

NEIGHBORHOODS, STRESS, AND CVD RISK AMONG WOMEN WITH HIV IN  
CHICAGO WIHS

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## DEDICATION

To my partner, parents, siblings, family, friends, peers, and mentors, I am so thankful for the lifetime of support and love I have received. I truly stand on the shoulders of giants.

“Hope is the belief that our tomorrows can be better than our todays. Hope is not magic; hope is work.”

— *DeRay Mckesson, On the Other Side of Freedom: The Case for Hope*

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## **ABSTRACT**

### **NEIGHBORHOODS, STRESS, AND CVD RISK AMONG WOMEN WITH HIV IN CHICAGO WIHS**

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As women living with HIV (WLWH) have aged in the United States, more and more are experiencing common comorbidities associated with aging. Cardiovascular diseases (CVDs) are among the most common chronic diseases that WLWH experience. HIV-positive women are uniquely vulnerable to CVD as they age due to a mix of intersecting circumstances, including general- and HIV-associated factors. Since an individual's perception of their neighborhood environment is a key contributor to cardiovascular health, it is important to examine the relationship between neighborhoods and cardiovascular health among WLWH. The purpose of this dissertation study was to examine associations between perception of neighborhood environment, stress, and cardiovascular disease risk among HIV-positive women. In order to describe the existing evidence regarding perception of neighborhood environment, chronic stress, and CVD risk among WLWH, I developed a conceptual framework of the interaction between neighborhood environment, and various HIV-associated and general factors linked to stress and CVD risk. Further, this study was completed as a secondary analysis of a data set from the Chicago site of the Women's Interagency HIV Study (WIHS) in 2012. A total of 147 HIV-positive women were included in this study. I examined associations between neighborhood perception, chronic stress, and risk for cardiovascular disease with multivariable linear regression analyses. Results from this study did not demonstrate

significant associations between neighborhood perception, chronic stress, and CVD risk among WLWH. This study can be used to develop clinical, behavioral, and policy interventions to promote cardiovascular health among women with HIV.

*Keywords: women, HIV, CVD, neighborhood, chronic stress*

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# CHAPTER 1

## Introduction

### The Issue

As treatment for HIV and access to antiretroviral medications has increased around the globe, women living with HIV/AIDS (WLWH) are reaching advanced ages at greater proportions than ever in the history. Currently, 36.7 million individuals are living with HIV/AIDS worldwide (Joint United Nations Programme on HIV/AIDS, 2016). In the United States, roughly 30% of individuals living with HIV are age 50 or older (United Nations Programme on HIV/AIDS, 2013), and more WLWH are experiencing common non-infections comorbidities in the United States, such as cardiovascular disease (CVD). CVD is a disease that affects the heart or circulatory tissues, is characterized by circulatory dysfunction due to chronic irritation and narrowing of vascular tissues, and includes coronary artery disease, heart failure, and myocardial infarction (American Heart Association, 2017). CVD is the greatest contributor to mortality for the United States general population, and accounts for a quarter of all deaths each year (Center for Disease Control and Prevention, 2017a). Further, CVD is the greatest cause of mortality of women in the United States, accounting for one in five deaths among women in 2017 (Center for Disease Control and Prevention, 2017b).

Several studies have suggested additional mechanisms of CVD among WLWH. First, HIV-associated immune activation (Borges et al., 2016; Dolan et al., 2005; Duprez et al., 2012; Grund et al., 2016; Kaplan et al., 2012; Keating et al., 2011; Lurain et al., 2016; Palella Jr et al., 2010; Triant, Meigs, & Grinspoon, 2009) metabolic changes and alterations in body fat distribution (Currier et al., 2008; Dolan et al., 2005; El-Sadr et al.,

2005; Grunfeld et al., 2007; Hadigan et al., 2003) have been suggested to contribute to CVD risk. Additionally, WLWH also tend to experience hormonal changes related to the virus, including earlier menopause compared to women without HIV (Fan, Maslow, Santoro, & Schoenbaum, 2008), which leads to changes in hormone production (e.g. increased androgens, decreased estrogen) that can contribute to increased risk for cardiovascular disease (Grady & Sawaya, 2005; Karim et al., 2013; Mesch et al., 2008; Schoenbaum et al., 2005; Soares, 2008). Furthermore, various antiretroviral medication regimens have been associated with elevated risk for CVD, and cause dyslipidemia, insulin resistance, lipodystrophy, endothelial tissue damage, and diastolic dysfunction (Butler et al., 2018; Carr & Cooper, 2000; Friis-Møller et al., 2003; Tien et al., 2010; Zanetti et al., 2018).

Women represent 23% of individuals in the United States living with HIV (Center for Disease Control and Prevention, 2018). HIV-positive women demonstrate a disproportionate burden of CVD relative to both HIV-positive men and HIV-negative women (Al-Kindi et al., 2016; Blackstock et al., 2013; Womack et al., 2014). For instance, studies of health disparities in CVD mortality have demonstrated that there is increasing morbidity and mortality due to CVDs among women with HIV relative to both men with HIV and women without HIV (Al-Kindi et al., 2016; Alcaide et al., 2013; Feinstein et al., 2016; Gardner et al., 2003; Khalsa et al., 2007). In comparison to men with HIV, WLWH demonstrate increased risk for a variety of CVDs, including MI and atherosclerosis (Capili, Anastasi, & Ogedegbe, 2011; Fitch et al., 2013; Mangili et al., 2006). Additionally, relative to women without HIV, WLWH may have increased vulnerability to CVD as it relates to general risk factors- such as obesity, hypertension,

and cigarette smoking- and HIV associated factors-such as chronic effects of ART, immune system changes, and accelerated aging and early menopause (Fan et al., 2008). Therefore, it is critical to understand causal mechanisms beyond the individual, such as neighborhood-level factors, that influence CVD risk among WLWH.

### **Inferences from Related Literature**

Stress can be defined as “a state manifested by a specific syndrome which consists of all the non-specifically induced changes in a biologic system” and incorporated both physiologic and psychological components of stress and a stress response (Selye, 1959). Stress is an individual’s psychological and biological responses to challenges and circumstances that are caused by stressors (Dimsdale, 2008). The continuation of an individual’s stress responses across the life course is chronic stress and can be caused by a variety of circumstances that often influence individual behaviors, including neighborhood stressors. In turn, chronic stress contributes to suppression of both cellular and humoral immune function, reducing the ability of the immune system to respond across the lifespan (Segerstrom & Miller, 2004). Therefore, chronic stress can exacerbate changes in immune function and further predispose WLWH to CVD.

As noted in cognitive theories of stress and coping, stress is a relationship between an individual and their environment (Folkman, 1984). Social (e.g. relationships with neighbors) and physical (e.g. access to affordable food) aspects of neighborhood environments can be sources of stressors and resources, and may also effect an individual’s stress response and resources for health (Elliott, 2000). Neighborhood-related stressors can cause distinct challenges for individuals, as stressors at the neighborhood-level are difficult to avoid and exist in an individual’s daily life (Matheson

et al., 2006). Neighborhood-related stressors are distinct from individual-level or role-related stressors, as neighborhood-related stressors happen at a societal level above the individual and their interactions and roles within their daily lives (Piazza, Charles, Sliwinski, Mogle, & Almeida, 2012; Serido, Almeida, & Wethington, 2004). These chronic neighborhood-level stressors examined in this study are process by which perception of neighborhood characteristics are internalized and impact CVD risk among WLWH. Neighborhood perception is an individual's appraisal and experience in the neighborhood in which they reside. A person's perception of their neighborhood is also shaped by their experiences and exposures within their neighborhood. Individual perceptions of neighborhoods are often measured as via self-report, and have been associated with objective (e.g. census-level measures) of neighborhood data (Burke-Miller et al., 2017; Echeverría, Diez-Roux, Shea, Borrell, & Jackson, 2008; Echeverria, Diez-Roux, & Link, 2004).

