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Neighborhood-Level Adversity and Inflammation Among Sexual Minority Men Living With HIV

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Objective: This cross-sectional study investigated the associations of neighborhood-level factors with immune activation, systemic inflammation, and leukocyte telomere length in 110 sexual minority men with human immunodeficiency virus. ***Method:*** From 2013 to 2017, sexual minority men with human immunodeficiency virus who used stimulants were recruited in San Francisco, California and provided blood samples to measure the markers of immune activation, systemic inflammation, and leukocyte telomere length. To measure neighborhood-level indices, the home address for each participant was geocoded and linked to data from the Centers for Disease Control and Prevention. Hierarchical linear modeling was employed to investigate the associations of neighborhood-level factors with systemic inflammation and leukocyte telomere length. ***Results:*** After adjusting for age, stimulant use, self-reported income, level of education, and race and ethnicity, residing in neighborhoods with greater percentages of poverty ($\beta = .33$, $p < .001$) and a higher proportion of racial/ethnic minority residents ($\beta = .26$, $p < .05$) were independently associated with higher levels of interleukin-6. Additionally, residing in neighborhoods with higher percentage of uninsured individuals was independently associated with higher tumor necrosis factor-alpha ($\beta = .24$, $p < .05$). Indices of neighborhood-level adversity were additionally associated with providing a urine sample that was reactive for stimulants ($OR = 1.31$, $p = .002$), which was, in turn, associated with shorter leukocyte telomere length ($\beta = -.31$, $p < .05$). ***Conclusions:*** Future longitudinal research should examine the biobehavioral pathways linking neighborhood-level factors and stimulant use with systemic inflammation and cellular aging.

Public Significance Statement
This study shows how neighborhood factors can impact the health of sexual minority men with human immunodeficiency virus. The research found that living in resource-poor neighborhoods was linked to higher systemic inflammation, substance use, and in turn faster aging at the cellular level. These findings highlight the need to address community- and neighborhood-level inequalities to improve the health of sexual minority men with human immunodeficiency virus.

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There is burgeoning evidence that where individuals live—including their homes, natural, and built environments, schools, workplaces, and neighborhoods and communities—significantly influences health outcomes, susceptibility to diseases, and overall well-being (Centers for Disease Control and Prevention, 2020; U.S. Department of Health and Human Services, 2021). Recent findings from a cross-sectional study using the National Neighborhood Data Archive indicated that residing in neighborhoods with lower socioeconomic status was associated with higher levels of cytomegalovirus immunoglobulin G and greater rates of immunosenescence (Noppert et al., 2024). Immunosenescence, which also occurs with chronological aging, is characterized by a gradual decline in immune system function, as evidenced by a reduced ratio of effector memory to naïve cluster of differentiation 4 T-helper cells (Weyand & Goronzy, 2016). Interestingly, the association of neighborhood-level factors with higher cytomegalovirus immunoglobulin G levels and immunosenescence persisted after adjusting for individual-level socioeconomic status and race and ethnicity. Comparatively, the Detroit Neighborhood Health Study observed the associations of poorer neighborhood quality with a faster epigenetic clock—a measure of accelerated cellular aging derived from measures of deoxyribonucleic acid (DNA) methylation—associated with early-onset chronic disorders (Martin et al., 2021). These associations were moderated by neighborhood-level social cohesion such that the association of poorer neighborhoods quality with a faster epigenetic clock was significant only in those residing in neighborhoods with lower social cohesion. Similarly, a recent study using data from the 1999–2020 National Health and Nutrition Examination Surveys observed that a medium and high neighborhood deprivation index rates was in fact inversely associated with shorter leukocyte telomere length, a measure of the protective cap on chromosomes that indexes accelerated cellular aging, linked to early-onset chronic disorders such as a variety of cardiovascular diseases (Powell-Wiley et al., 2020).

It is important to note that some adverse neighborhood-level factors such as neighborhood rates of poverty serve as a proxy for segregation and redlining—the discriminatory practice of denying or limiting financial services—such as loans and insurance to certain neighborhoods or communities based on racial or ethnic composition (Egede et al., 2023). This may lead to displacement to less desirable neighborhoods because of gentrification and socioeconomic and demographic changes and other forms of structural racism such as housing discrimination and healthcare disparities based on disadvantaging certain racial or ethnic groups while advantaging others (Lynch et al., 2021). Redlining and segregation are additionally associated with higher rates of involvement with the criminal justice system (Poulson et al., 2021), which can significantly impact an individual's health, both physically and mentally. In fact, interactions with the justice system—such as arrest, incarceration, or legal proceedings—can lead to increased distress, anxiety, and depression, which can significantly impact the immune function (Boen, 2020; Ghanooni et al., 2024).

