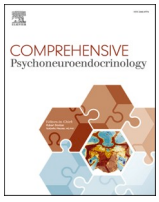
Comprehensive Psychoneuroendocrinology 11 (2022) 100145

Contents lists available at ScienceDirect

Comprehensive Psychoneuroendocrinology

journal homepage: www.sciencedirect.com/journal/comprehensive-psychoneuroendocrinology



Advancing health equity through integrated biology and population health research: A community-based sample cortisol feasibility and exploratory study

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ARTICLE INFO

Keywords:
Cortisol
Cortisol dynamic range
Allostatic load
Environment
Exposome
Community-based

ABSTRACT

Background: Community-based research inclusive of self-assessment and objective environmental metrics can be enhanced by the collection of biomarker data in unity toward assessing the health impacts of the totality of environmental stress driven by structural racism. Cortisol dynamic range (CDR), a measure of chronic stress burden, may underpin place-based connections to health, but a gap remains in elucidating community-based CDR methodology.
Purpose: To 1) assess the feasibility of cortisol collection and CDR measurement in a community-based study with home-based, participant-directed specimen collection, and 2) explore the association between CDR and other individual and environmental measures in a sample of predominantly Black participants. **Methods:** In this cross-sectional, observational study in predominantly Black urban neighborhoods, participants (n = 73) completed health assessments and in-home, self-collected salivary cortisol. For feasibility, CDR (peak-nadir) was compared to cortisol awakening response (CAR) slope over time. Comparisons of CDR quartile by person and place variables were explored (ANOVA).
Results: The cohort (77% Black, 39.7% <$15 k/year income, high perceived stress) completed 98.6% of cortisol collection timepoints. CDR was calculated in all participants without interruptions to sleep-wake cycle as seen with CAR collection. Participants in the lowest quartile of CDR were the oldest (p = 0.03) with lowest reported mental health (p = 0.048) with no associations seen for CAR.
Conclusion: Participant-collected CDR is more feasible than cortisol measures dependent on slopes over time in a community-based, predominately Black cohort with exploratory findings supporting relevance to outcomes of interest to future work. Future community-based studies should integrate CDR with environment and psychosocial measures.

1. Introduction

Comprehensively assessing the totality of exposures or stressors experienced by an individual across the life-course, including by way of their environment, in order to understand the impact of those exposures on health, known as the "exposome" has emerged as an important area

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https://doi.org/10.1016/j.cpnec.2022.100145
Received 17 December 2021; Received in revised form 20 May 2022; Accepted 20 May 2022
Available online 28 May 2022

of research [1]. Studying the exposome, however, will be incomplete if not inclusive of the impact of structural racism as a fundamental driver of health, particularly including stress-related health consequences. This imperative was highlighted by a 2020 National Academies of Sciences, Engineering, and Medicine workshop and publication as a call to action for work aiming to advance racial health equity [1].

Structural racism manifests through inequities in policies and practices, including the built and natural environment, housing quality and availability, and access to healthcare, which overlay with individual factors like psychosocial and material resources, experiences of discrimination, and social support [2,3]. Each of these layers of inequality impacts the exposome and ultimately health through a variety of biologic pathways that result in deeply entrenched racial health disparities[4]. Importantly, the biological impacts of structural racism may occur independent of experiences of interpersonal or psychosocial adversity as through environmental sleep disturbances and inequitable exposure to endocrine disrupting chemicals, for example [5,6]. While the impacts of structural racism on health are often concentrated in racially and economically segregated neighborhoods, much exposome-related research, which includes many metrics such as neighborhood and biologic-level measures, has not been inclusive of communities of color [1].

Various methods can be utilized to measure the hypothesized pathophysiologic stress-related drivers of health inequities relevant to community-based studies of the exposome, including allostatic load (AL) and its main component cortisol [7]. AL, a metric used to assess the physiologic manifestation of chronic, layered, and often intergenerational stress, is operationalized by combining multi-system biomarkers (e.g., neuroendocrine, immune/inflammatory, cardiovascular—blood pressure, cholesterol; and metabolic—glycosylated hemoglobin (A1C)) [8,9]. A core feature of AL is that it reflects the physiological burden of the stress pathway, or hypothalamic-pituitary-adrenal (HPA) axis. Cortisol, a biomarker of the HPA axis, lends way to a cascade of physiologic processes inclusive of the other AL-included systems, dependent on the stress exposure characteristics [10,11]. Dysregulation of the cortisol diurnal (daily) rhythm and pathway has been linked to a variety of poor mental and physical health outcomes [12–15]. Cortisol dynamic range (CDR), which measures the range of cortisol level from peak to nadir in an individual's diurnal cycle, is hypothesized to represent the flexibility of response to stress of an individual (e.g., capacity of HPA axis self-regulation) and has been directly correlated with AL [7,16]. While specific numeric values of CDR are not standardized, the larger the range of nadir to peak, the greater the capacity of the HPA axis to self-regulate in the face of stress [16]. Recent studies have demonstrated CDR decreases with age, poor cognitive function, and exposure to childhood adversity and/or social isolation [7,16,17]. Chronic exposure to structural racism across the life-course may manifest as altered diurnal cortisol regulation, ultimately leading to chronic disease risk in populations made vulnerable [18,19].

In aiming to inform the design of needed community-based interventions to address inequities in exposome-related exposures and outcomes, research can improve by applying methods that bridge social sciences, biology, and population health toward a "united view of health" aiming to reduce health disparities [20]. Community-based interventions that seek to directly change the ways in which structural racism harms health cannot be limited to survey collection, objective environmental measurement, or biomarker assays in isolation, but rather in unity toward addressing the multifactorial contributors to inequities and health disparities [1]. However, there is a dearth of literature that is inclusive of survey or subjective data with both environmental measures and biomarker analysis.

While a 2018 scoping review highlighted a significant association between neighborhood socioeconomic deprivation and AL, only fourteen studies were included, and only seven included cortisol, of which five were in racial/ethnically diverse populations [21]. The authors reported only three (two inclusive of Black participants) accounted for diurnal fluctuations. Importantly, all fourteen studies were observational rather than interventional [21]. Though some studies about neighborhood impact on health have measured cortisol as a stress biomarker [22], few, if any, to our knowledge have assessed a metric similar to CDR, and none have been intervention studies [23]. Further, there is a lack of clear methodological reporting on the form of data collection as field- (vs. clinic/laboratory-) based, which may be crucial for community engagement and participation.

There are several gaps and challenges to address toward full optimization of community-based integrated biospecimen methodology for health equity-advancing research. For example, in order for participants from communities that have been subject to historical and ongoing manifestations of structural racism agree to biospecimen collection in their communities, the formation of trust between investigators and individuals is paramount. Trust may build off a sense of embeddedness with academics and investigators rooted in the same social network [24], and therefore may be enhanced by bilateral, community-initiated and investigator-partnered data collection rather than a top-down attempt to collect data in institutional settings. Further, for generalizability, the specifics of HPA measurement must be standardized. Specifically, diurnal cortisol measurement, while requiring multiple collection points throughout the day, has greatest reliability [25]. Therefore, further research is needed to shed light on methodological considerations for diurnal biomarker sampling integration into community-based work.

This study was completed in partnership with a large citywide trial of an environmental intervention aimed at addressing dilapidated neighborhood conditions that result from structural racism and disinvestment (South et al. n. d.). While structural racism impacts many layers of the exposome through environment, we used data gathered from this partnered study related to, and with focus on, stress physiology. We aimed to, 1) assess the feasibility of cortisol collection and CDR measurement in an observational, cross-sectional community-based study with home-based, participant-directed specimen collection, and 2) explore the association between the more novel cortisol parameter, CDR, with biomarkers of other physiological systems of allostasis (e.g., cardiovascular, metabolic), psychological state (e.g., perceived stress and health), and neighborhood environment (e.g., exposure to green space) in a cohort of predominantly Black participants, toward hypothesis-generation. Though these were hypothesis-generating analyses, given prior work demonstrating a relationship between cortisol and dysglycemia [13,15], and between cortisol and depression [12], as well as specifically lower CDR with age [7], we did a-priori hypothesize that greater CDR would be associated with younger age, lower A1C, and highest scores of self-reported mental health (e.g., greater wellbeing). The findings of this study may offer insights for future work in community-based research integrated with biological studies of environment and stress exposures toward dismantling the multi-layered impacts of structural disadvantages on physical and mental health.

