



Vicarious Racism Stress and Disease Activity: the Black Women's Experiences Living with Lupus (BeWELL) Study

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Abstract

Background Indirect or vicarious exposure to racism (e.g., hearing about or observing acts of racism or discrimination) is a salient source of stress for African Americans. Emerging research suggests that these “secondhand” experiences of racism may contribute to racial health inequities through stress-mediated pathways. Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease that disproportionately impacts African American women and is characterized by racial disparities in severity. Health outcomes in this population may be susceptible to vicarious racism given that SLE is shown to be sensitive to psychosocial stress.

Methods Data are from 431 African American women with SLE living in Atlanta, Georgia in the Black Women's Experiences Living with Lupus (BeWELL) Study (2015–2017). Vicarious racism stress was measured with four items assessing distress from (1) hearing about racism in the news; (2) experiences of racism among friends or family; (3) witnessing racism in public; and (4) racism depicted in movies and television shows. Multivariable linear regression was used to examine associations with disease activity measured using the Systemic Lupus Activity Questionnaire.

Results Adjusting for sociodemographic and health-related covariates, vicarious racism stress was associated with greater disease activity ($b = 2.15$; 95% CI = 1.04–3.27). This association persisted even after adjustment for personal experiences of racial discrimination ($b = 1.80$; 95% CI = 0.67–2.92).

Conclusions Vicarious racism may result in heightened disease activity and contribute to racial disparities in SLE. Our findings suggest that acts of racism committed against members of one's racial group may have distinct health consequences beyond the immediate victim or target.

Keywords Vicarious racism · Systemic lupus erythematosus · African American women · Racial discrimination

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Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease characterized by a myriad of symptoms which are often unpredictable in timing and severity [1, 2]. SLE phenotypes are characterized by a range of mild to life-threatening clinical manifestations, including skin rashes, fever, arthritis, oral ulcers, nephritis, cognitive impairment, and neurologic and hematologic disorders [1, 2]. SLE is estimated to affect up to 322,000 people in the USA, although its distribution is patterned along gender and racial lines [3–5]. Nationally, women are 8–10 times more likely than men to be diagnosed with SLE, and African American women are 2–4 times as likely to have SLE compared with White women [6]. Moreover, African American women are disproportionately burdened by greater disease severity, including earlier onset, increased organ damage, greater comorbidities, and higher mortality rates and at earlier ages compared with White women [5, 7, 8]. Despite well-documented racial disparities in

incidence, prevalence, and disease progression, there remain significant gaps in knowledge on risk factors for SLE outcomes among African American women [4, 8].

Racism, defined as a system that disadvantages particular racial groups, is a distinct risk factor for worse health outcomes among African Americans [9, 10]. Racial discrimination is conceptualized as a level of racism and a qualitatively unique form of psychosocial stress experienced among African Americans [11]. Racial discrimination has been linked with adverse health outcomes through stress-mediated pathways involved in physiologic “weathering” [12, 13]. Prior research has consistently associated racial discrimination with poor mental health and maladaptive health behaviors, albeit to a lesser extent with physical health and biological indicators of disease and aging [14–18]. In the context of SLE, only two studies have linked unfair treatment and racial discrimination to worse disease outcomes among African American women [19, 20].

The majority of empirical research on the health consequences of racism have focused on direct interpersonal experiences of racial discrimination [10, 21, 22]. Investigations of other facets of racism that go beyond direct victimization are in their infancy. For example, emerging lines of research suggest that vicarious racism, as an indirect form of exposure to racism, is a salient source of psychosocial stress and may contribute to racial health inequities [17, 23, 24]. Vicarious racism is described as the “secondhand” exposure to racism, including racial discrimination directed at another individual [17, 25]. It is pervasive and can include witnessing others’ experiences of maltreatment based on race and hearing about racist incidents in the news, as well as the experiences of friends and family [25]. The concept of “linked lives,” which refers to the interconnection of persons and social embeddedness of individual lives, suggests that events which affect one person may have a concurrent impact on others [24, 26]. “Secondhand” exposure to the racist experiences of others may be shared among members of a social group and has the potential to elicit a stress response [27]. Accordingly, public manifestations of racism as well as the racist experiences of others have potential to result in adverse physiological health implications beyond the immediate target.