Among sexual minority men (SMM), the use of methamphetamine (meth) and other stimulants (e.g., cocaine and crack cocaine) is additionally prevalent and associated with immune activation, systemic inflammation, and accelerated cellular aging, beyond the effects of human immunodeficiency virus (HIV) infection and the impacts of macro-level factors. In the United States, one in five (i.e., 21%; 95% confidence interval [CI] = [13%, 28%]) SMM report recent meth use (Lodge et al., 2024). The prevalence of meth use is generally higher among SMM with HIV because it is a risk factor for HIV acquisition and unsuppressed viral load, which amplifies risk for onward HIV transmission (Grov et al., 2020). SMM with HIV who use meth are additionally more likely to experience difficulties with antiretroviral therapy (ART) adherence and persistence resulting in unsuppressed viral load (i.e., ≥200 copies/ml), which amplifies further immune dysregulation and inflammation (Passaro et al., 2015). Irrespective of HIV status, however, there is evidence that stimulant use such as meth is associated with elevations in soluble markers of immune activation, systemic inflammation, and shorter leukocyte telomere length (Cherenack et al., 2023; Mehta et al., 2021). Previous cross-sectional studies with treated SMM who were virally suppressed further observed stimulant-associated elevations in soluble cluster of differentiation 14 and soluble cluster of differentiation 163 (sCD163), measures of monocyte and macrophage activation (Carrico, Cherenack, et al., 2018; Miller et al., 2020). Moreover, recent stimulant use and injection meth use are additionally associated with measures of systemic inflammation such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and soluble tumor necrosis factor-α receptor I (sTNF-αRI) in SMM with treated HIV (Carrico, Cherenack, et al., 2018; Miller et al., 2020). Although meth use and individual-level involvement with the criminal justice system and specifically having a history of arrest are associated with greater immune activation and systemic inflammation (Ghanooni et al., 2024), studies on associations of meth use and neighborhood-level factors with markers of immune dysfunction and accelerated cellular aging in SMM with and without HIV are scarce.

In addition, an important gap is that prior studies have not sufficiently placed stimulant use such as meth in its social and structural context by examining the broader macro-level determinants. The relevance of macro-level determinants is supported in part by findings that neighborhood-level factors are associated with diminished effectiveness of HIV treatment as prevention in SMM (Mannheimer et al., 2019). In densely populated economically disadvantaged neighborhoods, SMM with HIV additionally face an increased risk of experiencing delays in initiating ART and achieving viral suppression (Latkin et al., 2013). Even with more available resources and transportation in urban areas, individuals in economically disadvantaged neighborhoods face challenges such as higher demands for services, lower rates of available preventive care, longer wait times, and fewer opportunities to take time off work, which are compounded by individual-level risk factors such as housing instability and negative mental health outcomes (e.g., depressive symptoms) that can collectively lead to delays in ART initiation and adherence (Brawner et al., 2022). These difficulties with managing ART may explain the associations of neighborhood-level factors with unsuppressed

viral load, which amplifies onward HIV transmission risk (Rodger et al., 2019). More research is needed to elucidate the complex biobehavioral mechanisms, whereby neighborhood-level adversity could influence markers of immune activation, inflammation, and cellular aging that are relevant to health outcomes among people with and without HIV.