2. Methods

The overall schema for the study is outlined in Fig. 1. Data for this study was collected in partnership with a neighborhood intervention study in which clusters of urban abandoned houses were selected at random to receive varying degrees of remediation (South et al. n. d.). For the present study, we enrolled participants who lived near study abandoned houses in one section of the city. We first attempted to contact participants enrolled in the parent study and conducted additional door-to-door recruitment within study clusters between September 2017 and March 2019. The field team consented participants who met the following inclusion criteria: age ≥18 years and English-language proficiency with exclusion criteria as use of steroid or interferon medications, recent major surgery, current pregnancy, heavy cigarette smoking (≥50 pack-year history), and reported daytime sleeping and/or night work. The current analysis included participants with at least one salivary

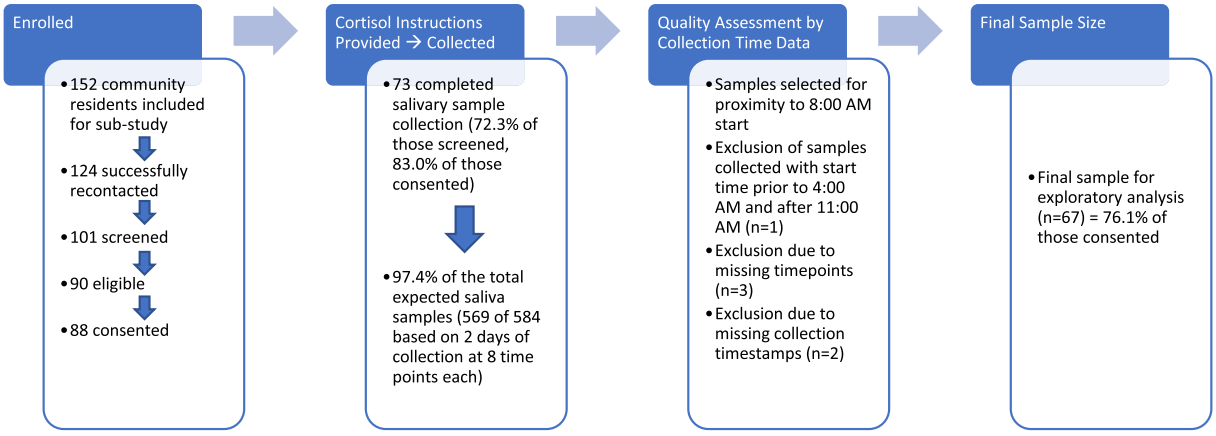

Fig. 1. Study Flow Chart
The overall schema for the study from enrollment to cortisol collection, quality assessment based on data for cortisol collection timing, and ultimate study sample for exploratory analyses (76.1% of those consented, 67/88).

cortisol sample. Budget constraints prevented follow-up, post-intervention biological data collection. The study was approved by the Institutional Review Board of the University of Pennsylvania.

2.1. Community engagement

Vacant and abandoned spaces in Philadelphia are primarily located in segregated, low-income Black neighborhoods, the result of historical and ongoing structural racism in public and private policy, as well as attendant disinvestment [26–29]. We knew, therefore, that most of our potential participants would be Black. Our research team has cultivated relationships and engagement methods involving door-to-door outreach for many years prior to the start of this study, and our engagement strategies for this study built on prior work [30–32]. One of our first studies was a qualitative effort to understand how residents in Black neighborhoods view vacant space as impacting individual and community health, as well as gathering intervention ideas [33]. An important aspect of all of our community-based research is hiring research team members who are from the neighborhoods we are working with and who share lived experience with potential participants. These research team members are vital to developing outreach protocols that are respectful, address common concerns that may be rooted in deserved institutional mistrust [34]. Further, once the team is in neighborhoods doing recruitment, they are uniquely able to quickly develop rapport with potential participants and establish a relationship built on trust. Our research field team members were hired from community and as part-time members of the study team.

2.2. Outcomes measurement

Outcomes measurement methods are detailed in Supplementary Table 1. Participants completed standardized questionnaires for self-assessment of perceived stress and physical and mental health using the validated Perceived Stress Scale-10 (PSS-10), and the 20-item Short Form Health Survey (SF-20).(Cohen and Williamson, n. d. [35]; Notably, PSS scores of 27–40 are considered high perceived stress.(Cohen and Williamson, n. d.) Each scale of the SF-20 ranges from 0 to 100, where a higher score indicated better self-rated health (lower scores indicate lower rated health) [35]. The study team then collected systolic and diastolic blood pressure, waist-hip ratio (WHR), and a finger stick blood sample to measure glycated hemoglobin (A1C), and total cholesterol. Clinical measurements were provided on a health card to participants. Neighborhood environment was measured by participants' reported time spent in greenspace (days), and objectively measured tree canopy coverage per 50- and 100-m diameter around the participant's home address using administrative tree canopy data (Supplementary Table 1). Tree canopy data was linked with participant address through geocoding with ArcGis Pro 10.0 (Esri, Redlands, California). We chose to include measurements of greenspace utilization and presence based on a significant body of literature demonstrating the health and safety benefits of nature, as well as the fact that greenspace, including tree canopy, is patterned by racial composition of neighborhoods [32,36–38]. Further, greenspace is hypothesized to influence health in part through the experience of stress, which was directly measured in this study.

2.3. Cortisol collection

The field team first learned how to properly collect salivary cortisol based on instructions from the collection company, including videos (SalivaBio Passive Drool methods using a saliva collection aid and cryovials from Salimetrics). The team practiced collection on themselves many times, and noted what techniques seemed to work best and how to describe the process to participants. Based on this experience, participant facing training materials were developed to both assist the field team in real time while teaching to participants, as well as to leave with participants to remember how to collect saliva. In participants homes, the field team first demonstrated the use of the salivary collection system, while showing participants each step on a picture-based "how-to" guide." Participants then performed a collection themselves in front of the field team to return-demonstrate the technique and ensure full understanding of a proper collection (detailed in Supplementary Fig. 1). Subjects were asked to self-collect saliva 4 times per day (immediately upon waking, 30 min after waking, mid-day, and at bedtime; estimated to take 10 min each) in the 2 weekdays which followed the day of enrollment and to freeze samples immediately after collection. The team brainstormed methods with participants to remember timely collection (i.e., alarms, visual reminders, etc.). For the majority of participants, a secure text message service schedules text reminders sent the day prior to collection and the afternoon and evening of collection days. A time was scheduled for the team to pick up the frozen samples which were then placed in a cooler of ice and transported to a University of Pennsylvania laboratory freezer where they were later analyzed for concentration in micrograms per deciliter (ug/dL) (Supplementary Fig. 1).

2.4. Cortisol measurements

Given the most physiologically applicable start time of cortisol curve data collection is considered 8 a.m. (with circadian rhythmic morning peak) [25], we used the data that was closest to the 8 a.m. start time per participant of the two collection days. We assessed the cortisol curve