WLWH are exposed to these stressors chronically, and over time, contribute to a variety of health outcomes. Evidence that contextualizes disparities in CVD outcomes among WLWH is growing, yet the relationship between CVD risk among WLWH and environmental health determinants is poorly understood (Burke-Miller et al., 2017). Previous research connects various aspects of neighborhoods to the health outcomes of WLWH. HIV-positive women often resides in segregated, urban areas of the United States (AIDSvu, 2016), with high concentration of poverty, which, in turn, has been associated with key risk factors for cardiovascular comorbidities among WLWH. Risk factors for CVD associated with concentrated poverty among WLWH include decreased likelihood of viral suppression, reduced CD4 cell counts, and poor retention in HIV care



(Burke-Miller et al., 2016; Castel et al., 2012; Eberhart et al., 2015; Shacham, Lian, Önen, Donovan, & Overton, 2013; Wiewel, Borrell, Jones, Maroko, & Torian, 2017). Further, one study demonstrated an association between urban hotspots of poor viral suppression and poor retention in HIV care with increased distance to public transit, shorter distance to pharmacies and medical care, and female sex (Eberhart et al., 2015). In other studies of neighborhoods among HIV-negative individuals, socioeconomic deprivation, low social cohesion, decreased safety, and residential instability are associated with increased risk for CVD (Chaix, Lindström, Rosvall, & Merlo, 2008; Chaix, Rosvall, & Merlo, 2007; Echeverría et al., 2008; Kim, Diez Roux, Kiefe, Kawachi, & Liu, 2010).

Despite this evidence, the direct association between neighborhood features with cardiovascular health outcomes among WLWH has seldom been examined. Most notably, many studies have utilized United States Census-derived measures for examination of neighborhoods. While these studies have revealed important areas for CVD prevention linked to poverty, these measures do not capture the processes by which aspects of neighborhoods get “under the skin” and contribute to health outcomes. Neighborhood perception more directly assesses the impact of neighborhoods on individual health outcomes as an individual’s appraisal of their neighborhood environment influences their health decisions (Echeverria et al., 2004). Studies have linked neighborhood perception to behaviors linked to increased risk for CVD, which include perceived lack of healthy foods, and perceived limited dietary options for cardiovascular health (Diez-Roux & Mair, 2010; Evenson et al., 2012). Additionally, perceived lack of safety and reduced social cohesion are associated with decreased

physical activity, increased sedentary behavior, increased alcohol consumption, stress, and depression (Echeverría et al., 2008; Evenson et al., 2012; Strong, Reitzel, Wetter, & McNeill, 2013). This dissertation addresses this gap in the literature by describing and examining the associations between perceived aspects of neighborhood environment, chronic stress, and CVD risk among WLWH.

### **Summary, Study Purpose, and Specific Aims**

In total, WLWH are distinctly vulnerable to CVD as they age, and a variety of studies suggests their risk factors are multifaceted. The neighborhood environments of WLWH likely play a significant role in shaping their daily lives and cardiovascular health. Investigations are underway into the underlying disease processes and symptomology of CVD among WLWHs, yet there is a lack of investigation of specific neighborhood-level health determinants that may contribute to CVD among HIV-positive women. Understanding factors that contribute to risk for CVD among WLWH is critical so that preventative interventions can be developed to promote cardiovascular health and wellness across the lifespan.

The specific aims of this study were to:

1. Describe a conceptual framework of chronic stress and CVD risk among WLWH as it relates to neighborhood environment.
2. Examine the associations between perception of neighborhood environment and chronic stress among WLWH.

*Hypothesis:* Decreased (poor) perception of neighborhood environment will be associated with increased chronic stress.

3. Examine the associations between neighborhood perception and risk for CVD.

*Hypothesis 1:* Increased CVD risk will be associated with poor (decreased) perception of neighborhood.

*Hypothesis 2:* Poor (decreased) perceived availability of healthy food, physical activity/walking environment, and social cohesion of neighborhoods will be associated with increased CVD risk.

- a. Exploratory aim: Examine whether the relationship between risk for cardiovascular disease and perceived aspects of neighborhood is mediated by chronic stress.
  - i. *Hypothesis:* Chronic stress will partially mediate the relationship between neighborhood perception and cardiovascular disease risk.

## **Study Overview**

To achieve the study aims, this dissertation utilized a secondary analysis of data collected as part of the site-specific Chicago Women's Interagency HIV Study (WIHS). Since its initiation in 1993, this longitudinal, prospective, multi-site study of women with HIV has examined the natural history and progression of HIV. The WIHS study also serves as a leading source of investigation into reproductive health, clinical outcomes (such as cardiovascular disease, diabetes, and neurocognitive disorders), and the efficacy of antiretroviral therapies (WIHS Data Management and Analysis Center, 2017). I used data collected from the cardiovascular disease, psychoneuroimmunology (PNI), and hair cortisol sub studies. These studies, within the larger framework of WIHS, seek to better understand cardiovascular function, stress response, and the utility of hair cortisol as a biomarker among WLWH. This study also incorporated data from WIHS clinical examinations and data from Chicago WIHS sub studies to achieve the study aims.

Inclusion criteria for this study were HIV-positive status, residence in the Chicago area, and participation in the previously mentioned Chicago WIHS sub studies. Table 1.2 displays the variables that were used in this study to accomplish the aims. All statistical analyses were conducted utilizing Stata 15 software (StataCorp, 2017).

The first aim of this study was to describe a conceptual framework for CVD risk among WLWH as it relates to their neighborhood environment and is discussed in the second chapter (manuscript one) of the dissertation study. The conceptual framework in this chapter was developed by a synthesis of ecological and behavioral theories as well as emerging evidence regarding the incidence of CVD among WLWH. Further, I adopted a health equity lens in development of this conceptual theory in addressing structural aspects of neighborhood environments that are linked to CVD risk. Therefore, this conceptual framework can inform interventions to promote cardiovascular health for WLWH in the neighborhoods in which they reside.

To achieve the second aim of this study, WIHS data was used to examine the relationship between neighborhood environment and chronic stress among women with HIV in Chicago WIHS and is discussed in the third chapter (manuscript two) of the dissertation study. Descriptive statistics of demographic and health data were completed to observe trends within this sample. Bivariate analyses between these variables and both the predictor variables- as measured Perception of Neighborhood and Environments Scale (PNES) and subscales- and the outcome variable- chronic stress as measured by Perceived Stress Scale (PSS) scores and hair cortisol concentration (HCC). The psychometric performance of the PNES in this sample is reported in Tables 1.4-1.5. I

evaluated bivariate relationships and multivariable linear regression models to achieve the study aims.

Similarly, WIHS data was utilized to examine the association between neighborhood perception and CVD risk among WLWH and is discussed in the fourth chapter (manuscript three) of the dissertation study. To achieve the third aim of the dissertation study, descriptive statistics of demographic and health data were used to examine trends with each study variable. Bivariate analyses between these variables and both the predictor variables- as measured Perception of Neighborhood and Environments Scale (PNES) and subscales- and the outcome variable- CVD risk as measured by the Framingham Risk Score (FRS) 10-year algorithm. I evaluated bivariate relationships and multivariable linear regression analyses. For the exploratory sub-aim of study, I sought to examine the extent to which chronic stress- as measured by responses to the Perceived Stress Scale (PSS) and hair cortisol concentration (HCC) - mediates the relationship between neighborhood perception and CVD risk. Preacher and Hayes mediation was the selected method of mediation to determine if this effect occurred in the hypothesized direction (Preacher & Hayes, 2004).

Effect size calculation for this study are included in Table 1.2. A total number of participants eligible for this study from the Chicago WIHS sample includes 147 HIV-positive women. The total number of Chicago WIHS women that provided hair cortisol samples is 55 HIV-positive women. For the analyses I conducted to complete the aims of this dissertation study, I included PNES subscales as independent variables. For analyses with the PSS and FRS, we calculated an effect size  $f^2$  of 0.057 with a sample size of 147, power calculated at 0.80, and alpha at 0.05. For the analyses with HCC, we calculated an

effect size  $f^2$  of 0.177, with a sample size of 55, power calculated at 0.80, and an alpha of 0.05. Effect size was calculated using PASS software (Hintze, 2004).

### **Key Definitions, Approach, and Conceptual Model**

Key terms and definitions of concepts included in the study are listed in Table 1.1. This dissertation study sought to examine the associations between neighborhood environments, chronic stress, and CVD risk among WLWH to reduce health disparities and move toward health equity. Health disparities, as defined in Healthy People 2020, are the variations in health outcomes that are “closely linked with social, economic, and/or environmental disadvantage” and “adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; gender; age; mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion” (Health & Services, 2008). In turn, health equity, as defined by Braveman (2014), is “the principle underlying a commitment to reduce- and, ultimately, eliminate- disparities in health and in its determinants, including social determinants”. This definition of health equity implies that the goals of health interventions should be developed with consideration of the structure of societies and power. This incorporated a health equity approach as a means of investigating the ways in which WLWH experience various disparities in CVD rates and outcomes. With this approach, this study can inform neighborhood-level or multi-level interventions that move towards health equity.