This cross-sectional study leveraged data from the baseline assessment of a randomized controlled trial that enrolled SMM with HIV with biologically verified, recent stimulant use (Carrico, Gómez, et al., 2018). As seen in Figure 1, we investigated the associations of indices of neighborhood-level adversity with immune activation, systemic inflammation, and leukocyte telomere length in an urban setting, San Francisco, California, United States. The primary objective was to determine the independent associations of neighborhood-level factors (e.g., estimated percentage of neighborhood poverty below 150% federal poverty level [FPL], estimated percentage of neighborhood rates of unemployment, estimated percentage of residing individuals without health care insurance, and neighborhood estimated percentage of individuals reporting a racial/ethnic minority status) with markers of immune activation, systemic inflammation, and leukocyte telomere length in this high priority population. Specifically, we hypothesized that residing in an urban neighborhood with greater adversity would be independently associated with higher levels of soluble markers of immune activation and inflammation as well as accelerated cellular aging after adjusting for age, stimulant use, self-reported income, level of education, and race and ethnicity. Guided by Social Action Theory (Ewart, 1991), we additionally proposed that indices of neighborhood-level adversity would function as key action contexts to influence individual-level self-regulatory behaviors such as stimulant use that, in turn, are associated with the biological outcomes of interest. As shown in Figure 1, we also tested the indirect associations of neighborhood-level factors with immune activation, systemic inflammation, and cellular aging via stimulant use.

Method

From 2013 to 2017, SMM with HIV who used stimulants in the San Francisco metropolitan area were enrolled in a randomized controlled trial (Carrico, Gómez, et al., 2018; Carrico et al., 2019). Participants were all cisgender SMM who met the following inclusion criteria: (a) 18 years of age or older, (b) reported engaging in anal sex with a man within the past 12 months, (c) fluent in English, (d) provided documentation proving HIV-positive serostatus (such as a diagnosis letter or evidence of being on ART medications), and (e) provided a urine or hair sample that was reactive for stimulant metabolites. This cross-sectional study used baseline data from 110 SMM with HIV that provided blood plasma and extracted leukocyte DNA to measure soluble markers of immune activation, inflammation, and leukocyte telomere length.

Measures

Sociodemographic Factors and ART Adherence

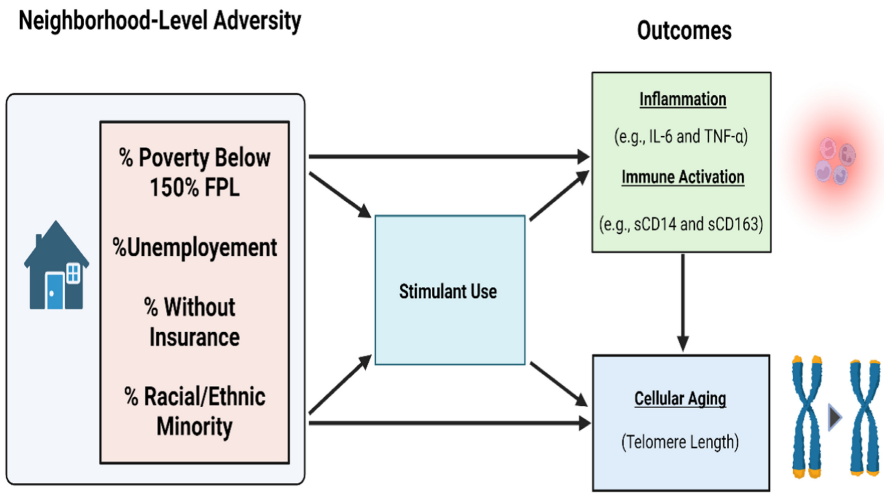
Sociodemographic factors included age, race/ethnicity, time since HIV diagnosis (years), education level, and income. Participants additionally reported their current ART regimen and adherence over the past 30 days using a visual analog scale (Finitsis et al., 2016).

Stimulant Use

Participants self-reported the frequency of recent stimulant use including meth, powder cocaine, and crack-cocaine in the past 3 months. Each stimulant drug was reported separately on a Likert-type scale from 0 (*not at all*) to 7 (*daily*). In addition, participants provided urine samples, which were collected for on-site screening of stimulant urine metabolites using the

Figure 1

Hypothesized Associations of Neighborhood-Level Factors With Immune Activation, Systemic Inflammation, and Leukocyte Telomere Length in SMM With HIV Who Use Stimulants



Note. SMM = sexual minority men; HIV = human immunodeficiency virus; FPL = federal poverty level; IL-6 = interleukin-6; TNF-α = tumor necrosis factor-alpha; sCD14 = soluble CD14; sCD163 = soluble CD163. See the online article for the color version of this figure.

iCup device (Redwood Biotech, Inc., Santa Rosa, California). Participants engaging in recent stimulant use had reactive urine toxicology results for meth, cocaine, or both within the past 72 hr.