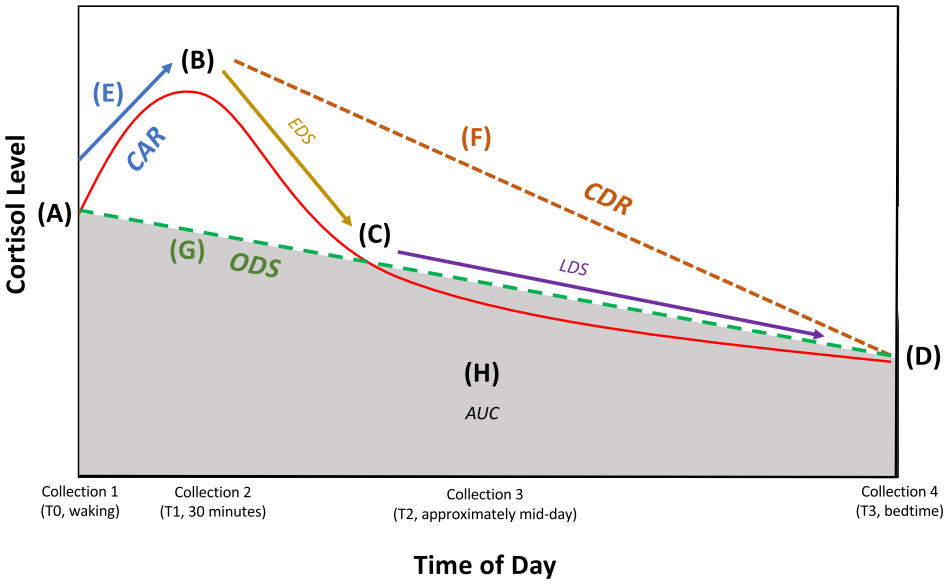

Fig. 2. Diurnal Cortisol Curve and Associated Measures
The graphic represents parameters of the cortisol diurnal curve (red line) with associated measurements. In this study we used assessed cortisol dynamic range (CDR) depicted in this figure as line F, and equal the difference between cortisol curve peak (here, point B) and the cortisol curve trough (here, point D). We also assessed cortisol awakening response (CAR) depicted here as the slope of line E (time 0 to time 30 min over time), and overall decline slope (ODS) or difference between morning and bedtime cortisol depicted as the slope of line G. Other cortisol measures include wake-up cortisol (time 0, point A), early decline slope cortisol (EDS, 30 min to 2 h, points B to C), late-decline slope cortisol (LDS, 2 h to bedtime, points C to D), bedtime cortisol (point D), and area under the curve (AUC, point H). Importantly, CDR is not dependent on time as it is calculated as a range via a difference between two values. CAR, ODS, EDS, and LDS are all slopes requiring the calculation of time passed for denominators, and AUC is also calculated with respect to time (change over time). . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

(Fig. 2) for cortisol dynamic range (CDR), cortisol awakening response (CAR; 0 to 30-min post-awakening slope), and overall decline slope (ODS; first morning cortisol to bedtime slope). Cortisol dynamic range (CDR) was calculated as described prior [7,16], by log-cortisol peak minus log-cortisol nadir. This translates to log of the cortisol diurnal peak-to-nadir ratio. CAR is calculated here as the second cortisol collection level (ug/dL) minus the first (ug/dL) then divided by the time difference between the two given not all participants collections were exactly 30 min apart. ODS is also calculated as a slope (over time), dividing the difference between morning and bedtime cortisol levels (each in ug/dL) by the difference in time between collections.

2.5. Statistical analysis

For our first aim, we applied descriptive statistics to assess feasibility of the study such as percent participation and adherence to instructions (timeline) for cortisol collection. Additionally, given that it is anticipated that CDR per physiologic prediction would be the difference of the last point of cortisol collection and the second point of cortisol collection (Fig. 2), we assessed the number of participants whose CDR indeed relied on these two time points as a checkpoint. Completion of collection at the points of measurement necessary for calculation were compared between CDR and CAR.

For our second aim, to explore the associations of CDR with other available biomarkers of physiologic dysregulation or disease risk (A1C, WHR, systolic blood pressure), environmental variables, and perceived stress and health, we applied ANOVA across quartiles of CDR measurement. Flatter CDR, or a smaller difference between the peak and nadir cortisol levels over the course of the day, is considered less dynamic of a response range to stress (blunted) [7], therefore, the first quartile would be the lowest or least dynamic range and the fourth quartile would be the highest or most dynamic range. As a robustness check, we also tested for association between these variables and quartile cortisol measures CAR and ODS.

3. Results

3.1. Sample

Of 192 residents screened for eligibility from the parent intervention study, a subset (n = 152) was selected for the sub-study based on clusters designated for the field staff who were a part of and trained for this sub-study. Of these, 124 were successfully recontacted by phone calls or door-to-door knocking. Of these, 101 participants were screened and 90 were eligible, of which, 88 consented to participant and 2 refused. Of the 88 consented participants, 73 completed salivary sample collection (equivalent to 73.3% of those screened, 81.1% of those eligible, and 83.0% of those consented). Of the 23 participants we had contact with but did not screen, 16 refused and 7 expressed initial interest but did not have time to talk further with us and we were not able to get back in touch with them either by phone or knocking on their door.

The cohort had an average age of 43.8 years (Table 1) and was comprised of mostly of individuals identifying as Black (n = 56, 76.7%) and female (n = 45, 61.6%). Most participants reported an annual household income of under $15,000 (n = 29, 39.7%), with just 12 (16.4%) reporting an income greater than $45,000. The average number of years reported living in each participant's current zip code was 17.13 ± 18.99. Nearly half (49.4%) of the sample had some college education or above, though the average household income was low. Black participants were of low income even in strata of higher educational attainment and lived in the same zip code for an average of 13 more years than other participants. Analyses of descriptive demographic variables stratified by education, race, and sex can be found in Supplementary Tables 2–4.

The clinical characteristics of the sample show the population had, on average, prediabetes (A1C > 5.7), adiposity (waist >92 cm for men, >88 cm for women, see Supplementary Table 4, Table 3, stratified by sex), and elevated blood pressure or hypertension (>120 mmHg, ≥ 130 mmHg systolic). The average PSS score was 28.8 (7.7), falling within the range of high perceived stress on the scale.

3.2. Feasibility

The 73 participants collected 97.4% (569/584) of the total expected saliva samples. After selection for the day based on start closest to 8:00AM, the analyzed data included 98.6% (288/292) of timepoints. Of the "immediately upon waking" samples, 87.5% were collected between 6:00 and 10:00 a.m.. Of these, the majority of participants provided the first sample within 1 h of 8:00 a.m. (68.1% between 7:00 and 9:00 a.m.). Remaining analyses excluded the subject with a collection start time

Table 1
Demographics of the community sample.

Demographics (n = 73)	n (% or SD)
Sex	
Female	45 (61.6%)
Male	27 (37.0%)
Other	1 (1.4%)
Age	43.8 (14.7)
Race	
Black	56 (76.7%)
Multiracial	9 (12.3%)
White	6 (8.2%)
Refused/Don't know	2 (2.7%)
Hispanic	
Yes	3 (4.11%)
No	70 (95.9%)
Annual household income	
Less than $15,000	29 (39.7%)
$15,000-$25,000	16 (21.9%)
$25,000-$45,000	11 (15.1%)
Greater than $45,000	12 (16.4%)
Education	
Less than high school	9 (12.3%)
High school or GED equivalent	28 (38.4%)
Some college	15 (20.6%)
College graduate	13 (17.8%)
More than college	8 (11.0%)
Years living in current zip code	17.13 (18.97)
Clinical characteristics (N = 73)	
Salivary Cortisol (ug/dL)	
Collection 1 (n = 73)	0.3718 (0.301)
Collection 2 (n = 73)	0.442 (0.31)
Collection 3 (n = 72)	0.249 (0.29)
Collection 4 (n = 70)	0.212 (0.26)
A1C	6.0 (1.3)
Total cholesterol	186.8 (42.3)
Waist	96.1 (17.8)
Systolic blood pressure	133.55 (19.8)
Perceived Stress	28.8 (7.7)
Physical Health	51.8 (26.0)
Mental Health	66.7 (10.1)
Greenspace Time (days)	3.2 (1.5)
50 Meter Canopy	1339.2 (552.8)
100 Meter Canopy	5137.5 (1346.9)

prior to 4:00 a.m. (n = 72). For CDR analysis, three more subjects were excluded due to samples incomplete at later timepoints.

Roughly half (52.8%) of participants were within 5 minutes of the instructed 30-min period between the first and second sample of the day, with 84.7% within 45 min of the first sample. When calculating CAR, 34.8% (24/69) were noted to have negative slopes (cortisol level at the second collection decreased from first).

In calculating CDR, 33.8% of subjects' CDR used the second cortisol collection time point measure as the peak and the fourth collection as the nadir, while the remainder of subjects' minimum or maximum was a different collection time (e.g., peak other than timepoint 2, and nadir other than timepoint 4). All those with CDR using second and fourth collection time also had positive CAR slopes.