Further, discussion of sex/gender is warranted for this study examining neighborhood-level factors that are associated with chronic stress and CVD risk among

WLWH. In the presented conceptual model of CVD among HIV-positive women (manuscript one), a discussion of sex/gender is warranted. The Canadian Institutes of Health Research (2013) defines sex as “a set of biological attributes in humans and animals” and is “primarily associated with physical and physiological features including chromosomes, gene expression, hormone levels and function, and reproductive/sexual anatomy”, whereas gender is the “socially constructed roles, behaviors, expressions and identities of girls, women, boys, men, and gender diverse people”. Critical feminist scholars have argued that, as some scholars conceive sex as an objective and biological construct, what is deemed objective and biologic is constructed through the social cultural lens of investigators (Davis & Preves, 2017). Therefore, this study defines WLWH as cisgender, meaning a gender identity that is socioculturally aligned with female sex (Canadian Institutes of Health Research, 2013; Davis & Preves, 2017; Fausto-Sterling, 2000). By making this distinction, this dissertation intentionally focuses on the intersection of social and biologic functions that specifically occur among cisgender women.

### **Significance and Innovation**

A call from the National Institutes of Health Office of AIDS Research advocates for critical investigation into the aging process among women with HIV and urges investigators to explore how their environmental and cultural context shapes their health and wellness (High et al., 2012). This study sought to work towards addressing health inequities and health disparities among WLWH to promote cardiovascular health as they age. Prior to 1992, many women failed to receive an AIDS diagnosis due to limited scope of CDC criteria that excluded common manifestations among women (Amaro, 1995).

Women historically and continually are underrepresented in HIV research and clinical trials (Diaz et al., 1995; Gifford et al., 2002; Levine, 1990). This tendency to exclude or underrepresent women has also occurred in CVD research and interventions, as CVD was largely considered a “man’s disease” despite the evidence that CVD has contributed to the greatest deaths among women in the United States (Center for Disease Control and Prevention, 2017b). Therefore, this study contributes to a body of work that examines the cardiovascular health of WLWH as a means of shedding light on their unique experiences and circumstances that can inform health interventions.

Additionally, findings from this study can inform structural interventions within neighborhoods to support the cardiovascular health of WLWH, such as increasing spaces of physical activity and increased access to affordable foods. These processes that promote cardiovascular health and wellness may in turn reduce healthcare costs. Individuals with HIV who experience CVD events have increased healthcare costs when compared to HIV-negative matched controls (Gallant, Hsue, Budd, & Meyer, 2018). Therefore, this study can contribute to healthcare and policy interventions towards addressing neighborhood-level structural factors associated with CVD risk that can reduce health disparities, promote health equity.

Furthermore, this dissertation has incorporated innovative measures for study analyses. First, this study utilized the Perception of Neighborhood Environments Scale (PNES) as a measure of the quality of neighborhood environment as interpreted by WLWH in the Chicago WIHS sample. Utilizing this measure offers several innovative advantages. For example, many studies of neighborhood environment utilize census-level data, which serve as useful aggregate measures (e.g. zip code-level data for education,



green spaces, housing, etc.), of neighborhoods for systematic analysis. Additionally, studies that have incorporated aggregate measures are often limited due to: reduced basis in theory; arbitrary units of spatial analysis, and indirect connection to individual health (Diez-Roux & Mair, 2010; Echeverria et al., 2004; Roux, 2008). As an alternative measure to aggregate neighborhood-level data, the PNES and subscales can be used for direct examination of neighborhood attributes as perceived by the women in the study that influence health as reported by WLWH, and has been validated in the Chicago WIHS sample (Burke-Miller et al., 2017). Further, the self-reported nature of the PNES is more closely tied to the chronic stress experience of WLWH than aggregate neighborhood measures. Secondly, hair cortisol concentration (HCC) was used as a measure of chronic stress among WLWH. HCC is a relatively new stress measure, and few studies have utilized it as a tool for measuring chronic stress (Russell, Koren, Rieder, & Van Uum, 2012). As an alternative measure of stress, HCC can be utilized as a composite measure of stress over several months and is not susceptible to fluctuations related to situational stressors like salivary or serum cortisol levels (Sauvé, Koren, Walsh, Tokmakejian, & Van Uum, 2007). Therefore, HCC was an ideal and innovative measure for this study.

### **Protection of Human Subjects**

This study received a waiver of Institutional Review Board review prior to any data analysis given that all study data were de-identified prior to data transfer from Chicago WIHS to the investigative team. All data for this analysis were maintained on password-protected and secured servers maintained by the University of Pennsylvania School of Nursing. Only personnel on the study team viewed data for analysis and publication.

## References

- AIDSvu. (2016). Rates of Females Living with Diagnosed HIV, 2014. Retrieved from <https://map.aidsvu.org/map>
- Al-Kindi, S. G., ElAmm, C., Ginwalla, M., Mehanna, E., Zacharias, M., Benatti, R., . . . Longenecker, C. T. (2016). Heart failure in patients with human immunodeficiency virus infection: epidemiology and management disparities. *International journal of cardiology*, 218, 43-46.
- Alcaide, M. L., Parmigiani, A., Pallikkuth, S., Roach, M., Freguja, R., Della Negra, M., . . . Pahwa, S. (2013). Immune activation in HIV-infected aging women on antiretrovirals—implications for age-associated comorbidities: a cross-sectional pilot study. *PLoS One*, 8(5), e63804.
- Amaro, H. (1995). Love, sex, and power: Considering women's realities in HIV prevention. *American psychologist*, 50(6), 437.
- American Heart Association. (2017). What is cardiovascular disease? Retrieved from [http://www.heart.org/HEARTORG/Conditions/What-is-Cardiovascular-Disease\\_UCM\\_301852\\_Article.jsp#.Wrv3CaIwgUc](http://www.heart.org/HEARTORG/Conditions/What-is-Cardiovascular-Disease_UCM_301852_Article.jsp#.Wrv3CaIwgUc)
- Blackstock, O. J., Tate, J. P., Akgün, K. M., Crystal, S., Duggal, M., Edelman, E. J., . . . Rodriguez-Barradas, M. C. (2013). Sex disparities in overall burden of disease among HIV-infected individuals in the Veterans Affairs healthcare system. *Journal of general internal medicine*, 28(2), 577-582.
- Borges, Á. H., O'connor, J. L., Phillips, A. N., Neaton, J. D., Grund, B., Neuhaus, J., . . . Lundgren, J. D. (2016). Interleukin 6 is a stronger predictor of clinical events than

- high-sensitivity C-reactive protein or D-dimer during HIV infection. *The Journal of infectious diseases*, 214(3), 408-416.
- Braveman, P. (2014). What are health disparities and health equity? We need to be clear. *Public Health Reports*, 129(1\_suppl2), 5-8.
- Burke-Miller, J. K., Weber, K., Cohn, S. E., Hershow, R. C., Sha, B. E., French, A. L., & Cohen, M. H. (2016). Neighborhood community characteristics associated with HIV disease outcomes in a cohort of urban women living with HIV. *AIDS care*, 28(10), 1274-1279.
- Burke-Miller, J. K., Weber, K. M., Cohn, S. E., Hershow, R. C., Sha, B., French, A. L., & Cohen, M. H. (2017). Measurement of Neighborhood Context in an Urban Cohort of HIV-infected or at risk Low-Income Women. *Journal of poverty*, 21(1), 80-96.
- Butler, J., Kalogeropoulos, A. P., Anstrom, K. J., Hsue, P. Y., Kim, R. J., Scherzer, R., . . . Hernandez, A. F. (2018). Diastolic Dysfunction in Individuals With Human Immunodeficiency Virus Infection: Literature Review, Rationale and Design of the Characterizing Heart Function on Antiretroviral Therapy (CHART) Study. *Journal of cardiac failure*, 24(4), 255-265.
- Canadian Institutes of Health Research. (2013). Gender, sex, and health research guide: a tool for CIHR applicants. Retrieved from <http://igar-tool.gender-net.eu/en/reference/gender-sex-and-health-research-guide-a-tool-for-cihr-applicants>
- Capili, B., Anastasi, J. K., & Ogedegbe, O. (2011). HIV and general cardiovascular risk. *Journal of the Association of Nurses in AIDS Care*, 22(5), 362-375.