Neighborhood-Level Factors

Neighborhood-level data were obtained from merging participants' addresses with previously published geodata by Centers for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry, and Social Vulnerability Index outcomes using geographic information systems (Centers for Disease Control and Prevention, 2020). Estimated rates of neighborhood-level poverty below 150% FPL, unemployment, individuals without health care insurance, and neighborhood estimated percentage of individuals with a racial/ethnic minority status were measured. Estimated rates of neighborhood poverty below 150% FPL, unemployment, individuals without health care insurance, and percentage of individuals with a racial/ethnic minority status were specifically selected as proxies for neighborhood population income, residential stability, structural racism, and levels of investment and quality of resources in residing neighborhoods (Swaroop & Krysan, 2011; Yang & South, 2020).

Soluble Markers of Immune Activation and Systemic Inflammation

Soluble markers of immune activation included sCD14 and sCD163. Soluble markers of systemic inflammation included IL-6, TNF-α, soluble TNF-α receptor I (sTNF-αRI), and soluble tumor necrosis factor-alpha-α receptor II (sTNF-αRII). The soluble markers of immune activation and inflammation were quantified in plasma using the Human Quantikine Immunoassay (R&D Systems, Minneapolis, Minnesota, United States), following the manufacturer's instructions.

Leukocyte Telomere Length

Mean relative telomere length was indirectly measured as the ratio of telomeric product/single copy gene obtained from the quantitative polymerase chain reaction (qPCR) technique as described elsewhere (Cawthon, 2002; Lin et al., 2010). The purpose of measuring a single copy gene (i.e., one that occurs once in the human genome) is to normalize the estimated number of telomere repeats in the sample by the number of genome equivalents as the proxy for the number of cells in the sample. Samples were amplified using the QuantiNova SYBR Green polymerase chain reaction kit from QIAGEN. All samples were measured in quintuplicate, and the mean of at least three valid replicates was used in subsequent analyses. Outlier estimates (defined as $\geq$1.5 *SD* units) were excluded. If three replicates could not be retained, the qPCR sample was repeated. For each reaction, 4 ng of genomic DNA for each unknown sample was used as the template for polymerase chain reaction. For each qPCR experiment, one intraplate and one interplate control sample were included to assess for intraplate and interplate variability using the coefficient of variation. The purchased control genomic DNA sample was employed to create the standard curve and was also used to normalize assay plates by computing the geometric mean of the control DNA sample on each assay plate.

Statistical Analyses

Hierarchical linear modeling was employed to examine the associations of neighborhood-level factors with markers of immune activation, systemic inflammation, and leukocyte telomere length. In this model, Level 1 model represented individual predictors and the outcome, while Level 2 represented neighborhood-level predictors and the Level 1 coefficients. Given the nested nature of study participants within neighborhoods, mixed procedure in SAS statistical software was used to examine the associations of indicators of neighborhood-level factors with plasma levels of sCD14, sCD163, IL-6, TNF-α, soluble sTNF-αRI, sTNF-αRII, and leukocyte telomere length. Due to skewness of data, sTNF-αR and sTNF-αRII were $\log_{10}$ transformed.

The bivariate associations among indices of neighborhood-level adversity were primarily examined to avoid multicollinearity in hierarchical linear modeling models (Johnston et al., 2018). To minimize multicollinearity, we subsequently removed neighborhood-level factors that exhibited Pearson correlation coefficients of 0.5 or higher with the variable of poverty below 150% FPL. This resulted in the exclusion of the following neighborhood-level factors: neighborhood-level rates of housing cost burden, multiunit housing structures, crowding, and residing in group quarter facilities.

After the assessment of the unconditional models, estimated percentage of neighborhood individuals living below 150% FPL, neighborhood-level percentages of unemployment, proportion of individuals without health care insurance, and estimated percentage of neighborhood individuals with a racial/ethnic minority status were introduced as Level 2 predictors of immune activation, systemic inflammation, and leukocyte telomere length. All models were adjusted for chronological age, stimulant use, self-reported income, level of education, and race/ethnicity. Moreover, we performed sensitivity analyses to specifically determine how variations in neighborhood-level factors affect our outcomes while restricting the sample to participants with an undetectable viral load (<40 copies/ml) to determine if these associations remained among those who were achieving adequate levels of ART adherence.

