
Level 1, ϵ	0.050	0.003			
Intercept1/Intercept2, $\upsilon 00$	0.020	0.000	125	145.01	.11
Intercept1/General Stress, $\upsilon 03$	0.003	0.000	125	95.21	.50

Potential Mediators	**Coefficient**	**SE**	***t* Ratio**
CES-D	0.000	0.001	0.251
Negative life events	0.000	0.000	1.233
No. domains of chronic stress	−0.000	0.001	−0.162

SE = standard error; SD = standard deviation.
Data were analyzed using HLM 7.
Multilevel models using random intercepts and random slope for general chronic stress were used in these analyses (47).

attenuated in African Americans after adjustment for CVD risk factors, which represents both a potential confound and a potential consequence of the effects of psychosocial stress on CVD risk, with cortisol activity serving as a possible mediator. Because very few people changed status between Year 1 and Year 5, possibly a result of their already advanced ages and the fact that the study covered only 4 full years, it was not possible to determine the direction of significant associations of higher BMI and diabetes with flatter cortisol rhythms. White males in this sample also were characterized by flatter cortisol slopes in conjunction with yearly increases in general chronic stress. This is consistent with prior studies that have found no significant

sex differences in slopes (19,48) but have identified significant sex differences in stress reactivity or morning cortisol levels (49–51). It is possible that adult men may be particularly sensitive to psychosocial stressors as a result of physiologic and/or social differences, and this may have implications for understanding higher morbidity and mortality rates among adult men, as compared with their same-age female counterparts.

Study Limitations

Although this study contributes to our understanding of the stability of racial and ethnic differences in cortisol diurnal rhythms, as it is the first study to examine this particular question longitudinally, the psychosocial factors examined in these analyses failed to completely explain these differences. It is unclear whether variability in cortisol rhythms both within and across racial and ethnic groups would be more pronounced among younger cohorts, who may experience greater variation in daily activities, income levels, and types of psychosocial stressors. Moreover, the absence of information on prenatal environmental factors and birth outcomes, which have been demonstrated to be important predictors of postnatal HPA axis activity in other studies (52), made it impossible to assess whether such early experiences may have had long-term consequences for HPA axis activity in this sample.

The generalizability of these findings may be influenced by several factors. The sample size is rather limited, and the diversity among Hispanic/Latino ethnic subgroups cannot possibly be explored with a sample of this size. Because this is a genetically and culturally group that extends across racial categories, with Puerto Ricans and Cubans differing significantly from one another as well as from Mexicans, the most populous group, it is unclear how these findings might differ according to subgroup. Similarly, there is substantial intraracial diversity with respect to genetics, behaviors, and social factors among African Americans and whites in the United States as well. Given the sample size and nature of these data, one cannot determine the extent to which differences might be due to genetic versus social and/or behavioral factors. In particular, wakeup cortisol levels have been found to be more strongly influenced by genetics and long-term chronic stress, whereas bedtime levels tend to be more sensitive to current and recent social stressors (53). However, we believe that the highly detailed cortisol protocol (assessed for 3 days per year over four waves in a 5-year period) represents an important contribution to the literature, as the very few large-scale studies of racial and ethnic differences in cortisol have not examined stability in racial and ethnic differences longitudinally (19,21). Additional research and replication in a larger, multisite study, and ideally, a nationally representative sample would help to confirm the generalizability of these findings.

In addition, racial and ethnic minority participants were slightly less likely than whites to complete all requirements necessary for inclusion in the longitudinal analyses, compared with those who began the study at Wave 1. Because participants were required to be ambulatory and well enough to go to the laboratory to complete all interviews and questionnaires and provide biological samples, those in poorer health, who may be disproportionately minorities, may be more likely to leave the study. Conversely, those in poor health may be less likely to work and thus more readily available to participate in the study, as work obligations were among reasons cited for study refusal. Thus, the nature of any potential bias in estimates of the racial and ethnic gap due to attrition is unclear. Nonetheless, the final analytical sample did not differ significantly from those included in the noncortisol portions of the individual study waves on any of the covariates, providing some indication that attrition was not systematic.

Finally, the Chicago Health, Aging, and Social Relations Study does not include any specific measures of exposure to racial discrimination, which has previously been found to be associated with sympathetic-adrenal-medullary system activity and other health outcomes (8,16). However, if discrimination were associated cortisol slopes, such effects could influence our results only if discrimination interacted with race/ethnicity but would not otherwise alter the current findings. Moreover, one prior study of this question found that discrimination did not mediate racial and ethnic differences in cortisol rhythms (19), making it unclear whether its inclusion would dramatically influence these results.

Despite these possible limitations, the current study provides strong evidence for the robustness of group-level racial and ethnic differences in basal cortisol activity over an extended period and revealed greater sensitivity of minority racial-ethnic groups to yearly changes in chronic stress, both of which support the idea that the HPA axis may serve as important biological mediator of the impact of psychosocial stress on health and racial and ethnic health disparities.

Although higher levels of general chronic stress among minorities also predicted flatter cortisol rhythms, they did not explain racial and ethnic differences in cortisol activity. Therefore, additional research is needed to identify the origins of flatter diurnal rhythms. Longitudinal research over a more extended time frame, beginning as early as the prenatal period, may provide some insight regarding this matter. Finally, that participants of lower SES experienced a gradual flattening of their cortisol rhythms over the course of the study provides some evidence that basal HPA axis activity is a reasonable avenue to explore as a potential contributor to socioeconomic health disparities in later adulthood. Overall, these results provide preliminary support for the theory that HPA axis activity may play a role in racial and ethnic and socioeconomic health disparities.

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