- Carr, A., & Cooper, D. A. (2000). Adverse effects of antiretroviral therapy. *The Lancet*, 356(9239), 1423-1430.
- Castel, A. D., Befus, M., Willis, S., Griffin, A., West, T., Hader, S., & Greenberg, A. E. (2012). Use of the community viral load as a population-based biomarker of HIV burden. *Aids*, 26(3), 345-353.
- Center for Disease Control and Prevention. (2017a). Heart Disease Facts. Retrieved from <https://www.cdc.gov/heartdisease/facts.htm>
- Center for Disease Control and Prevention. (2017b). Women and Heart Disease. Retrieved from [https://www.cdc.gov/dhdsp/data\\_statistics/fact\\_sheets/fs\\_women\\_heart.htm](https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_women_heart.htm)
- Center for Disease Control and Prevention. (2018, 7/5/2018). HIV among women. Retrieved from <https://www.cdc.gov/hiv/group/gender/women/index.html>
- Chaix, B., Lindström, M., Rosvall, M., & Merlo, J. (2008). Neighbourhood social interactions and risk of acute myocardial infarction. *Journal of Epidemiology & Community Health*, 62(1), 62-68.
- Chaix, B., Rosvall, M., & Merlo, J. (2007). Neighborhood socioeconomic deprivation and residential instability: effects on incidence of ischemic heart disease and survival after myocardial infarction. *Epidemiology*, 18(1), 104-111.
- Currier, J., Scherzer, R., Bacchetti, P., Heymsfield, S., Lee, D., Sidney, S., & Tien, P. C. (2008). Regional adipose tissue and lipid and lipoprotein levels in HIV-infected women. *Journal of acquired immune deficiency syndromes (1999)*, 48(1), 35.
- Davis, G., & Preves, S. (2017). Intersex and the social construction of sex. *Contexts*, 16(1), 80-80.

- Diaz, T., Chu, S. Y., Sorvillo, F., Mokotoff, E., Davidson, A. J., Samuel, M. C., . . . Fann, S. A. (1995). Differences in participation in experimental drug trials among persons with AIDS. *Journal of acquired immune deficiency syndromes and human retrovirology: official publication of the International Retrovirology Association*, 10(5), 562-568.
- Diez-Roux, A. V., & Mair, C. (2010). Neighborhoods and health. *Annals of the New York Academy of Sciences*, 1186(1), 125-145.
- Dimsdale, J. E. (2008). Psychological stress and cardiovascular disease. *Journal of the American College of Cardiology*, 51(13), 1237-1246.
- Dolan, S. E., Hadigan, C., Killilea, K. M., Sullivan, M. P., Hemphill, L., Lees, R. S., . . . Grinspoon, S. (2005). Increased cardiovascular disease risk indices in HIV-infected women. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 39(1), 44-54.
- Duprez, D. A., Neuhaus, J., Kuller, L. H., Tracy, R., Belloso, W., De Wit, S., . . . Lundgren, J. (2012). Inflammation, coagulation and cardiovascular disease in HIV-infected individuals. *PLoS One*, 7(9), e44454.
- Eberhart, M. G., Yehia, B. R., Hillier, A., Voytek, C. D., Fiore, D. J., Blank, M., . . . Brady, K. A. (2015). Individual and community factors associated with geographic clusters of poor HIV care retention and poor viral suppression. *Journal of acquired immune deficiency syndromes (1999)*, 69(0 1), S37.
- Echeverría, S., Diez-Roux, A. V., Shea, S., Borrell, L. N., & Jackson, S. (2008). Associations of neighborhood problems and neighborhood social cohesion with

- mental health and health behaviors: the Multi-Ethnic Study of Atherosclerosis. *Health & place*, 14(4), 853-865.
- Echeverria, S. E., Diez-Roux, A. V., & Link, B. G. (2004). Reliability of self-reported neighborhood characteristics. *Journal of Urban Health*, 81(4), 682-701.
- El-Sadr, W., Mullin, C., Carr, A., Gibert, C., Rappoport, C., Visnegarwala, F., . . . Raghavan, S. (2005). Effects of HIV disease on lipid, glucose and insulin levels: results from a large antiretroviral-naïve cohort. *HIV medicine*, 6(2), 114-121.
- Elliott, M. (2000). The stress process in neighborhood context. *Health & place*, 6(4), 287-299.
- Evenson, K. R., Block, R., Roux, A. V. D., McGinn, A. P., Wen, F., & Rodríguez, D. A. (2012). Associations of adult physical activity with perceived safety and police-recorded crime: the Multi-ethnic Study of Atherosclerosis. *International journal of behavioral nutrition and physical activity*, 9(1), 146.
- Fan, M. D., Maslow, B.-S., Santoro, N., & Schoenbaum, E. (2008). HIV and the menopause. *Menopause International*, 14(4), 163-168.
- Fausto-Sterling, A. (2000). *Sexing the body: Gender politics and the construction of sexuality*: Basic Books.
- Feinstein, M. J., Bahiru, E., Achenbach, C., Longenecker, C. T., Hsue, P., So-Armah, K., . . . Lloyd-Jones, D. M. (2016). Patterns of cardiovascular mortality for HIV-infected adults in the United States: 1999 to 2013. *American Journal of Cardiology*, 117(2), 214-220.
- Fitch, K. V., Srinivasa, S., Abbara, S., Burdo, T. H., Williams, K. C., Eneh, P., . . . Grinspoon, S. K. (2013). Noncalcified coronary atherosclerotic plaque and

- immune activation in HIV-infected women. *The Journal of infectious diseases*, 208(11), 1737-1746.
- Folkman, S. (1984). Personal control and stress and coping processes: A theoretical analysis. *Journal of personality and social psychology*, 46(4), 839.
- Friis-Møller, N., Weber, R., Reiss, P., Thiébaud, R., Kirk, O., Monforte, A. d. A., . . . Law, M. (2003). Cardiovascular disease risk factors in HIV patients—association with antiretroviral therapy. Results from the DAD study. *Aids*, 17(8), 1179-1193.
- Gallant, J., Hsue, P., Budd, D., & Meyer, N. (2018). Healthcare utilization and direct costs of non-infectious comorbidities in HIV-infected patients in the USA. *Current medical research and opinion*, 34(1), 13-23.
- Gardner, L. I., Klein, R. S., Szczech, L. A., Phelps, R. M., Tashima, K., Rompalo, A. M., . . . Greenberg, A. (2003). Rates and risk factors for condition-specific hospitalizations in HIV-infected and uninfected women. *Journal of acquired immune deficiency syndromes (1999)*, 34(3), 320-330.
- Gifford, A. L., Cunningham, W. E., Heslin, K. C., Andersen, R. M., Nakazono, T., Lieu, D. K., . . . Bozzette, S. A. (2002). Participation in research and access to experimental treatments by HIV-infected patients. *New England Journal of Medicine*, 346(18), 1373-1382.
- Grady, D., & Sawaya, G. F. (2005). Discontinuation of postmenopausal hormone therapy. *The American journal of medicine*, 118(12), 163-165.
- Grund, B., Baker, J. V., Deeks, S. G., Wolfson, J., Wentworth, D., Cozzi-Lepri, A., . . . Neaton, J. D. (2016). Relevance of interleukin-6 and D-dimer for serious non-

- AIDS morbidity and death among HIV-positive adults on suppressive antiretroviral therapy. *PLoS One*, *11*(5), e0155100.
- Grunfeld, C., Rimland, D., Gibert, C. L., Powderly, W. G., Sidney, S., Shlipak, M. G., . . . Heymsfield, S. B. (2007). Association of upper trunk and visceral adipose tissue volume with insulin resistance in control and HIV-infected subjects in the FRAM study. *Journal of acquired immune deficiency syndromes (1999)*, *46*(3), 283.
- Hadigan, C., Meigs, J. B., Wilson, P. W., D'agostino, R. B., Davis, B., Basgoz, N., . . . Grinspoon, S. (2003). Prediction of coronary heart disease risk in HIV-infected patients with fat redistribution. *Clinical infectious diseases*, *36*(7), 909-916.
- Health, U. D. o., & Services, H. (2008). The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Phase I report: Recommendations for the framework and format of Healthy People 2020. Section IV. Advisory Committee findings and recommendations.
- High, K. P., Brennan-Ing, M., Clifford, D. B., Cohen, M. H., Currier, J., Deeks, S. G., . . . Goronzy, J. J. (2012). HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. *Journal of acquired immune deficiency syndromes (1999)*, *60*(Suppl 1), S1-18.
- Hintze, J. (2004). NCSS and PASS software. *Kaysville, UT: Number Cruncher Statistical Systems*.
- Hipp, J. R. (2010). A dynamic view of neighborhoods: The reciprocal relationship between crime and neighborhood structural characteristics. *Social Problems*, *57*(2), 205-230.