Finally, we examined the associations of neighborhood-level factors with the self-reported frequency of stimulant use in the past 90 days as well as recent stimulant use to determine whether neighborhood factors were directly associated with stimulant use. Informed by these results and our hypothesized model (see Figure 1), we additionally examined the indirect associations of neighborhood-level factors with immune activation, systemic inflammation, and shorter telomere length via stimulant use.

Results

As shown in Table 1, the current study enrolled a diverse sample of 110 SMM living with HIV between 2013 and 2017 from eight neighborhoods out of 65 census tracts in San Francisco metropolitan area. The distribution of participants across neighborhoods varied significantly. Most participants (43.7%) resided in a single neighborhood (Tenderloin), while the remaining participants were distributed as follows: Mission District (14.5%), South of Market (9%), Chinatown (15.5%), Sunset District (6.4%), Castro (2.8%), Richmond District (3.7%), and Pacific Heights (4.5%). While the study neighborhoods had an average household income of $100,000 (*SD* = $35,355.34), a large portion of participants ($n = 48$) resided in San Francisco's

Table 1
Demographic Characteristics at Baseline (N = 110)

Demographic characteristics	*M* (*SD*)
Age	43.2 (9.2)
Time since HIV diagnosis (years)	13.4 (8.9)
Demographic characteristics	***N*** **(%)**
Race/ethnicity	
Black/African American	18 (16.4)
White	47 (42.7)
Hispanic/Latino	32 (29.0)
Other ethnic minority	13 (11.8)
Education	
Less than high school	8 (7.3)
High school graduate	17 (15.5)
Some college/trade school	57 (51.8)
College graduate	17 (15.25)
Postgraduate	11 (10.0)
Income	
<$4,999	16 (14.7)
$5,000–$11,999	28 (25.7)
$12,000–$15,999	27 (24.8)
$16,000–$24,999	12 (11.0)
$25,000–$34,999	9 (8.3)
$35,000–$49,999	7 (6.4)
>$50,000	2 (0.9)

Note. HIV = human immunodeficiency virus.

Tenderloin neighborhood, which has the lowest median household income ($45,000), the highest rate of uninsured residents (20%), and a predominantly racial or ethnic minority population, comprising 85% of households (see Supplemental Table in the online supplemental materials). Participants' ages varied from 24 to 59 years, with an average age of 43.2 ($SD = 9.2$). Approximately 47% of the participants were non-Hispanic White, while 32% identified as Hispanic/Latino, 18% as Black/African American, and 13% as other including Asian, Native Hawaiian and Pacific Islander, and multiracial. Most participants (57%) had completed at least some college education with an unemployment rate of 39%. Additionally, most study participants (71%) had undetectable HIV viral load (<40 copies/ml).

Table 2 summarizes the standardized associations of neighborhood-level factors with markers of immune activation, systemic inflammation, and leukocyte telomere length. After adjusting for chronological age and recent stimulant use as well as individually reported annual income, level of education, and race and ethnicity, residing in neighborhoods with higher estimated percentages of poverty below 150% FPL was independently associated with greater plasma IL-6 levels ($\beta = .32$, $p < .001$). Similarly, residing in neighborhoods with higher estimated percentages of individuals reporting a racial/ethnic minority status were associated with higher levels of plasma IL-6 ($\beta = .26$, $p < .05$). Moreover, residing in neighborhoods with higher estimated percentage of individuals without a health care insurance was independently associated with higher TNF-α ($\beta = .24$, $p < .05$), after adjusting for age, recent stimulant use, individually reported annual income, level of education, and race and ethnicity. The findings remained consistent after performing sensitivity analyses that restricted the sample to participants with an undetectable viral load while controlling for self-reported ART adherence.

Subsequently, residing in neighborhoods with higher estimated rates of poverty below 150% FPL were significantly associated with greater odds of recent biologically confirmed stimulant use ($OR = 1.31$, $p = .002$) as well as greater self-reported use of stimulants at least once per week ($OR = 1.24$, $p = .01$). Residing in neighborhoods reporting a greater percentage of racial and ethnic minority individuals was associated with higher odds of recent biologically confirmed stimulant use ($OR = 1.22$, $p = .04$). There were no significant indirect associations of neighborhood-level factors on markers of immune activation, immune dysregulation, and leukocyte telomere length via biologically confirmed recent stimulant use or self-reported stimulant use at least weekly. However, recent stimulant use was associated with shorter telomere length ($\beta = -.31$, $p = .002$).