3.3. Exploratory analyses

Exploratory analyses included 67 participants as 6 were excluded due to time of collection outside the window of 4 a.m –11 a.m. or missing cortisol at all 4 collection timepoints (76.1% of those consented, Fig. 1). The greatest quartile of CDR (4th quartile, "Q4" of Table 2, quartile with the most dynamic/greatest range between peak and nadir), is indicative of the most adaptable physiological stress response. Individuals in this quartile were the youngest (35.19 ± 13.76 years, p = 0.031). Specifically, age in those with the greatest quartile of CDR (4th quartile), had an average age of nearly 9 years more than those in the lowest CDR quartile (1st quartile). Though the 4th quartile for CDR also had the lowest total cholesterol and A1C, this was not significant. A trend toward significance was with the lowest dynamic range CDR (quartile 1) having the highest perceived stress (p = 0.05). Those in the fourth quartile for CDR had the greatest mental health score (p = 0.048). Specifically, mental health scores in those with the greatest quartile of CDR (4th quartile), was 9 units higher on average than those in the lowest CDR quartile (1st quartile). A significant association was seen for green space time across quartiles (p = 0.014), but with those of the lowest CDR having the greatest time in green space. No associations were found with CAR or ODS (Supplementary Tables 7 and 8).

Given the observation that nearly half (49.4%) of the sample had some college education or above, though the average household income was low, we conducted an exploratory analysis of the association between CDR and education (education was the independent variable and CDR was the dependent) and found it significant (B = 0.141, (95%CI 0.12, 0.270), p = 0.033), though a similar model using household income as the independent variable was not significant.

Analyses of cortisol outcomes stratified by race and adjusted for sex can be found in Supplementary Tables 7 and 8.

4. Discussion

Our study demonstrated the feasibility of community-engaged exposome research, inclusive of participant-led collection, specifically to allow analyses using the cortisol dynamic range measure. Our sample was community-based and comprised of participants who were predominantly Black and of low income and relatively poor health. The impact of structural racism may be evident from our sample characteristics. For example, we observe that individuals who identified as Black were of low income even with higher educational attainment and were more likely to remain in the same zip code than individuals of other

Table 2
Subject characteristics by quartile of CDR.

Var	Q1 (SE)	Q2 (SE)	Q3 (SE)	Q4 (SE)	P-value (ANOVA)
CDR	0.545 (0.051)	1.162 (0.038)	1.759 (0.041)	2.254 (0.066)	–
Age	46.765 (3.793)	43.176 (3.697)	49.706 (2.969)	35.188 (3.440)	0.031**
A1C	6.376 (0.449)	5.853 (0.189)	6.347 (0.363)	5.606 (0.110)	0.237
Total Cholesterol	184.765 (9.280)	187.0 (12.127)	201.294 (12.380)	180.75 (6.950)	0.5419
WHR	97.641 (4.567)	95.647 (4.766)	95.324 (4.230)	96.688 (4.011)	0.982
SBP	136.5 (5.367)	128.735 (4.112)	131.529 (5.668)	137.125 (5.020)	0.601
Perceived Stress	31.882 (1.968)	25.118 (1.803)	29.529 (1.490)	27.063 (1.852)	0.050
Mental Health	60.625 (3.180)	68.333 (1.407)	67.647 (2.318)	69.583 (2.432)	0.048**
Physical Health	55.208 (6.756)	48.148 (6.446)	55.882 (6.053)	46.875 (6.670)	0.672
Green Space Time (days)	4.000 (0.309)	2.647 (0.352)	3.647 (0.342)	2.750 (0.359)	0.014*
50 Meter Canopy	1508.513 (170.772)	1186.655 (97.377)	1466.249 (129.072)	1199.16 (129.541)	0.194
100 Meter Canopy	5481.481 (433.020)	4843.256 (244.567)	5137.024 (361.666)	5110.459 (283.359)	0.617

SE = Standard Error, CDR = Cortisol Dynamic Range (log-cortisol peak minus log-cortisol nadir), A1C = glycosylated hemoglobin A1c, WHR = waist to hip ratio, SBP = systolic blood pressure.
**$p < 0.05$ and trend through quartiles, *$p < 0.05$ no trend by quartiles.

racial identity, which are both corroborated by nationally representative findings and trends(Board of Governors of the Federal Reserve System (U.S.) et al., 2017 [39,40]. Racial wealth gaps in education attainment coupled with inequities in opportunities for social and geographic mobility are some of many examples of structural racism [40]. Notably, this study cohort was also overall in poor health with average clinical metrics showing evidence of prediabetes, adiposity, hypertension, and elevated stress, for example. We included individual subjective and objective measures of health (e.g., survey, physical exam, and clinical laboratory data), metrics of individual and neighborhood interaction (greenspace), and stress-burden biomarker data (e.g., cortisol dynamic range, or CDR). We observed feasibility in, 1) successful participant retention and methodological integration inclusive of in-home cortisol collection, and 2) CDR collection compared to other diurnal metrics of cortisol in community-engaged collection methodology (CAR, ODS), particularly due to greater vulnerability of the later to accuracy in timing of sample collection because they are slopes (values divided by time) [25]. Following a timed schedule is recommended by expert consensus on methodology for salivary cortisol awakening response, but is challenging to attain [41].

Specifically, using door-to-door recruitment in our study neighborhoods, we saw 97.8% were retained from consent to participate in the study through to sample collection, demonstrating the acceptability of study methods by community members. Of note, the racial makeup and life experience of the study field team was largely reflective of the participants being recruited, potentially facilitating trust between investigators and participants. Our field team methodology is a crucial strength of our study and may indicate why we had a higher retention rate of participation than prior studies (which showed a retention rate of 45%) [42]. Though the response rate for participants screened was high (73%), this may be improved by future studies that should aim to involve community members who are hired full-time as part of research teams (ours were part-time employees). This increase in community-based researcher involvement and time can also enable frequent check-ins with participants regarding methods, for example. We also demonstrated feasibility of using participant-led, in-home saliva collection, with 98.6% adherence to full collection of samples at all time points. Though challenges were observed in meeting precision of collection times, when using data from the day of collection where the participant started closest to 8:00 a.m., the majority of individuals provided an initial sample within an hour (68.1%) and a second sample within 45 min later (84.7%).

CDR may provide a more feasible alternative to CAR or ODS in community biomarker sampling. Because CAR and ODS are measured slopes (e.g., change in cortisol over time), they may be less accurate with methodological challenges around timed collections (e.g., given dependence on a denominator of time that is more variable in field collection than may be if lab-collected). Further, the observation that nearly 35% of participants had negative CAR slopes, despite that a positive slope is consistent with a physiological diurnal cortisol curve, suggests measurable impact on CAR measurement by altered sleep-wake cycles (e.g., waking during the night, starting collection much after morning wake time). Importantly, the observation that 66.2% of participants' CDR used collection times outside of the second for peak and the fourth for nadir, emphasizes that even with the feasibility of CDR, more than two daily samples and accuracy of associated collection times are still needed in methods to ensure reliable data for CDR calculation.

Our exploratory analysis supports feasibility and relevance of the CDR measure to community-engaged exposomics research. The observation of a trend toward greater dynamic range with younger age is consistent with the CDR literature [7,16,17], suggesting internal validity of CDR in our sample. Further, though lower CAR measurement is also known to occur with older age [43], this was not seen in our sample via CAR or ODS measurements again suggesting feasibility favoring CDR compared to other measures of cortisol diurnal pattern in this community-based study. Of note, other diurnal metrics of cortisol, like area under the curve, also rely on change over time [12].

With this establishment of CDR as feasibly collected in our study, we were able to consider the impact of the exposome via cortisol on physical and mental health in an exploratory analysis of our sample. While a trend toward significance was observed with the lowest dynamic range CDR quartile having the highest perceived stress, the association likely did not reach significance given the high baseline perceived stress of the entire cohort (average 28, with scores above 27 are considered high (Cohen and Williamson, n. d.)). While we hypothesized a relationship between CDR and A1C would be observed, the null observation is consistent with prior literature particularly in predominantly Black cohorts [13–15,44], which is hypothesized to be due to sensitization of the HPA axis in the face of chronic intergenerational exposure to structurally imposed stressors by way of racism and trauma. Importantly, these findings taken together support the need for future community-based studies of the multi-layered origins of stress especially as they may inter-relate with aspects of interpersonal and structural racism.