Joint United Nations Programme on HIV/AIDS. (2016). Global AIDS update 2016.

*Geneva: UNAIDS.*

Kaplan, R. C., Landay, A. L., Hodis, H. N., Gange, S. J., Norris, P. J., Young, M., . . .

Lazar, J. (2012). Potential cardiovascular disease risk markers among HIV-infected women initiating antiretroviral treatment. *Journal of acquired immune deficiency syndromes (1999)*, *60*(4), 359.

Karim, R., Mack, W. J., Kono, N., Tien, P. C., Anastos, K., Lazar, J., . . . Greenblatt, R.

M. (2013). Gonadotropin and sex steroid levels in HIV-infected premenopausal women and their association with subclinical atherosclerosis in HIV-infected and-uninfected women in the women's interagency HIV study (WIHS). *The Journal of Clinical Endocrinology & Metabolism*, *98*(4), E610-E618.

Keating, S. M., Golub, E. T., Nowicki, M., Young, M., Anastos, K., Crystal, H., . . .

Desai, S. (2011). The effect of HIV infection and HAART on inflammatory biomarkers in a population-based cohort of US women. *AIDS (London, England)*, *25*(15), 1823.

Khalsa, A., Karim, R., Mack, W. J., Minkoff, H., Cohen, M., Young, M., . . . Levine, A.

M. (2007). Correlates of prevalent hypertension in a large cohort of HIV-infected women: Women's Interagency HIV Study. *Aids*, *21*(18), 2539-2541.

Kim, D., Diez Roux, A. V., Kiefe, C. I., Kawachi, I., & Liu, K. (2010). Do neighborhood

socioeconomic deprivation and low social cohesion predict coronary calcification? The CARDIA study. *American journal of epidemiology*, *172*(3), 288-298.

- Levine, C. (1990). Women and HIV/AIDS research: The barriers to equity. *Evaluation Review, 14*(5), 447-463.
- Lurain, N. S., Hanson, B. A., Hotton, A. L., Weber, K. M., Cohen, M. H., & Landay, A. L. (2016). The association of human cytomegalovirus with biomarkers of inflammation and immune activation in HIV-1-infected women. *AIDS research and human retroviruses, 32*(2), 134-143.
- Mangili, A., Gerrior, J., Tang, A. M., O'leary, D. H., Polak, J. K., Schaefer, E. J., . . . Wanke, C. A. (2006). Risk of cardiovascular disease in a cohort of HIV-infected adults: a study using carotid intima-media thickness and coronary artery calcium score. *Clinical infectious diseases, 43*(11), 1482-1489.
- Matheson, F. I., Moineddin, R., Dunn, J. R., Creatore, M. I., Gozdyra, P., & Glazier, R. H. (2006). Urban neighborhoods, chronic stress, gender and depression. *Social science & medicine, 63*(10), 2604-2616.
- Mesch, V., Siseles, N., Maidana, P., Boero, L., Sayegh, F., Prada, M., . . . Berg, G. (2008). Androgens in relationship to cardiovascular risk factors in the menopausal transition. *Climacteric, 11*(6), 509-517.
- Palella Jr, F. J., Gange, S. J., Benning, L., Jacobson, L., Kaplan, R. C., Landay, A. L., . . . Elion, R. (2010). Inflammatory biomarkers and abacavir use in the Women's Interagency HIV Study and the Multicenter AIDS Cohort Study. *AIDS (London, England), 24*(11), 1657.
- Piazza, J. R., Charles, S. T., Sliwinski, M. J., Mogle, J., & Almeida, D. M. (2012). Affective reactivity to daily stressors and long-term risk of reporting a chronic physical health condition. *Annals of Behavioral Medicine, 45*(1), 110-120.

- Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior research methods, instruments, & computers*, 36(4), 717-731.
- Roux, A. D. (2008). Next steps in understanding the multilevel determinants of health. *Journal of Epidemiology & Community Health*, 62(11), 957-959.
- Russell, E., Koren, G., Rieder, M., & Van Uum, S. (2012). Hair cortisol as a biological marker of chronic stress: current status, future directions and unanswered questions. *Psychoneuroendocrinology*, 37(5), 589-601.
- Sauvé, B., Koren, G., Walsh, G., Tokmakejian, S., & Van Uum, S. H. (2007). Measurement of cortisol in human hair as a biomarker of systemic exposure. *Clinical & Investigative Medicine*, 30(5), 183-191.
- Schoenbaum, E. E., Hartel, D., Lo, Y., Howard, A. A., Floris-Moore, M., Arnsten, J. H., & Santoro, N. (2005). HIV infection, drug use, and onset of natural menopause. *Clinical infectious diseases*, 41(10), 1517-1524.
- Seegerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychological bulletin*, 130(4), 601.
- Selye, H. (1959). Perspectives in stress research. *Perspectives in biology and medicine*, 2(4), 403-416.
- Serido, J., Almeida, D. M., & Wethington, E. (2004). Chronic stressors and daily hassles: Unique and interactive relationships with psychological distress. *Journal of health and social behavior*, 45(1), 17-33.

- Shacham, E., Lian, M., Önen, N., Donovan, M., & Overton, E. (2013). Are neighborhood conditions associated with HIV management? *HIV medicine*, *14*(10), 624-632.
- Soares, C. N. (2008). Practical strategies for diagnosing and treating depression in women: menopausal transition. *The Journal of clinical psychiatry*, *69*(10), e30-e30.
- StataCorp. (2017). Stata Statistical Software. College Station, TX: StataCorp LLC.
- Strong, L. L., Reitzel, L. R., Wetter, D. W., & McNeill, L. H. (2013). Associations of perceived neighborhood physical and social environments with physical activity and television viewing in African-American men and women. *American journal of health promotion*, *27*(6), 401-409.
- Suttles, G. D. (1972). *The social construction of communities*: University of Chicago Press.
- Tien, P. C., Schneider, M. F., Cox, C., Cohen, M., Karim, R., Lazar, J., . . . Glesby, M. J. (2010). HIV, Highly Active Antiretroviral Therapy and Lipoprotein Particle Concentrations in the Women's Interagency HIV Study. *AIDS (London, England)*, *24*(18), 2809.
- Triant, V. A., Meigs, J. B., & Grinspoon, S. K. (2009). Association of C-reactive protein and HIV infection with acute myocardial infarction. *Journal of acquired immune deficiency syndromes (1999)*, *51*(3), 268.
- United Nations Programme on HIV/AIDS. (2013). HIV and Aging: A special supplement to the UNAIDS report on the global AIDS epidemic, 2013. *Retrieved online: December, 4.*

- US Department of Health and Human Services. (2008). The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Phase I report: Recommendations for the framework and format of Healthy People 2020. Section IV. Advisory Committee findings and recommendations.
- Wiewel, E. W., Borrell, L. N., Jones, H. E., Maroko, A. R., & Torian, L. V. (2017). Neighborhood characteristics associated with achievement and maintenance of HIV viral suppression among persons newly diagnosed with HIV in New York City. *AIDS and Behavior*, 21(12), 3557-3566.
- WIHS Data Management and Analysis Center. (2017). Our Study: The Women's Interagency HIV Study. Retrieved from <https://statepi.jhsph.edu/wihs/wordpress/>
- Womack, J. A., Chang, C. C. H., So-Armah, K. A., Alcorn, C., Baker, J. V., Brown, S. T., . . . Goetz, M. B. (2014). HIV infection and cardiovascular disease in women. *Journal of the American Heart Association*, 3(5), e001035.
- Zanetti, H. R., Mendes, E. L., Chagas, A. C. P., Douglas, M. O. G., Lopes, L. T. P., Roeber, L., . . . Resende, E. S. (2018). Triad of the Ischemic Cardiovascular Disease in People Living with HIV? Association Between Risk Factors, HIV Infection, and Use of Antiretroviral Therapy. *Current atherosclerosis reports*, 20(6), 30.