Discussion

The findings from this cross-sectional study underscore the importance of placing individual-level risk factors such as stimulant use in their social and structural context by examining neighborhood-level factors. Drawing on Social Action Theory (Ewart, 1991), we proposed that neighborhood-level factors would serve as a critical context influencing individual self-regulatory behaviors, such as stimulant use, which are subsequently linked to this study's biological outcomes. This perspective suggests that the neighborhood and social environment play pivotal roles in shaping biological changes that directly impact health. After adjusting for chronological age, recent stimulant use, and individually reported annual income, level of education, and race/ethnicity, indices of neighborhood-level adversity were independently associated with greater systemic inflammation but not immune activation. Participants who resided in neighborhoods with higher rates of poverty also had higher odds of recent stimulant use that was, in turn, significantly associated with accelerated cellular aging indexed by shorter leukocyte telomere length.

The findings from this study align with previous research in the broader population (Sullivan et al., 2019). Living in impoverished neighborhoods may function as a chronic stressor that leads to physiological dysregulation of the sympathetic nervous system. In fact, adverse neighborhood-level factors have been collectively linked to the dysregulation of the hypothalamus–pituitary–adrenal axis and the activation of autonomous nervous system, resulting in increased levels of immune dysregulation and systemic inflammation (Boscolo et al., 2012; McWilliams, 2009; Meyer, 2003). This, in turn, contributes to a chronic inflammatory state that is highly detrimental, playing a significant role in accelerated cellular aging and the subsequent early onset and progression of chronic conditions such as cardiovascular disease and specific types of cancer (Donath & Shoelson, 2011; Libby, 2006).

Residing in resource-poor neighborhoods often limits health care access, routine preventive checkups, and necessary screenings and treatments (Cattell, 2001). Financial barriers, such as inability to afford health insurance or higher out-of-pocket expenses, often prevent individuals from seeking timely and appropriate preventive and medical attention. This lack of access can lead to inadequate management of chronic conditions and worse health outcomes (Murray, 2006). Regardless, the existing body of knowledge on the associations of neighborhood-level rates of poverty and low socioeconomic status with dysregulated immune responses in SMM with and without HIV is limited. Cohort studies with national sampling frames are needed to examine the macro-level determinants of systemic inflammation and cellular aging in SMM with and without HIV across geographic regions. These studies should include other

Table 2

Standardized, Cross-Sectional Associations of Neighborhood-Level Factors With Markers of Immune Activation, Inflammation, and Leukocyte Telomere Length (N = 110)

Results	IL-6 β [95 % CI]	sCD14 β [95 % CI]	sCD163 β [95 % CI]	TNF-α β [95 % CI]	TNF-α receptor I β [95 % CI]	TNF-α receptor II β [95 % CI]	Telomere length β [95 % CI]
Percent below 150% the federal poverty level	.32*** [.007, .001]	.10 [.02, .07]	.05 [.01, .07]	.09 [.03, 1.07]	.16 [1.2, 1.6]	.07 [1.5, 2.8]	.20 [2.6, 4.5]
Percent unemployed	−.13 [.008, .02]	.004 [.05, .09]	.18 [.02, 1.06]	.03 [.04, .09]	.02 [1.4, 2.5)	.10 [1.3, 2.7]	−.01 [2.4, 3.5]
Percent uninsured	−.03 [.01, .04]	−.14 [.01, .07]	−.04 [.04, .08]	.24* [.03, .05]	−.24 [1.8, 2.5]	−.18 [1.5, 2.8]	−.01 [2.1, 3.9]
Percent of racial/ethnic minority residents	.26* [.03, .065]	.04 [.04, 1.09]	.13 [.05, .1]	.06 [.03, 1.07]	.06 [1.7, 2.6]	.15 [1.7, 2.6]	−.20 [2.3, 4.8]
R^2 (%)	13	3	4	12.5	3	6	6.5
Model significance	.70*	.08	.60	.04*	.05	.04	.02