Recent studies have found evidence for negative health consequences associated with indirect exposure to race-related stress. For example, “spillover” effects of unarmed Black Americans killed by police evince mental health tolls for Black American adults in the general population [28]. Immigration raids and severe sociopolitical stressors have been linked to area-level increases in adverse birth outcomes among infants of racial and ethnic minorities living in the USA [29, 30]; and a racially divisive campus climate has been associated with dysregulated physiologic reactivity among African American college students [31]. Research among children highlights common associations between a child’s

vicarious exposure to parental experiences of racism and adverse mental and socioemotional health outcomes [25]. Similarly, studies on African American mothers have identified that indirect exposure to racism through their children’s experiences with discrimination is a major source of stress [32]. These studies suggest that vicarious racism may be an important health hazard to consider given its salience and prevalence particularly among African American women [32, 33].

As is the case for direct interpersonal discrimination as a source of stress, vicarious racism may negatively impact health outcomes through mental health, behavioral, and physiologic channels [14, 17]. Chronic exposure to stress elicits a cascade of biological processes mediated by the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system which, over time, can cause the “wear and tear” of physiologic systems and accelerate disease progression [12, 34]. Accordingly, repetitive experiences of acute stress result in a heightened inflammatory state which can lead to the premature aging of cells. Racial discrimination has been associated with elevated inflammatory markers, including C-reactive protein and interleukin-6 [16, 35]; these indicators have in turn been linked with worse SLE processes [36, 37]. Exposure to vicarious racism may similarly exacerbate disease progression by undermining shared inflammatory stress-response pathways that have been associated with increased SLE activity.

In an age of increasing media coverage, accessibility of information and nationally publicized events, exposure to vicarious racism may play an increasing role in the health of individuals, especially those with chronic illness [38]. However, to our knowledge, no studies have examined the association between witnessing or observing acts of racism and SLE progression, despite the optimal context given SLE’s inflammatory disease processes and sensitivity to psychosocial stressors. In this study, we examined associations between vicarious racism stress, direct experiences of racial discrimination, and disease activity among African American women with SLE.

Methods

Sample

Data used in this study are from the Black Women’s Experiences Living with Lupus (BeWELL) Study [20]. The BeWELL Study recruited 438 African American women from the Georgians Organized Against Lupus (GOAL) cohort, largely from a population-based registry of validated SLE cases in metropolitan Atlanta, Georgia, with supplemental sampling of participants from the Lupus Clinic of Grady Memorial Hospital and private community rheumatologist

practices [39]. BeWELL includes a full spectrum of participants with validated SLE of varying severity and socioeconomic status, and represents one of the largest studies on the social epidemiology of SLE to date. Data were collected from April 2015 to April 2017. All protocols and procedures were approved by the Institutional Review Board of Emory University and all study participants gave informed signed consent.

Measures

Disease Activity

SLE is characterized by periods of disease activity which wax and wane often unpredictably and are sensitive to psychosocial stress [40, 41]. Disease activity has been shown to predict several SLE outcomes, including irreversible and permanent organ damage [42]. We measured SLE activity using the Systemic Lupus Activity Questionnaire, a validated patient-reported measure developed to assess the presence and severity of disease activity in SLE populations when physician assessment is unfeasible [42]. The scale assesses symptoms of disease activity over the previous 3 months, including fatigue, fevers, oral ulcers, chest pain, and joint swelling, among others [42]. Items are grouped and weighted, with possible scores ranging from 0 to 44. Higher scores represent greater disease activity.

Vicarious Racism Stress

Distress in response to the indirect exposure to racism was measured as the mean of four items developed for the BeWELL Study and based on previous literature [43]. Participants were asked to rate on a 4-point scale from 0 (“not at all”) to 3 (“very much”; Cronbach $\alpha = .83$) “how distressed or bothered you get by the following situations”: (1) hearing people being the victims of racism in the news, (2) hearing about family members or friends who experienced racism, (3) seeing other people in public being treated unfairly because of their race, and (4) seeing racism depicted in movies or television shows.