## Appendices

*Table 1.1 Key Terms and Definitions*

Term	Definition
Cardiovascular disease (CVD)	A disease characterized by circulatory dysfunction due to chronic irritation and narrowing of vascular tissues; can include common illness such as coronary artery disease, myocardial infarction, and heart failure (American Heart Association, 2017)
Sex	Sets of biological attributes in humans and animals that are primarily associated with physical and physiological features including chromosomes, gene expression, hormone levels and function, and reproductive/sexual anatomy (Canadian Institutes of Health Research, 2013)
Gender	Socially constructed roles, behaviors, expressions and identities of girls, women, boys, men, and gender diverse people (Canadian Institutes of Health Research, 2013)
Women	Individuals who identify with the socially constructed roles, behaviors, expressions, and identity of women (Canadian Institutes of Health Research, 2013)
Cisgender women	Individuals of female sex who identify as women
Women living with HIV	Individuals of female sex who identify as women that are of HIV-positive status
Neighborhood	The dynamic physical spaces, locations, and meanings of home areas, localities, and urban districts/regions (Hipp, 2010; Suttles, 1972)
Stress	An individual's psychological and biological responses to challenges and circumstances that are caused by stressors (Dimsdale, 2008)
Chronic stress	The continuation of an individual's stress responses throughout the lifespan (Seegerstrom & Miller, 2004)
Social determinants of health	The conditions in the environments in which people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks (US Department of Health and Human Services, 2008)
Health disparities	Variations in health outcomes that are closely linked with social, economic, and/or environmental disadvantage and adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; gender; age; mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion (US Department of Health and Human Services, 2008)
Health equity	The principle underlying a commitment to reduce- and, ultimately, eliminate- disparities in health and in its determinants, including social determinants (Braveman, 2014)

Table 1.2: Effect Size Calculations to Achieve the Study Aims

Analysis	Power	N	Independent Variables-Controlled (kc)	Independent Variables-Tested (kt)	Effect Size ( $f^2$ )	Alpha	Beta
<i>Aim 2</i>							
PSS							
	0.800	147	4	1	0.057	0.05	0.200
HCC							
	0.800	55	6	1	0.177	0.05	0.200
<i>Aim 3</i>							
FRS							
	0.800	147	4	1	0.057	0.05	0.200

Table 1.2 Displays the effect size calculations to complete the aims of this study. Separate effect size calculations were completed based differences in sample sizes for study analyses and varying independent, controlled variables for each analysis.

## **CHAPTER 2**

### **A conceptual model of neighborhood factors associated with chronic stress and CVD among women living with HIV**



## **Abstract**

As women continue to age with HIV, they are increasingly predisposed to noncommunicable diseases, such as cardiovascular disease (CVD), that contribute to increasing morbidity and mortality around the world. The intersection of individual and contextual factors, such as sex/gender, race/ethnicity, and geographic location contribute to health disparities and increased burden of CVD among women with HIV. As demonstrated, the conceptual framework calls into attention the various factors- ranging from neighborhood and community level to the individual- that contribute to chronic stress, inflammation, and cardiovascular disease as experienced by women with HIV. This conceptual is seeks to consider neighborhood and individual health determinants that are associated with CVD among HIV-infected women. Future clinical practice, research, and policy interventions are needed in order to meet the complex needs of women with HIV to promote health equity, cardiovascular wellness, and healthy aging in their neighborhoods and communities.

*Keywords: HIV, women, CVD, neighborhood, chronic stress, health disparities*

## Exemplar

*Rebecca is a 55-year-old African American woman who lives in an urban neighborhood on the South side of Chicago. She was first diagnosed with HIV in 1995 when she was hospitalized with an opportunistic infection. She recovered and was given a complicated and difficult medication regimen that she often had difficulties affording. She experienced severe depression and stigma because of her diagnosis, and she along with many of her family and friends thought that she was near death. Her family and friends often avoided her. As she continued to take her medications and found a supportive provider, she began to feel better about her prognosis. Rebecca eventually went back to work to support her three children and her mother. She has moved around various apartment complexes in her neighborhood, and she and her children had periods of unstable housing. They currently live with her partner of five years in a house. Rebecca complains about the litter in the neighborhood and feels that the city does little to keep the neighborhood clean. She has strong connections to her neighbors, friends, and church community, but many of them do not know that she is HIV-positive. She fears for the safety of her children as they walk to school, yet she is hopeful that they will stay focused on school and go to college. Rebecca often puts her children's, partner's, and mother's needs over her own, and some nights she goes without eating or gets a cheap snack from her nearby convenience store. She walks to and from the bus stop to work, but otherwise does not have an exercise routine. She occasionally experiences chest pain with straining physical activity. Rebecca feels that everything she experienced in her life, especially after HIV diagnosis, helped her find meaning and purpose. She values every day that she has with her family, friends, and neighbors.*

## **Introduction**

### **Background**

As treatment for HIV and access to antiretroviral medications has increased around the globe, women with HIV are reaching advanced ages at proportions that push the boundaries of the HIV/AIDS pandemic. It is estimated that 287,400 women were living with HIV at the end of 2013 and comprise of about 23% of individuals in the United States living with the virus (Center for Disease Control and Prevention, 2017b). Additionally, roughly 30% of individuals living with HIV are age 50 or older (High et al., 2012). The NIH Office of AIDS Research advocates for critical investigation into the aging process among individuals with HIV and identifies critical areas of investigation such as mechanisms of immune senescence, multi-variable outcome indicators, and focus towards building infrastructure that supports individuals with HIV in their communities (High et al., 2012). The Office of AIDS Research also encourages investigators to specifically explore the health of women living with HIV/AIDS, and how their environmental and neighborhood contexts shape their health outcomes.

Increasingly, HIV-infected women are experiencing common comorbidities that are associated with aging in the United States general population, such as cardiovascular disease (Al-Kindi et al., 2016). Cardiovascular disease (CVD) is characterized by inflammation and plaque formation within coronary arteries, leading to atherosclerosis and reduced blood flow to cardiac tissue, weakened cardiac muscles, and irregular heart rhythms. CVD, over time, can lead to severe and life-threatening events, such as myocardial infarction, atrial fibrillation, and heart failure (Center for Disease Control and Prevention, 2017a). About 370,000 people die annually due to CVD, and it is the number

one cause of death in the United States (Centers for Disease Control and Prevention & National Center for Health Statistics, 2017). CVD is associated with individual-level factors that promote inflammation and plaque build-up over time, such as increased caloric and fat in diet, reduced physical activity, and increased stress. Additionally, hypertension, hyperlipidemia, and diabetes further increase risk for CVD (Torpy, Burke, & Glass, 2009). As women with HIV are increasingly experiencing CVD, disparities have been noted relative to HIV-infected men and HIV-uninfected women. In the following section, I will describe the intersectional factors that impact disparities in CVD that impact WLWH.

## **Methods**

### **Purpose**

Currently, it is unclear the extent to which HIV and aspects of an individual's environment and circumstances that influence health behaviors contribute to CVD among women with HIV. Therefore, the purpose of this article is to describe a conceptual framework of neighborhood and community factors that contribute to CVD among women aging with HIV. Further, the presented conceptual framework seeks to promote investigation into causal mechanisms that contribute to CVD incidence among HIV-infected women such that interventions can be developed to reduce health disparities and promote health equity. This conceptual framework is situation-specific, which is characterized by a focus on a population and context associated with a phenomenon of interest. Additionally, situation-specific theories are critical for describing and depicting phenomena to promote interventions (A. Meleis & Im, 2001; A. I. Meleis, 1997, 1998). Therefore, this situation-specific framework of neighborhood factors that influence CVD

among WLWH intends to describe key concepts and their interrelations that are salient for policy, community, and behavioral interventions to prevent CVD and promote cardiovascular health and wellness among WLWH.