We also observed that poorer mental health was reported in those with the least dynamic CDR, corroborating prior literature demonstrating that HPA axis dysfunction is associated with mental illness such as depression [12]. As it is known that exposure to greenspace mitigates symptoms of depression and poor self-reported mental health [31], quantifying such neighborhood characteristics in exposomics work is as crucially important as biologic measurements. While we did not observe a relationship between greater CDR and greater time in greenspace or canopy coverage, one might still hypothesize that there is an association given CDR decreases with age (as we observed) and greenspace time and access may increase with age (e.g., more day time to walk in retirement). As in this example, our study supports the need for further research to continue to incorporate each of these components of the exposome (biologic—as cortisol with other allostatic load metrics, environmental—as neighborhood factors) in future mental health studies and health services research (Fig. 3). Additionally, our findings combined with knowledge that HPA function and measurement correlate with adiposity, age, and dysglycemia [13–15], suggest such future work be powered to explore the interplay between CDR, age, adiposity, environmental, and psychological variables.

Though a few community-based studies have begun to bridge cortisol biology and social data collection in recent years based on our review, they often restrict cortisol collection to an in-clinic approach, which is not reflective of the broader community of individuals who may never interact with investigators if they are not met directly in their homes [45,46]. One recent neighborhood study did use only in-home cortisol collection in a large sample ($n > 2000$) of adolescents, however, cortisol collection occurred pre and post stressor and so did not account for the diurnal cortisol response [47]. Prior studies with population-level cohorts have also met challenges in adopting systematic methods of salivary cortisol collection [48]. Notably, one such study most inclusive of Black individuals only collected morning serum cortisol. [49]; p.) Three large epidemiological studies in the United States that have attempted to collect salivary cortisol at multiple time points all have cited time precision as a challenge [50–53], two of which explicitly mention how this led to limitations in CAR data calculation and/or use [50–52], and one which attempted to use time tracking devices that were cost prohibitive for wide-spread use or applicability to community-sampling methods [53]. Our findings taken together in context of these studies suggests that time of cortisol collection is a significant barrier to study and so future work should aim to enhance instruction of, and adherence to, collection timing. Importantly, though our study demonstrated feasibility of collection throughout the day, future research should aim to include participants' own feedback with respect to the collection process including training and timing.

Ultimately, our findings build on prior literature to indicate some crucial methodological considerations for future studies aiming to be inclusive of community-based (in-home, participant-led) cortisol biomarker collection. Our study specifically adds the importance in

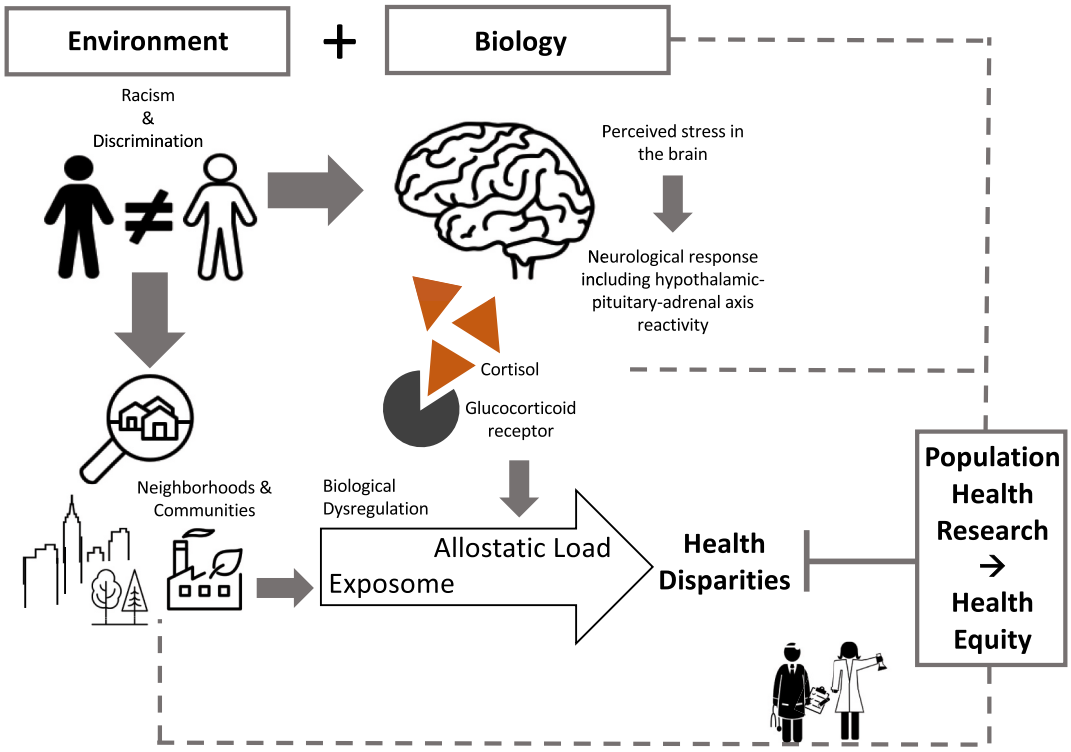

Fig. 3. The Exposome Meets Allostatic Load: The Impact of Structural Racism as an Integration of Environmental and Biologic Study in Community-based Research
While the psychological stress of chronic experiences of interpersonal racism and discrimination may trigger the stress pathway (hypothalamic-pituitary-adrenal axis) over time yielding dysfunction of cortisol diurnal patterns, structural racism simultaneously influences inequitable impacts to environmental factors such as decreased access to greenspace, and increased exposure to pollutants. Specifically, chronic cortisol may over occupy glucocorticoid receptors which feedback to the central HPA axis and with time may result in decreased ability of the axis, via cortisol, to respond to acute stress which may manifest as a shortening of cortisol dynamic range (CDR). Taken together, the totality of these exposures, known as the exposome, joins the allostatic load burden of imbalanced physiology across multiple systems to yield health disparities in mental and physical illness, inclusive of commonly comorbid illness known to bidirectionally link to cortisol dysregulation such as depression and cardiometabolic disease. If population health research is inclusive of biological, environmental, and subjective psychosocial metrics n design, potentially with the use of community field workers and participant-led sample collection, outcomes will be more likely to align toward a common goal of multi-layered solutions into achieved health equity.

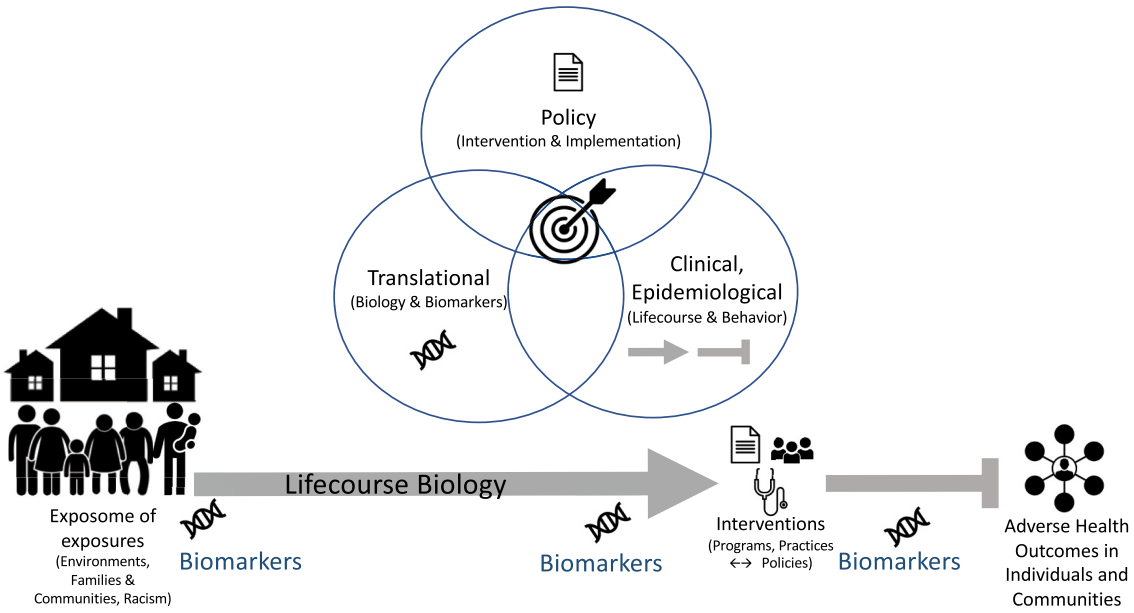

Fig. 4. Conceptual Framework for Future Integrated Biological and Population Health Research
The study of the exposome, inclusive of biological assessments, must be designed in a way that orients future work toward interventions (programs and practices that may influence policies) that may ultimately inhibit adverse health outcomes in individuals, communities, and populations. Work that considers translational biology from community-based level of study into larger-scale epidemiological studies will build evidence toward shaping anti-racist policies and outcomes oriented toward equitably attainable healthful exposomes (healthy environments and exposures).

considering CDR as it is potentially more feasible than other cortisol measures, while being particularly relevant to exposome-related study. Taken together this work yields the following recommendations: 1) provide participants with specific directions and supports especially around accurate timing of collection, 2) collect participant data inclusive of sleep-wake cycle specifics, and 3) include a minimum three samples (30 min after waking and evening nadir for CDR, and a third first morning sample at wake up for time quality check).