Everyday Discrimination

Experiences of direct interpersonal racial discrimination were measured using the 10-item Everyday Discrimination Scale [44]. The Everyday Discrimination Scale is a validated self-report instrument which asks participants, “In your day-to-day life, how often do any of the following things happen to you because of your race, ethnicity, or color?”. Items (e.g., being treated with less respect or courtesy, being called names or insulted, receiving poorer service compared with others) assess the frequency of chronic, day-to-day experiences of

unfair treatment [44]. In the current study, the Everyday Discrimination Scale was modified to examine these experiences specifically due to race (Cronbach $\alpha = .91$). We examined the mean response choice across items, which ranged in value from 0 (“never”) to 5 (“almost every day”).

Covariates

Several relevant potential confounders were included in analyses. Demographic variables included age in years and years since diagnosis. Socioeconomic variables included measures of education (less than high school, high school, some college, college graduate, or advanced degree), work status (full-time; part-time; out of labor force, including retired, homemaker, or student; or not working, including those unemployed, laid-off, or unable to work due to health or disability), insurance status (private, public, or none), and ratio of pre-taxed annual household income-to-federal poverty thresholds. Health-related variables included body mass index (weight in kilograms divided by the square of height in meters), measured continuously and based on measured height and weight; self-reported current smoking status (0 = no, 1 = yes); and current SLE medication use of either steroids, hydroxychloroquine, and/or immunosuppressive drugs (0 = no, 1 = yes). Cumulative organ damage was included to adjust for differences in disease severity within the sample and was measured using the Brief Index of Lupus Damage, a validated measure of irreversible damage across 12 organ systems [45]. The Brief Index of Lupus Damage consists of 26 self-reported items which assess cumulative organ damage since the onset of SLE and present for at least 6 months. Items (e.g., “Have you ever had a skin ulcer that lasted 6 months or longer?” and “Has a doctor ever told you that you had osteoporosis that resulted in a fracture?”) are endorsed as either present or absent. Possible scores range from 0 to 30 and higher scores indicate greater damage.

Statistical Analysis

Eleven participants reported their household income but were missing data on whether it was before or after taxes. For these participants, we averaged the corresponding pre-tax amount (assuming the figure reported was after taxes) with the amount that was reported assuming it was prior to taxes. Seven participants with missing data on any variable (1.6%) were excluded from analyses, yielding a final analytic sample size of 431.

Bivariate associations between disease activity and other continuous variables were assessed with Pearson’s correlation analyses. Bivariate correlations between disease activity and categorical variables were assessed with *t* tests for dichotomous variables and ANOVAs for variables with three or more categories. A series of nested regression models examining predictors of SLE activity was estimated with covariates

added in block groups. Model 1 examined vicarious racism stress in relation to SLE activity controlling for age and years since diagnosis. Model 2 additionally adjusted for socioeconomic covariates. In model 3, health-related covariates were added. Everyday discrimination was added in the final model (Model 4). Post hoc model diagnostics were examined, and exploratory moderation analyses investigated whether vicarious racism stress and direct interpersonal discrimination exacerbated the effects of one another on SLE activity.

Results

The mean participant age was 46.83 years (SD = 12.32) with a mean disease duration of 15.98 years (SD = 10.39). The mean SLE activity score was 15.11 (SD = 7.97). Participants reported being highly distressed or bothered due to vicarious exposure to racism (median = 2.75; interquartile range = 0.75). Participants most frequently reported experiencing at least one form of direct interpersonal racial discrimination less than once per year, with only 48 participants reporting no experiences of direct interpersonal racial discrimination. Bivariate correlations indicated significant associations between vicarious racism stress and SLE activity ($r = 0.11$; $p < 0.05$); everyday discrimination and SLE activity ($r = 0.17$; $p < 0.001$); and vicarious racism stress with everyday discrimination ($r = 0.17$; $p < 0.001$). Additional bivariate correlations with disease activity and sample characteristics are presented in Table 1.

Results from multivariable analyses for final models adjusting for additional covariates are shown in Table 2. In Model 1, vicarious racism stress was found to be associated with SLE activity adjusting for age and years since diagnosis ($b = 1.45$; 95% confidence intervals [CI] 0.17, 2.74). Vicarious racism stress remained significantly associated with SLE activity after adjusting for socioeconomic covariates (Model 2; $b = 1.92$; 95% CI 0.73, 3.11) and health-related covariates (Model 3; $b = 2.15$; 95% CI 1.04, 3.27). When models were further adjusted for everyday discrimination (Model 4; $b = 1.14$; 95% CI 0.42, 1.86), vicarious racism stress remained significantly associated with SLE activity ($b = 1.80$; 95% CI 0.67, 2.92).