### **Approach**

A theoretical synthesis was used to derive the description of this conceptual framework. A theoretical synthesis involved integrating and transforming existing evidence to generate a new theory for a specific phenomenon. A theoretical synthesis utilizes existing evidence to depict interconnections of key concepts that are salient to describe a phenomenon of interest (Walker & Avant, 2005). Therefore, a theoretical synthesis is an appropriate strategy for theory development for CVD risk among WLWH. Further, this conceptual framework was developed with a narrative review of the literature. A narrative review is a comprehensive narrative synthesis of peer-reviewed literature that can be useful for a broad presentation of information that supports theory development (Day, 1998; Green, Johnson, & Adams, 2006; Slavin, 1995). A narrative review was selected for development of this theory due to the broad expanse of the scientific and health literature that examines CVD, neighborhoods, health behaviors, chronic stress, and inflammation among WLWH. This narrative review contributed to the development of a situation-specific theory of neighborhood and community influences on the cardiovascular health among WLWH. As intended in the development of many situation-specific theories, this conceptual framework can be used to inform interventions for cardiovascular health promotion among WLWH beyond behavioral interventions and extend to neighborhood and policy interventions.

## Review of the Literature

### *Neighborhood and community factors*

Currently, there are a variety of definitions of operationalizations of neighborhood and community. Suttles (1972) defines neighborhoods based on geographic boundaries, and describes these in three levels: home area, locality, and urban district or region. Home area refers to an individual's sense of belonging, involving familiarity and community. A locality incorporates residential activities and social status through service provision, urban planning, and housing. Urban districts refer to the social and economic opportunities within a neighborhood, including employment connections, leisure opportunities, and social networks (Suttles, 1972). As this definition implies, the boundaries and functions of neighborhoods are dynamic and defined by individuals within these areas.

For the purposes of this conceptual model- to characterize the associations between neighborhood environment and CVD among WLWH- aspects of neighborhood environments have widely been examined as built and physical factors of neighborhoods or social and relational factors of neighborhoods. Built and physical factors of neighborhoods include the structures and objects that influence health and wellness (Macintyre, Ellaway, & Cummins, 2002). Resources and services allocated to neighborhoods that individuals utilize for daily living (e.g. food, water, utilities) that are embedded in the physical and build neighborhood environment have been linked to CVD. For example, several studies of neighborhoods have demonstrated the association of perceived lack of healthy foods, and limit the dietary options with CVD (Diez-Roux & Mair, 2010; Evenson et al., 2012). Perceived reduced safety and reduced social cohesion

are associated with decreased physical activity, increased sedentary behavior, increased alcohol consumption, stress, and depression (Echeverría, Diez-Roux, Shea, Borrell, & Jackson, 2008; Evenson et al., 2012; Strong, Reitzel, Wetter, & McNeill, 2013), which predispose individuals to CVD.

Further, the aesthetic qualities of neighborhoods, which include the cleanliness and maintenance of the physical and built neighborhood, have been a major area of policy and health research. The broken windows theory, for instance posits that criminal damages to property and that go unaddressed by police and policymakers will lead to broader crime and degradation of neighborhood environments (Kelling & Wilson, 1982). This prioritized the aesthetic quality of neighborhoods and advocated for surveillance and incarceration for low-level offenses and quality of life crimes (e.g. petty theft, public intoxication, prostitution, disorderly conduct, vandalism) as means of preventing neighborhood degradation (Herbert, 2001). Further, as Sampson and Raudenbush (2004) note, broken windows ideas of causal factors associated with neighborhood disorder can be influenced by systemic racism and stereotypes of neighborhoods related to the racial/ethnic and socioeconomic composition. Additionally, the success of broken windows policing and incarceration has often been overstated, and broken windows policing lead to disproportionate criminalization of Black and Hispanic/Latinx persons, reduced funding for social welfare programs, increased costs in the criminal justice system, undermined community policing strategies, and sowed distrust of police among racial and ethnic minorities (Kamalu & Onyeozili, 2018). As health research has focused on broken windows and aesthetic qualities, studies have consistently noted the link between neighborhood deprivation and risk of CVD (Chaix, Rosvall, & Merlo, 2007;

Diez-Roux et al., 1997; Kim, Diez Roux, Kiefe, Kawachi, & Liu, 2010). Although research and policies have moved beyond the focus of broken windows, the importance of neighborhood qualities and their association with cardiovascular health persists.

Additionally, neighborhoods and communities are often conceptualized as social systems, which develop specific functions (e.g. political, economic, etc.) that adapt to the needs of the community (Alinsky, 1972). Within this lens, communities organize to function based on the demands of their circumstances and respond to issues that impact them in a specific time and place (Alinsky, 1972; Sen, 2003). Lastly, the racial and ethnic background of inhabitants is inextricably tied to the functions and dynamics of neighborhoods and communities. Various non-White communities are impacted by systems of oppression (e.g. racism, sexism, etc.), and these systems influence the functions within and between communities and neighborhoods (Chávez, Minkler, Wallerstein, & Spencer, 2007; Rivera & Erlich, 2001).

When taking these various aspects of neighborhoods and community into account, there are several key assumptions that are made that are critical to the promotion of health equity in order to address CVD incidence among WLWH. First, in health research it is often assumed that neighborhoods and communities are fixed and limited to a specific place in time, particularly when neighborhood level data is aggregated by zip code or census tract. While this may be true in regard to the physical location of certain settings, neighborhood and communities are dynamic, with boundaries that are porous, flexible, and influenced by a variety of external forces, such as crime, housing, and economic opportunities (Brawner, Reason, Goodman, Schensul, & Guthrie, 2015; Hipp, 2010). Therefore, the conceptualization of neighborhood in this model recognizes aspects



of physical space, location, and meaning of neighborhoods as dynamic and defined by individuals.

Individuals in neighborhoods with fewer health care services, reduced transportation options, less affordable food options, less walkable neighborhoods, and increased crime and violence have an increased risk for CVD (Diez-Roux et al., 2001; Diez-Roux et al., 1997). Further, neighborhood socioeconomic deprivation and concentrated incarceration influence can negatively influence the cardiovascular health and wellness of individuals, including women living with HIV, who have experienced incarceration and their families and communities overall (Kim et al., 2010; Lee, Wildeman, Wang, Matusko, & Jackson, 2014; Lugalia-Hollon & Cooper, 2018; Nazmi, Roux, Ranjit, Seeman, & Jenny, 2010; Nazmi & Victora, 2007; Wildeman & Wang, 2017). There have been a wide variety of interventions that have focused directly on these aspects of neighborhoods and communities, yet there is a lack of specific focus on these environmental constructs and their specific impact on CVD among HIV-infected women. However, there is a body of literature that supports the impacts of neighborhood and community factors and their influence on HIV management among women, which if compromised, could influence coronary artery disease processes. Shacham, Lian, Önen, Donovan, and Overton (2013) demonstrated that HIV-infected individuals who reside in neighborhoods with higher poverty rates were more likely to have low CD4 cell counts, which could predispose WLWH to CVD.

In this model, health resources and services can be defined as the resources for daily living, health maintenance, and variety of services that are associated with cardiovascular functioning, and include clinics, pharmacies, and hospitals; restaurants,

grocery stores, and convenience stores, and other social services. Neighborhoods that have reduced or limited accessibility of resources and services can contribute to negative impacts on individual health (Block, Scribner, & DeSalvo, 2004). Additionally, social interactions and networks, are the interactions and relationships that women with HIV have with fellow members of their community that influence social cohesion and comfort within their neighborhood. Reduced social interaction and social networks are documented to contribute to poor health outcomes (Klijs, de Leon, Kibele, & Smidt, 2017), and it is likely that reduced social interactions and reduced social cohesion contribute to CVD among women with HIV. Lastly, transportation and movement can be defined as the resources (e.g. cars, busses, trains, sidewalks, etc.) and movement through and across communities. Transportation services and movement, and in particular, their relationship with physical inactivity, can increase the risk of CVD in the context of neighborhoods and communities (Sallis, Floyd, Rodríguez, & Saelens, 2012).

Within this model of CVD among WLWH, the neighborhood and community factors of decreased health resources and services, negative or reduced social interactions and networks, and limited transportation and movement options, can in combination, contribute to environmental constraints that serve as the context in which women with HIV make decisions and/or serve as locations in which women with HIV are exposed to factors that contribute to CVD. In the Integrated Behavioral Model (IBM), Fishbein and Yzer (2003) define environmental constraints as the barriers that may prevent individuals from partaking in protective health behaviors. In this conceptual model, reduced health resources and services, limited social networks and social isolation, and reduced

movement throughout neighborhoods can contribute to CVD among HIV-infected women over time.