Considering these methodological recommendations is especially pertinent, as the NIH calls for research to understand the role of structural racism on health disparities, ("Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities (R01 Clinical Trial Optional)," 2021) where integrating biomarker, psychosocial, and objective environment data collection is paramount to advancing knowledge (Fig. 4). First, racism and discrimination impact biology and clinical health outcomes. For example, Black individuals have flatter cortisol curves overall, but their curves may differ with exposure to discrimination (independent of socioeconomic status) [54–56]. Discrimination also impacts pathways toward increased allostatic load, mediated in part by poor sleep quality, in Black compared to white individuals [6]. Further, structural racism influences housing, healthy food, and educational access that transmit into mental illness, cardiovascular, diabetes, and other chronic disease disparities [12], and manifests into opportunity gaps for Black children which correlate with increased all-cause mortality rates [57]. Second, structural racism imposes inequitable distribution of toxic environmental exposures on health including limited neighborhood resources and access to greenspace [31], with simultaneous increases in endocrine disrupting chemical exposures [5] that both impact biology and disease outcomes. Third, these factors intersect with risk for psychosocial stressor exposures like adverse childhood experiences that occur from early life, but cause ripple effects on biology across the life-course leading to increased prevalence of chronic disease into adulthood and premature mortality [58–60]. Importantly, racial/ethnic experiences of discrimination may result in flattened cortisol curve for other minoritized populations including Hispanics and Asian Americans and Native Hawaiians [12,61].

The longitudinal and chronic nature of these exposures and the development of their associated outcomes lends to challenges in studying the impacts of interventions in short-term studies [45]. However, biomarkers may pose an opportunity to assess underlying physiological changes that occurs prior to clinical outcomes [9]. Therefore, self-report survey data, which provides only a snapshot in time may not provide a full assessment of outcomes and may be subject to response recall bias, can be complimented by biomarker work [62]. An integrated approach to research will better address the root cause of health disparities toward the attainment of community and neighborhood-level equity in policy and health impacts and, ultimately, population health justice [20].

This study has limitations including the small sample size, lack of comparison groups by demographic or exposure variables. Still, our cohort was inclusive of majority Black, low-income individuals, which is representative of our aim to assess feasibility and relevance of the CDR measure in community-based exposome research, where some large scale study samples have lacked diverse sampling [52], or accuracy of population representation [63]. The knowledge that structural racism impacts environment, exposomal, and ultimately biological systems on multiple levels was a framework for our study that focused on one aspect for those impacts, through CDR, we acknowledge that future studies could aim to include measures of structural and interpersonal racism in their methodology. Though our data was not inclusive of detailed participant sleep-wake cycles and vulnerable to inaccurate collection time data, we addressed the importance of diurnal timing on cortisol collection by excluding participants who reported daytime sleeping and/or night work, and in analyses, including samples from the day of collection beginning most proximate to 8:00 a.m., excluding the one sample which was collected outside of a 4:00 a.m. to 11:00 a.m. start time. Still, we found CDR a feasible measurement, which is also not directly dependent on of timed collection. Our analysis was limited by lack of collection of other metrics which may impact cortisol levels such as caffeine, or recent infection or antibiotic use. While our study corroborates prior literature in finding an association between older age and lower CDR, prior literature has also demonstrated an association between cognitive decline and lower CDR [7]. Though cognitive decline may correlate with older age, our study did not include a measure of cognitive function, suggesting an area for future research. As our data was limited to cross-sectional analysis, future work is needed in longitudinal and interventional community-based studies inclusive of CDR and exposomic investigations.

5. Conclusion

In conclusion, we demonstrate the feasibility of collecting participant self-collected salivary cortisol data in the field as part of bilateral community-engaged research with support for use of, specifically, the cortisol dynamic range metric. Further, our findings suggest areas for improvement in this space including better practices for data on sleep-wake cycles and time specifications of cortisol collection. Future work should aim to enhance methodological approaches to combining cortisol and biomarker data collection in population physical and mental health and intervention research toward understanding the impacts of structural racism. Integrating biological, population health and policy research, and epidemiological methods will maximize the potential for research to impact adverse health outcomes currently associated with structural racism and social inequities across the life-course (Fig. 4).

Disclosures

The authors have no conflicts of interest to disclose.

Declaration of interest

The authors received support in training and completion of the study from the University of Pennsylvania Perelman School of Medicine. The study was funded in part by grant 5R01AA024941 from the National Institutes of Health.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpnec.2022.100145.

References

[1] J.C. Nwanaji-Enwerem, C.L. Jackson, M.A. Ottinger, A. Cardenas, K.A. James, K.M. C. Malecki, J.-C. Chen, A.M. Geller, U.A. Mitchell, Adopting a "compound" exposome approach in environmental aging biomarker research: a call to action for advancing racial health equity, Environ. Health Perspect. 129 (2021) 45001, https://doi.org/10.1289/EHP8392.
[2] Z.D. Bailey, N. Krieger, M. Agénor, J. Graves, N. Linos, M.T. Bassett, Structural racism and health inequities in the USA: evidence and interventions, Lancet 389 (2017) 1453–1463, https://doi.org/10.1016/S0140-6736(17)30569-X.
[3] A.V. Diez Roux, C. Mair, Neighborhoods and health, Ann. N. Y. Acad. Sci. 1186 (2010) 125–145, https://doi.org/10.1111/j.1749-6632.2009.05333.x.
[4] D.R. Williams, J.A. Lawrence, B.A. Davis, Racism and health: evidence and needed research, Annu. Rev. Publ. Health 40 (2019) 105–125, https://doi.org/10.1146/annurev-publhealth-040218-043750.
[5] T.M. Attina, J. Malits, M. Naidu, L. Trasande, Racial/ethnic disparities in disease burden and costs related to exposure to endocrine-disrupting chemicals in the United States: an exploratory analysis, J. Clin. Epidemiol. 108 (2019) 34–43, https://doi.org/10.1016/j.jclinepi.2018.11.024.
[6] L.M. Tomfohr, M.A. Pung, J.E. Dimsdale, Mediators of the relationship between race and allostatic load in African and White Americans, Health Psychol. Off. J. Div. Health Psychol. Am. Psychol. Assoc. 35 (2016) 322–332, https://doi.org/10.1037/hea0000251.
[7] S.T. Charles, J. Mogle, J.R. Piazza, A. Karlamangla, D.M. Almeida, Going the distance: the diurnal range of cortisol and its association with cognitive and