Note. All models were adjusted for age, stimulant use, self-reported income, level of education, and race/ethnicity. Model significance is reported based on results of the Wald test. IL-6 = interleukin-6; β = degree of change in outcome variable for every 1-unit of change in predictor variable; CI = confidence interval; sCD14 = soluble CD14; sCD163 = soluble CD163; TNF-α = tumor necrosis factor alpha; TNF-α receptor I = tumor necrosis factor-alpha receptor I; TNF-α receptor II = tumor necrosis factor-alpha receptor II. TNF-α receptors I and II were $\log_{10}$ transformed.
* $p < .05$. *** $p < .001$.

indicators of neighborhood-level factors such as social cohesion and community engagement as well as indices of structural stigma including employment and housing discrimination to provide frameworks for understanding the consequences of systemic inequalities and discriminatory practices that are embedded within societal structures and institutions.

Similarly, residing in neighborhoods with high unemployment rates is associated with poorer health outcomes over and above individual-level socioeconomic characteristics (Ross & Mirowsky, 2001). In fact, studies have found that residing in neighborhoods with higher rates of unemployed individuals may be associated with elevated levels of inflammatory markers such as C-reactive protein and IL-6 (Chai et al., 2016; Iyer et al., 2022). Although neighborhood socioeconomic disadvantage is shown to be associated with higher levels of exposure to psychosocial stressors and substance use (Boardman et al., 2001), there is a dearth of research exploring the effects of neighborhood-level rates of unemployment on the immune responses and cellular aging both in the general population and among SMM.

Moreover, in the United States, higher rates of unemployment and lack of health care insurance are closely intertwined and can have significant consequences for individuals and their access to health care services. When individuals reside in neighborhoods with higher rates of unemployment, especially for an extended period, they may also experience losing access to employer-sponsored health insurance, leaving them without adequate or quality coverage for preventive and medical expenses (Centers for Disease Control and Prevention, 2017). The lack of regular access to primary care and preventive services, coupled with the absence of health care insurance, can contribute to worsening mental and physical health outcomes. In fact, chronic conditions can go undetected or poorly managed, leading to more severe health complications over time. This can ultimately contribute to health disparities, as individuals without access to regular quality health care are at a higher risk of experiencing adverse health outcomes compared to those with consistent and comprehensive health care (McWilliams, 2009). Although the lack of health care insurance has been associated with a myriad of negative health outcomes, research on the associations of neighborhood-level indicators of poor health care coverage with immune dysregulation and cellular aging is scant in both SMM and the broader population.

Finally, it is important to reemphasize that measuring the estimated percentage of racial/ethnic minority individuals in neighborhoods is not intended to perpetuate stereotypes or reinforce preconceived notions about racial/ethnic minority groups. Several studies indicate that racial/ethnic minority people, especially those belonging to marginalized communities, encounter disproportionate rates of contact, profiling, arrest, and other unfavorable interactions with law enforcement. Similarly, concentration of racial/ethnic minority groups likely reflects racist policies such as redlining and displacement of these communities because of gentrification. A recent study from our team has demonstrated that self-reported financial hardship, housing instability, and a history of arrest significantly predict dysregulated immune function among SMM with and without HIV (Ghanooni et al., 2024). Although cross-sectional, this study is among the first to investigate the associations of structural determinants with immune activation and systemic inflammation.

The results of this study should be interpreted in the context of some limitations. First, the utilization of a cross-sectional design, the relatively small sample size, and recruitment in the San Francisco area constrained our ability to establish a causal relationship between indices of neighborhood-level adversity with the outcomes examined. To provide more robust evidence, future research employing longitudinal designs is needed to elucidate the biobehavioral mechanisms whereby neighborhood-level adversity is associated with inflammation, cellular aging, and stimulant use. Additionally, most participants in this study were concentrated in just a few neighborhoods, with 43.7% coming from a single neighborhood of San Francisco alone. This limitation highlights potential challenges in generalizing the findings, as the experiences and characteristics of participants in these neighborhoods may not represent those in other areas. Additionally, the lack of significant indirect effects of stimulant use on associations between neighborhood-level factors and markers of immune activation, immune dysregulation, and leukocyte telomere length may be primarily attributed to insufficient statistical power because of the small sample sizes within certain neighborhoods.