Regression diagnostics were conducted to check for influential observations and outliers. Tests consistently revealed three observations with high values of Cook's D and DFFITS which indicate observations with the greatest residual and leverage. Removing these observations did not lead to substantively different conclusions; however, unstandardized effect estimates increased for vicarious racism stress ($b = 2.27$; 95% CI 1.17, 3.40) and marginally decreased for everyday discrimination ($b = 1.04$; 95% CI 0.34, 1.74).

Post hoc analyses examined moderation between vicarious racism and everyday discrimination using the corresponding

mean-centered terms and their interaction. No evidence for effect modification was found ($b = 0.30$; 95% CI - 0.90, 1.49).

Discussion

Only a handful of studies have examined how racial discrimination and racism-related incidents may have collateral effects on individuals beyond the immediate victim. Accordingly, scholars have highlighted the need for future research to examine vicarious racism in the context of racial health inequities [9, 24, 46]. This study is the first to our knowledge that examines vicarious racism in relation to disease severity specifically in the context of SLE, a condition that disproportionately burdens African American women with accelerated disease progression [5, 7, 8]. We found that both greater reports of vicarious racism stress and direct experiences of racial discrimination were positively associated with disease activity after adjusting for demographic, socioeconomic, and health-related covariates. Vicarious racism stress remained significantly associated with heightened disease activity even after adjusting for direct experiences of racial discrimination. Our results support previous research suggesting that, similar to more commonly studied direct experiences of racial discrimination, “secondhand” exposure to racism and racism-related stress may exacerbate disease processes and contribute to racial disparities in health.

Findings from this study are in line with past research on direct interpersonal experiences of unfair treatment, racial discrimination, and SLE outcomes [19, 20]. Direct experiences of racial discrimination are a form of psychosocial stress which may affect health through pathways involved with physiological “weathering” and the “wear and tear” of biological systems [12, 34]. Racial discrimination has been associated with biomarkers of inflammation, which are involved in the pathogenesis of SLE and relevant to accelerated disease activity [16, 35–37].

Although there are past studies on general perceptions about discrimination against one's racial group [47, 48], fewer have explicitly examined the health implications of vicarious racism, or directly witnessing, hearing about, or observing acts of discrimination and racism against one's racial group. Our findings extend research on group discrimination and are consistent with conceptualizations of “linked lives” which posit that the direct experiences of others may be shared among members of the same social group, and that such experiences may also become embodied [24, 26]. Previous research robustly demonstrates that indirect exposures to race-related trauma have deleterious effects on health, particularly for racial and ethnic minorities. For example, police killings of unarmed Black Americans are associated with increased poor mental health days for Black Americans in the general population, although not for White Americans [28]. State-level

Table 1 Descriptive characteristics of African American women with systemic lupus erythematosus (SLE), bivariate associations with disease activity (SLAQ), and mean SLAQ scores: BeWELL Study (2015–2017) ($n = 431$)