physiological functioning, Psychoneuroendocrinology 112 (2020), 104516, https://doi.org/10.1016/j.psyneuen.2019.104516.
[8] T.M. Beckie, A systematic review of allostatic load, health, and health disparities, Biol. Res. Nurs. 14 (2012) 311–346, https://doi.org/10.1177/1099800412455688.
[9] A. Danese, B.S. McEwen, Adverse childhood experiences, allostasis, allostatic load, and age-related disease, Physiol. Behav. 106 (2012) 29–39, https://doi.org/10.1016/j.physbeh.2011.08.019.
[10] D.Y. Lee, E. Kim, M.H. Choi, Technical and clinical aspects of cortisol as a biochemical marker of chronic stress, BMB Rep 48 (2015) 209–216, https://doi.org/10.5483/bmbrep.2015.48.4.275.
[11] R.M. Sapolsky, L.C. Krey, B.S. McEwen, The neuroendocrinology of stress and aging: the glucocorticoid cascade hypothesis, Endocr. Rev. 7 (1986) 284–301, https://doi.org/10.1210/edrv-7-3-284.
[12] J.J. Joseph, S.H. Golden, Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus, Ann. N. Y. Acad. Sci. 1391 (2017) 20–34, https://doi.org/10.1111/nyas.13217.
[13] B. Kluwe, R. Ortiz, J.B. Odei, S. Zhao, D. Kline, G. Brock, J.B. Echouffo-Tcheugui, J.-M. Lee, S. Lazarus, T. Seeman, P. Greenland, B. Needham, M.R. Carnethon, S. H. Golden, J.J. Joseph, The association of cortisol curve features with incident diabetes among whites and African Americans: the CARDIA study, Psychoneuroendocrinology 123 (2021) 105041, https://doi.org/10.1016/j.psyneuen.2020.105041.
[14] B. Kluwe, S. Zhao, D. Kline, R. Ortiz, G. Brock, J.B. Echouffo-Tcheugui, M. Sims, R. R. Kalyani, S.H. Golden, J.J. Joseph, Adiposity measures and morning serum cortisol in african Americans: jackson heart study, Obes. Silver Spring Md 29 (2021) 418–427, https://doi.org/10.1002/oby.23056.
[15] R. Ortiz, B. Kluwe, J.B. Odei, J.B. Echouffo Tcheugui, M. Sims, R.R. Kalyani, A. G. Bertoni, S.H. Golden, J.J. Joseph, The association of morning serum cortisol with glucose metabolism and diabetes: the Jackson Heart Study, Psychoneuroendocrinology 103 (2019) 25–32, https://doi.org/10.1016/j.psyneuen.2018.12.237.
[16] A.S. Karlamangla, S.S. Merkin, D.M. Almeida, E.M. Friedman, J.A. Mogle, T. E. Seeman, Early-life adversity and dysregulation of adult diurnal cortisol rhythm, J. Gerontol. B Psychol. Sci. Soc. Sci. 74 (2019) 160–169, https://doi.org/10.1093/geronb/gby097.
[17] C. Ayala-Grosso, F. Torrico, M. Ledezma-Ruiz, M. Busolo-Pons, Chronic stress in cognitive processes: cortisol dynamic range of secretion is associated with perception of unsafety environment in a Venezuelan population, J. Alzheimers Dis. JAD (2020), https://doi.org/10.3233/JAD-200886.
[18] M. Berger, Z. Sarnyai, More than skin deep": stress neurobiology and mental health consequences of racial discrimination, Stress Amst. Neth. 18 (2015) 1–10, https://doi.org/10.3109/10253890.2014.989204.
[19] A.S. Karlamangla, E.M. Friedman, T.E. Seeman, R.S. Stawksi, D.M. Almeida, Daytime trajectories of cortisol: demographic and socioeconomic differences–findings from the National Study of Daily Experiences, Psychoneuroendocrinology 38 (2013) 2585–2597, https://doi.org/10.1016/j.psyneuen.2013.06.010.
[20] K. Armstrong, D.A. Asch, Bridging polarization in medicine - from biology to social causes, N. Engl. J. Med. 382 (2020) 888–889, https://doi.org/10.1056/NEJMp1913051.
[21] A.I. Ribeiro, J. Amaro, C. Lisi, S. Fraga, Neighborhood socioeconomic deprivation and allostatic load: a scoping review, Int. J. Environ. Res. Publ. Health 15 (2018), https://doi.org/10.3390/ijerph15061092.
[22] R.A. Karb, M.R. Elliott, J.B. Dowd, J.D. Morenoff, Neighborhood-level stressors, social support, and diurnal patterns of cortisol: the Chicago Community Adult Health Study, Soc. Sci. Med. 75 (2012) 1038–1047, https://doi.org/10.1016/j.socscimed.2012.03.031, 1982.
[23] S.E. Wing, G. Bandoli, D. Telesca, J.G. Su, B. Ritz, Chronic exposure to inhaled, traffic-related nitrogen dioxide and a blunted cortisol response in adolescents, Environ. Res. 163 (2018) 201–207, https://doi.org/10.1016/j.envres.2018.01.011.
[24] D. Khodyakov, L. Mikesell, E. Bromley, Trust and the ethical conduct of community-engaged research, Eur. J. Pers. Centered Healthc. 5 (2017) 522–526, https://doi.org/10.5750/ejpch.v5i4.1263.
[25] S.H. Golden, G.S. Wand, S. Malhotra, I. Kamel, K. Horton, Reliability of hypothalamic-pituitary-adrenal axis assessment methods for use in population-based studies, Eur. J. Epidemiol. 26 (2011) 511–525, https://doi.org/10.1007/s10654-011-9585-2.
[26] D.S. Massey, American apartheid: segregation and the making of the underclass, Am. J. Sociol. 96 (1990) 329–357, https://doi.org/10.1086/229532.
[27] D. Pager, H. Shepherd, The sociology of discrimination: racial discrimination in employment, housing, credit, and consumer markets, Annu. Rev. Sociol. 34 (2008) 181–209, https://doi.org/10.1146/annurev.soc.33.040406.131740.
[28] R.J. Sampson, W.J. Wilson, H. Katz, Reassessing "toward a theory OF race, crime, and urban inequality": enduring and new challenges in 21 st century America, Bois Rev. Soc. Sci. Res. Race 15 (2018) 13–34, https://doi.org/10.1017/S1742058X18000140.
[29] W.J. Wilson, The Truly Disadvantaged: the Inner City, the Underclass, and Public Policy, second ed., University of Chicago Press, Chicago ; London, 2012.
[30] C.C. Branas, E. South, M.C. Kondo, B.C. Hohl, P. Bourgois, D.J. Wiebe, J. M. MacDonald, Citywide cluster randomized trial to restore blighted vacant land and its effects on violence, crime, and fear, Proc. Natl. Acad. Sci. Unit. States Am. 115 (2018) 2946–2951, https://doi.org/10.1073/pnas.1718503115.
[31] E.C. South, B.C. Hohl, M.C. Kondo, J.M. MacDonald, C.C. Branas, Effect of greening vacant land on mental health of community-dwelling adults: a cluster randomized trial, JAMA Netw. Open 1 (2018), e180298, https://doi.org/10.1001/jamanetworkopen.2018.0298.
[32] E.C. South, M.C. Kondo, R.A. Cheney, C.C. Branas, Neighborhood blight, stress, and health: a walking trial of urban greening and ambulatory heart rate, Am. J. Publ. Health 105 (2015) 909–913, https://doi.org/10.2105/AJPH.2014.302526.
[33] E. Garvin, C. Branas, S. Keddem, J. Sellman, C. Cannuscio, More than just an eyesore: local insights and solutions on vacant land and urban health, J. Urban Health Bull. N. Y. Acad. Med. 90 (2013) 412–426, https://doi.org/10.1007/s11524-012-9782-7.
[34] H.A. Edwards, D.Y. Monroe, C.D. Mullins, Six ways to foster community-engaged research during times of societal crises, J. Comp. Eff. Res. 9 (2020) 1101–1104, https://doi.org/10.2217/cer-2020-0206.
[35] A.L. Stewart, R.D. Hays, J.E. Ware, The MOS short-form general health survey. Reliability and validity in a patient population, Med. Care 26 (1988) 724–735, https://doi.org/10.1097/00005650-198807000-00007.
[36] T. Hartig, R. Mitchell, S. de Vries, H. Frumkin, Nature and health, Annu. Rev. Publ. Health 35 (2014) 207–228, https://doi.org/10.1146/annurev-publhealth-032013-182443.
[37] A. Nardone, K.E. Rudolph, R. Morello-Frosch, J.A. Casey, Redlines and greenspace: the relationship between historical redlining and 2010 greenspace across the United States, Environ. Health Perspect. 129 (2021) 17006, https://doi.org/10.1289/EHP7495.
[38] J. Roe, C. Thompson, P. Aspinall, M. Brewer, E. Duff, D. Miller, R. Mitchell, A. Clow, Green space and stress: evidence from cortisol measures in deprived urban communities, Int. J. Environ. Res. Publ. Health 10 (2013) 4086–4103, https://doi.org/10.3390/ijerph10094086.
[39] R. Chetty, N. Hendren, P. Kline, E. Saez, Where is the land of opportunity? The geography of intergenerational mobility in the United States, Q. J. Econ. 129 (2014) 1553–1623, https://doi.org/10.1093/qje/qju022.
[40] A.S. Venkataramani, R. O'Brien, G.L. Whitehorn, A.C. Tsai, Economic influences on population health in the United States: toward policymaking driven by data and evidence, PLoS Med. 17 (2020), e1003319, https://doi.org/10.1371/journal.pmed.1003319.
[41] T. Stalder, C. Kirschbaum, B.M. Kudielka, E.K. Adam, J.C. Pruessner, S. Wust, S. Dockray, N. Smyth, P. Evans, D.H. Hellhammer, R. Miller, M.A. Wetherell, S. J. Lupien, A. Clow, Assessment of the cortisol awakening response: expert consensus guidelines, Psychoneuroendocrinology 63 (2016) 414–432, https://doi.org/10.1016/j.psyneuen.2015.10.010.
[42] D.L. Hall, D. Blyler, D. Allen, M.H. Mishel, J. Crandell, B.B. Germino, L.S. Porter, Predictors and patterns of participant adherence to a cortisol collection protocol, Psychoneuroendocrinology 36 (2011) 540–546, https://doi.org/10.1016/j.psyneuen.2010.08.008.
[43] J.L.J. Heaney, A.C. Phillips, D. Carroll, Aging, health behaviors, and the diurnal rhythm and awakening response of salivary cortisol, Exp. Aging Res. 38 (2012) 295–314, https://doi.org/10.1080/0361073X.2012.672134.
[44] R. Ortiz, J.A.L. Gemmill, N. Sinaii, B. Stegmann, I. Khachikyan, G. Chrousos, J. Segars, P. Stratton, Hypothalamic-pituitary-adrenal Axis responses in women with endometriosis-related chronic pelvic pain, Reprod. Sci. Thousand Oaks Calif 27 (2020) 1839–1847, https://doi.org/10.1007/s43032-020-00201-x.
[45] A.L. Pearson, K.A. Pfeiffer, J. Gardiner, T. Horton, R.T. Buxton, R.F. Hunter, V. Breeze, T. McDade, Study of active neighborhoods in Detroit (StAND): study protocol for a natural experiment evaluating the health benefits of ecological restoration of parks, BMC Publ. Health 20 (2020) 638, https://doi.org/10.1186/s12889-020-08716-3.
[46] N. Razani, S. Morshed, M.A. Kohn, N.M. Wells, D. Thompson, M. Alqassari, A. Agodi, G.W. Rutherford, Effect of park prescriptions with and without group visits to parks on stress reduction in low-income parents: SHINE randomized trial, PLoS One 13 (2018), e0192921, https://doi.org/10.1371/journal.pone.0192921.
[47] K.E. Rudolph, G.S. Wand, E.A. Stuart, T.A. Glass, A.H. Marques, R. Duncko, K. R. Merikangas, The association between cortisol and neighborhood disadvantage in a U.S. population-based sample of adolescents, Health Place 25 (2014) 68–77, https://doi.org/10.1016/j.healthplace.2013.11.001.
[48] E.K. Adam, M. Kumari, Assessing salivary cortisol in large-scale, epidemiological research, Psychoneuroendocrinology 34 (2009) 1423–1436, https://doi.org/10.1016/j.psyneuen.2009.06.011.
[49] S. Barber, D.A. Hickson, I. Kawachi, S.V. Subramanian, F. Earls, Double-jeopardy: the joint impact of neighborhood disadvantage and low social cohesion on cumulative risk of disease among African American men and women in the Jackson Heart Study, Soc. Sci. Med. 153 (2016) 107–115, https://doi.org/10.1016/j.socscimed.2016.02.001, 1982.
[50] J.O. Allen, D.C. Watkins, L. Chatters, A.T. Geronimus, V. Johnson-Lawrence, Cortisol and racial health disparities affecting Black men in later life: evidence from MIDUS II, Am. J. Men's Health 13 (2019), 1557988319870969, https://doi.org/10.1177/1557988319870969.
[51] S. Cohen, J.E. Schwartz, E. Epel, C. Kirschbaum, S. Sidney, T. Seeman, Socioeconomic status, race, and diurnal cortisol decline in the coronary artery risk development in young adults (CARDIA) study, Psychosom. Med. 68 (2006) 41–50, https://doi.org/10.1097/01.psy.0000195967.51768.ea.
[52] B.T. Radler, The midlife in the United States (midus) series: a national longitudinal study of health and well-being, Open Health Data 2 (2014) e3, https://doi.org/10.5334/ohd.ai.
[53] X. Wang, B.N. Sánchez, S.H. Golden, S. Shrager, C. Kirschbaum, A.S. Karlamangla, T.E. Seeman, A.V.D. Roux, Stability and predictors of change in salivary cortisol measures over six years: mesa, Psychoneuroendocrinology 49 (2014) 310–320, https://doi.org/10.1016/j.psyneuen.2014.07.024.
[54] T.E. Fuller-Rowell, S.N. Doan, J.S. Eccles, Differential effects of perceived discrimination on the diurnal cortisol rhythm of African Americans and Whites,