Equally important, neighborhood-level factors were specifically linked to inflammation but did not show associations with immune

activation or leukocyte telomere length, which raises intriguing questions about the underlying mechanisms at play. One possible explanation is that neighborhood factors may directly influence inflammatory responses more than they affect broader immune activation processes. Inflammation can be a more immediate response to environmental stressors, whereas immune activation and dysfunction may involve more complex, longer-term adaptations that are less sensitive to neighborhood characteristics (Reale et al., 2018).

Furthermore, the lack of association observed between neighborhood-level factors and telomere length should not be interpreted as a complete absence of effect from neighborhood factors on cellular aging. While our findings indicated that telomere length was unaffected by neighborhood-level factors, it is important to recognize that other markers of cellular aging—which we did not measure—such as patterns of DNA methylation may have been influenced by neighborhood-level factors of adversity (Unnikrishnan et al., 2019). Similarly, limited panel of immune markers and sample size limitations may have reduced the statistical power needed to detect associations between stimulant use and markers of systemic inflammation and immune activation. While we observed associations between neighborhood factors and systemic inflammation, the subgroup of participants reporting regular stimulant use may not have been large enough to detect separate effects specific to stimulant use alone. Future studies could benefit from examining a broader array of markers of biological aging in a large sample to provide a more comprehensive understanding of how neighborhood environments contribute to the aging process at the cellular level. Addressing these limitations in future studies could provide a more comprehensive view of how neighborhood adversity shapes various health outcomes.

It is also important to note that although we considered using latent variable modeling with structural equation modeling, we decided against it because of the relatively small sample size. Although the study involved participants from eight neighborhoods in San Francisco, California, we did not have data on the duration of time participants had lived in their respective neighborhoods. Moreover, the data were collected from 2013 to 2017, prior to the COVID-19 pandemic. As a result, the associations observed may have been significantly affected by the pandemic, and these changes warrant further investigation. Finally, given that this study focused on SMM with HIV who had biologically confirmed stimulant use, it is possible that indices of neighborhood-level adversity are serving as proxies for a more severe stimulant use disorder. Future studies should focus on examining the relevance of neighborhood-level factors in national samples of the broader population of SMM with and without HIV.

Despite these limitations, this study is among the first to establish the associations of neighborhood-level factors with inflammation in SMM with HIV. The findings underscore the benefits of placing individual-level risk factors in their social and structural context to better understand multilevel determinants of immune activation and cellular aging among SMM with HIV.

Resumen

Objetivo: Este estudio transversal investigó las asociaciones de factores a nivel de vecindario con la activación inmune, la inflamación sistémica y la longitud de los telómeros de los leucocitos en 110 hombres de minorías sexuales (SMM, por sus siglas en inglés) con VIH. ***Métodos:*** de 2013 a 2017, se reclutó a SMM con VIH que usaron estimulantes en San Francisco, California, y proporcionaron muestras de sangre para medir marcadores de activación inmune, inflamación sistémica y longitud de los telómeros de los leucocitos. Para medir los índices a nivel de vecindario, se geo codificó la dirección de cada participante y se vinculó a datos de los Centros para el Control y la Prevención de Enfermedades (CDC, por sus siglas en inglés). Se empleó un modelo lineal jerárquico para investigar las asociaciones de factores a nivel de vecindario con la inflamación sistémica y la longitud de los telómeros de los leucocitos. ***Resultados:*** Después de ajustar por edad, uso de estimulantes, ingresos autodeclarados, nivel de educación y raza y etnia, residentes en vecindarios con mayores porcentajes de pobreza ($\beta = .33$, $p < .001$) y con una mayor proporción de minorías raciales/étnicas ($\beta = .26$, $p < .05$) se asociaron de forma independiente con niveles más altos de interleucina-6. Además, residir en vecindarios con un mayor porcentaje de personas sin seguro se asoció de forma independiente con un mayor factor de necrosis tumoral alfa ($\beta = .24$, $p < .05$). Los índices de adversidad a nivel de vecindario se asociaron adicionalmente con el suministro de una muestra de orina que reaccione a los estimulantes (OR = 1.31, $p = .002$), lo que, a su vez, se asoció con una longitud más corta de los telómeros de los leucocitos ($\beta = -.31$, $p < .05$). ***Conclusiones:*** Las futuras investigaciones longitudinales deberían examinar las vías bio conductuales que vinculan los factores a nivel de vecindario y el uso de estimulantes con la inflamación sistémica y el envejecimiento celular.

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