Variable	Mean (SD)	No. (%)	Mean SLAQ (SD)	Bivariate association with SLAQ
Disease activity (SLAQ)	15.11 (7.97)			
Vicarious racism stress	2.54 (0.59)			.11 [†] , *
Everyday discrimination	1.23 (0.95)			.17 [†] , ***
Age	46.83 (12.32)			−.01 [†]
Years since diagnosis	15.98 (10.39)			−.04 [†]
Education				3.89 [‡] , **
Less than high school		36 (8.35)	17.33 (7.47)	
High school		77 (17.87)	15.83 (7.15)	
Some college		196 (45.48)	16.61 (7.59)	
≥ Bachelor's degree		122 (28.31)	11.60 (8.15)	
Work status				18.44 [‡] , ***
Full-time		124 (28.77)	11.70 (7.71)	
Half-time		54 (12.53)	13.24 (7.03)	
Out of labor force		21 (4.87)	12.95 (7.91)	
Not working		232 (53.83)	17.57 (7.50)	
Insurance status				14.00 [‡] , ***
Private		155 (35.96)	12.57 (7.77)	
Public		228 (52.90)	16.83 (7.59)	
None		48 (11.14)	15.19 (8.27)	
Income-to-poverty ratio	2.01 (1.68)			−.32 [†] , ***
Body mass index ^a	30.93 (8.10)			.10 [†] , *
Smoking status				−39.31 [§] , ***
No		369 (85.61)	14.49 (7.79)	
Yes		62 (14.39)	18.85 (8.03)	
Steroids				−38.30 [§] , ***
No		192 (44.55)	13.54 (7.47)	
Yes		239 (55.45)	16.38 (8.14)	
Hydroxychloroquine				−37.27 [§] , ***
No		116 (26.91)	16.45 (8.50)	
Yes		315 (73.09)	14.62 (7.72)	
Other immunosuppressants				−38.27 [§] , ***
No		240 (55.68)	14.98 (7.93)	
Yes		191 (44.32)	15.28 (8.03)	
SLE organ damage	2.77 (2.50)			.32 [†] , ***

BeWELL Black Women's Experiences Living with Lupus

^a Weight (kg)/height (m)²* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ [†] Bivariate association from Pearson's correlation analysis, r [‡] Bivariate association from one-way analysis of variance, F -statistic[§] Bivariate association from t test

increases in adverse birth outcomes following an immigration raid have been documented for infants born to immigrant Latina mothers but not non-Latina White mothers [29]. The 2006 Duke lacrosse scandal demonstrated the effects of a racially divisive campus climate on African American students' heightened baseline cortisol and blunted stress response [31]. Taken together, results from this study contribute to the

increasing documentation on the health effects of "secondhand" exposure to racism-related stress among racial and ethnic minorities living in the United States.

Our findings advance the literature on vicarious racism and health in several ways. Previous research on vicarious racism has focused primarily in the context of caregiving or childrearing (e.g., caregiver-experienced discrimination or

Table 2 Multivariable linear regression analysis of disease activity among African American women in the Black Women’s Experiences Living with Lupus (BeWELL) Study (2015–2017) (*n* = 431)

Variable	Model 1		Model 2		Model 3		Model 4	
	<i>b</i>	95% CI	<i>b</i>	95% CI	<i>b</i>	95% CI	<i>b</i>	(95% CI)
Vicarious racism stress	1.45	(0.17, 2.74)	1.92	(0.73, 3.11)	2.15	(1.04, 3.27)	1.80	(0.67, 2.92)
Age	0.02	(−0.06, 0.09)	0.02	(−0.05, 0.10)	−0.01	(−0.08, 0.06)	−0.01	(−0.08, 0.06)
Years since diagnosis	−0.04	(−0.13, 0.05)	−0.05	(−0.13, 0.03)	−0.08	(−0.16, 0.00)	−0.08	(−0.16, −0.01)
Education (ref: < high school)								
High school			−1.09	(−4.02, 1.84)	−0.57	(−3.34, 2.20)	−0.32	(−3.07, 2.42)
Some college			0.17	(−2.47, 2.80)	−0.01	(−2.51, 2.49)	−0.17	(−2.65, 2.30)
≥ Bachelor’s degree			−2.47	(−5.40, 0.47)	−1.96	(−4.77, 0.85)	−2.27	(−5.06, 0.52)
Work status (ref: full-time)								
Half-time			−0.16	(−2.70, 2.38)	−0.55	(−2.96, 1.86)	−0.64	(−3.02, 1.75)
Out of labor force			1.24	(−2.41, 4.88)	1.55	(−1.91, 5.00)	1.73	(−1.69, 5.15)
Not working			3.83	(1.76, 5.90)	2.31	(0.28, 4.34)	2.34	(0.33, 4.35)
Insurance status (ref: private)								
Public			−0.58	(−2.61, 1.44)	−0.67	(−2.57, 1.22)	−0.47	(−2.35, 1.41)
None			−1.30	(−3.91, 1.31)	−0.96	(−3.42, 1.50)	−0.67	(−3.11, 1.77)
Income-to-poverty ratio			−1.05	(−1.58, −0.52)	−0.98	(−1.47, −0.48)	−0.94	(−1.43, −0.45)
Body mass index ^a					0.11	(0.03, 0.20)	0.08	(0.00, 0.17)
Smoker: yes vs no					3.53	(1.60, 5.45)	3.19	(1.28, 5.11)
Steroids: yes vs no					1.85	(0.41, 3.28)	1.90	(0.48, 3.32)
Hydroxychloroquine: yes vs no					−1.21	(−2.74, 0.32)	−1.22	(−2.73, 0.30)
Other immunosuppressants: yes vs no					−0.31	(−1.74, 1.11)	−0.32	(−1.72, 1.09)
SLE organ damage					0.85	(0.55, 1.14)	0.81	(0.52, 1.10)
Everyday discrimination							1.14	(0.42, 1.86)