Psychoneuroendocrinology 37 (2012) 107–118, https://doi.org/10.1016/j.psyneuen.2011.05.011.
[55] H.M. Lehrer, B.J. Goosby, S.K. Dubois, M.L. Laudenslager, M.A. Steinhardt, Race moderates the association of perceived everyday discrimination and hair cortisol concentration, Stress Amst. Neth. 23 (2020) 529–537, https://doi.org/10.1080/10253890.2019.1710487.
[56] L.J. Samuel, D.L. Roth, B.S. Schwartz, R.J. Thorpe, T.A. Glass, Socioeconomic status, race/ethnicity, and diurnal cortisol trajectories in middle-aged and older adults, J. Gerontol. B Psychol. Sci. Soc. Sci. 73 (2018) 468–476, https://doi.org/10.1093/geronb/gbw080.
[57] R. O'Brien, T. Neman, N. Seltzer, L. Evans, A. Venkataramani, Structural racism, economic opportunity and racial health disparities: evidence from U.S. counties, SSM - Popul. Health 11 (2020) 100564, https://doi.org/10.1016/j.ssmph.2020.100564.
[58] D.W. Brown, R.F. Anda, H. Tiemeier, V.J. Felitti, V.J. Edwards, J.B. Croft, W. H. Giles, Adverse childhood experiences and the risk of premature mortality, Am. J. Prev. Med. 37 (2009) 389–396, https://doi.org/10.1016/j.amepre.2009.06.021.
[59] V.J. Felitti, R.F. Anda, D. Nordenberg, D.F. Williamson, A.M. Spitz, V. Edwards, M. P. Koss, J.S. Marks, Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The adverse childhood experiences (ACE) study, Am. J. Prev. Med. 14 (1998) 245–258.
[60] J.P. Shonkoff, N. Slopen, D.R. Williams, Early childhood adversity, toxic stress, and the impacts of racism on the foundations of health, Annu. Rev. Publ. Health 42 (2021) 115–134, https://doi.org/10.1146/annurev-publhealth-090419-101940.
[61] J.K. Kaholokula, A. Grandinetti, S. Keller, A.H. Nacapoy, T.K. Kingi, M.K. Mau, Association between perceived racism and physiological stress indices in Native Hawaiians, J. Behav. Med. 35 (2012) 27–37, https://doi.org/10.1007/s10865-011-9330-z.
[62] D.M. Almeida, K. McGonagle, H. King, Assessing daily stress processes in social surveys by combining stressor exposure and salivary cortisol, Biodemogr. Soc. Biol. 55 (2009) 219–237, https://doi.org/10.1080/19485560903382338.
[63] K.M. Keyes, D. Westreich, UK Biobank, big data, and the consequences of non-representativeness, Lancet Lond. Engl. 393 (2019) 1297, https://doi.org/10.1016/S0140-6736(18)33067-8.