CI confidence interval

^a Weight (kg)/height (m)²

offspring-experienced discrimination); in laboratory settings; with sole emphasis on socioemotional, behavioral, or mental health outcomes; or with measures which assess direct and indirect discrimination concurrently [17, 25, 43, 49]. This is one of few studies that examine vicarious racism in relation to physical health outcomes among a relatively large sample of adult African American women. Our results suggest that exposure to vicarious racism has deleterious effects on physical health among this group. Additionally, our findings indicate that vicarious racism stress is associated with disease activity independent of direct interpersonal experiences of racial discrimination. This is important to consider in light of the continued perpetration and increasing visibility of racism, and a broader hostile racial climate in the United States. Recent reports indicate a 17% increase in hate crimes from 2016 to 2017, and that 92% of African Americans believe that discrimination against their group is prevalent in the USA [50–52]. The modern age of social media, news coverage, and continuous stream of nationally publicized events serves to amplify the pervasiveness of vicarious racism stress and its potential health effects [38]. Accordingly, the timing of this

study (2015–2017) and changing sociopolitical climate may have affected the salience of vicarious racism for African American women in the BeWELL sample [38]. Using data from the same time period, a recent study found post-inauguration increases in preterm birth rates among immigrant, Hispanic, and Muslim populations in New York City compared with the pre-inauguration period, which the authors attribute to severe sociopolitical stressors [30].

Several study limitations are important to note. Conclusions regarding the causal direction cannot be determined given the cross-sectional nature of the data. Our interpretation, however, is consistent with other literature showing that direct experiences of racial discrimination may lead to poor disease outcomes [10, 17, 22]. The inconsistency of exposure assessment between measures of direct racial discrimination (e.g., frequency) and vicarious racism (e.g., perceived severity) limits the ability for direct comparison of racism-related stressors. BeWELL participants are from a specific geographic area and our results may not be generalizable to those living in other regions of the USA. Although the outcome measure of disease activity (Systemic Lupus Activity

Questionnaire) has demonstrated reliability and validity in previous epidemiologic research, it is limited by its self-report nature [42]. Moving forward, longitudinal and nationally representative data will be critical in understanding how exposure to vicarious racism stress, including frequency and perceived severity, may be associated with changes in SLE activity and other objective measures of disease over time. Future research should consider potential mediators and moderators of this relationship to identify protective factors or coping strategies which may buffer the effects of vicarious racism on SLE activity.

This study advances the scientific literature on the social epidemiology of SLE and is the first to provide evidence of the deleterious health effects of vicarious racism stress, an understudied dimension of racism, in the context of this disease. Importantly, findings from this study have critical public health and policy implications considering heightened racial tensions and visibility of racism. Moving forward, public health efforts should raise awareness of the “secondhand” exposure to racism as a potential health risk factor more broadly. Similar to reducing the harmful effects of secondhand smoke by targeting underlying rates of smoking, an appropriate public health response to vicarious racism is to address racial discrimination and racism itself. Relevant policy implications may involve the enactment and strict enforcement of anti-discrimination policies to reduce the continued perpetration of racism. Additional public health implications include the formation of support groups in the aftermath of high-profile racist events, similar to mass shootings and other traumatic events, which may provide an effective coping mechanism for those experiencing distress [53, 54]. Results from this study join a growing body of evidence which highlights the need to eliminate racial discrimination and the structural systems which foster and perpetuate these acts in order to advance health equity and improve population health.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Institutional Review Board approval was obtained for the study.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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