### ***Interaction between neighborhoods and individuals***

Within this conceptualization of neighborhoods/communities and women with HIV, it is critical to incorporate the various interactions that occur over time that impact health and wellness. Within the socioecological perspective, Bronfenbrenner (1977) discussed the interactions an individual has within their environment as being dynamic and reciprocal as they develop over their life course. Additionally, social cognitive theory defines the nature of the interaction between individuals and their environment as reciprocal determinism, which is the process by which individual behavior is shaped by the continued and ever-changing interaction between individual, social, and environmental factors (Bandura, 1978, 1983). Influencing factors within neighborhoods and communities on individuals include racism, sexism, neighborhood deprivation, and economic status, and have been shown to influence cardiovascular diseases (Calvin et al., 2003; Diez-Roux et al., 1997; Jackson, 1994; LaVeist, Nickerson, & Bowie, 2000). Additionally, individuals can influence and change their neighborhood and community. For instance, individuals may demonstrate political agency, economic and resource contribution, and socialization in their neighborhoods and communities (Chitewere, Shim, Barker, & Yen, 2017). In the context of WLWH, women often contribute to their communities based on the gender normative roles and commonly perform caretaking positions (Asuquo, Etowa, & Akpan, 2017). In this process, women often place their role as caretaker above their individual needs, which can have negative impacts on health and wellness. In both cardiovascular and HIV literature, this role strain has negatively

influenced health outcomes (Caiola, Barroso, & Docherty, 2017). In this model of CVD pathogenesis, the directionality of women contributing to their neighborhood and community can have negative health impacts regarding the potential lack of individual health prioritization relative to their neighborhood and community engagement.

### *Individual factors*

Individual factors that contribute to CVD pathogenesis include a variety of characteristics that uniquely contribute to CVD among WLWH. Within the domain of individual factors, each woman's unique combination of attributes and behaviors contribute to their cardiovascular health over time. Within this model, individual factors that contribute to the CVD disease process include general factors, those commonly regarded as factors for CVD within non-HIV infected persons, and HIV-related factors, which include specific aspects of HIV that influence CVD. Within individuals, general and HIV-related risk factors contribute to increased stress and inflammation that, in turn, advances aging. These processes, over time, contribute to CVD and associated health problems among women with HIV.

### *General factors*

Personal traits comprise of demographic characteristics, socioeconomic position and status, education, race/ethnicity, and aspects of individual personality and health among women with HIV. As describe previously, women with HIV are impacted by a variety of intersecting personal traits, such as race/ethnicity and sex/gender, that predispose them to CVD related to inequitable distribution of resources that promote health and wellness. Therefore, in this model, the various intersecting traits of women

with HIV and their associations with increased stress and experiences of discrimination and adversity are important forces in the onset of CVD.

Discrimination refers to the unfair, unethical, and demeaning treatment of individuals based on individual characteristics, and can include race and gender discrimination (Newman, Williams, Massaquoi, Brown, & Logie, 2008). Experiences of discrimination impact individual health when discrimination is perceived and/or internalized, and can cause individuals to hold negative attitudes or beliefs about oneself that contribute to stress and negative affect and self-concept (Armstead, Lawler, Gorden, Cross, & Gibbons, 1989; Fang & Myers, 2001; Klonoff, Landrine, & Ullman, 1999). Perceived discrimination has been associated with depression, post-traumatic stress, and low health satisfaction (Bird, Bogart, & Delahanty, 2004; Boarts, Bogart, Tabak, Armelie, & Delahanty, 2008). Further, perceived and internalized discrimination have been associated with CVD as the stress of interpersonal experiences and/or negative self-concept contribute to increased stress throughout the lifespan (Calvin et al., 2003). Additionally, discrimination has been associated with hypertension, diabetes, and CVD, as well as all-cause mortality as it contributes to chronic stress and health behavior (Paradies, 2006). Critical consciousness- which can be defined as the awareness of social discrimination- has been associated with better health outcomes among WLWH, and demonstrates the benefits of confronting discriminatory practices and ideas that impact HIV-infected women (Kelso et al., 2014).

Behaviors can be defined as the various health-related actions that women with HIV may conduct that protect or predisposes them to CVD. Health behaviors have been widely studied among individuals with HIV and within CVD literature as several

behavioral theories, such as the Health Belief Model, the Integrative Behavioral Model, Social Cognitive Theory, and Ecosocial Models- to name a few- have supported the development of behavioral interventions for HIV management and CVD prevention (Glanz, Rimer, & Viswanath, 2008). As described previously, risk or protective behaviors include diet and nutrition, physical activity, central obesity, alcohol and substance abuse, and cigarette smoking, which can contribute to increased risk of CVD (Center for Disease Control and Prevention, 2015). Several behavioral theories indicate that these risk factors are heavily influenced by environment, and various environmental constraints can lead to CVD among women with HIV. Studies that have examined health behaviors of WLWH with a focus on CVD have found that general behavioral factors, such as elevated caloric diet, physical inactivity, cigarette smoking, and illicit drug use (e.g. crack/cocaine, methamphetamine, heroin, and marijuana use) are associated with elevated CVD risk and disease severity (Duran, Almeida, Segurado, & Jaime, 2008; Hessol et al., 2013; Koczor et al., 2015; Lai et al., 2016; Okafor et al., 2017; Patterson et al., 2015; Petoumenos & Law, 2016; Reece, Norman, & Hulse, 2016; Vallecillo et al., 2013; Webel et al., 2015). Importantly, the development and promotion of behavioral interventions that seek to encourage dietary change, physical activity, and smoking cessation among WLWH have demonstrated cardiovascular health benefits (Dubé et al., 2003; Fitch et al., 2006; Hessol et al., 2014; Stradling et al., 2012). Therefore, in this theoretical model, behavior is broadly defined and can encompass a variety of health behaviors that influence cardiovascular health.

Genetic and metabolic factors that influence general risk for CVD involve the various genetic and metabolic functions that contribute to cardiovascular and

inflammatory system health and function. Evidence regarding genetic factors that influence risk for CVD is increasing, and genes linked to increased cholesterol have been associated with CVD pathogenesis (Khera & Kathiresan, 2017). As inherited DNA has been shown to play a role in CVD and cardiovascular health, this relationship is complex and prevalence of large genetic contributions to CVD are rare (Kathiresan & Srivastava, 2012). Genetic factors may predispose WLWH to cardiometabolic dysfunctions, such as hypertension, elevated blood glucose and diabetes, and hypercholesteremia contribute to CVD and the formation of coronary plaque and calcification (Center for Disease Control and Prevention, 2015).

Reproductive hormonal function regards the activity of reproductive system functions that contribute to the production of hormones, such as estrogen, progesterone, and testosterone (National Cancer Institute, n.d.). In females, estrogen and progesterone play vital roles in the development of sex characteristics, menstruation, fertility, and pregnancy. Further, estrogen and progesterone are theorized to be health protective, and reduced production of these hormones has been associated with the onset of a variety of noncommunicable diseases among women, including CVD (Schoenbaum et al., 2005). In addition, post-menopausal status has been associated with accelerated and accentuated aging among HIV-infected women (Mesch et al., 2008). WLWH have demonstrated hastened menopause when compared with HIV-uninfected women (Fan, Maslow, Santoro, & Schoenbaum, 2008), which can contribute to increased risk for CVD.

#### *HIV-related factors*

Independent of general factors that contribute to CVD, women have additional factors related to HIV-associated stigma, HIV viral activity, side effects of antiretroviral

medications, in particular metabolic and body fat distribution changes as a result of antiretroviral medications. Individuals with HIV often experience internalized stigma, which refers to the self-perceptions of cultural and societal conceptions about individuals with HIV/AIDS that involves feelings that damage one's character and identity (Goffman, 2009). Internalized stigma is common among women with HIV, and it is associated with depression (Simbayi et al., 2007). HIV viral activity, within the context of this conceptual model, refers to the latent or active state of the HIV virus and its interactions with various cells and tissues. Several studies have demonstrated that HIV-infected individuals with elevated HIV viral load and low CD4 cell count, clinical markers of HIV disease progression, demonstrate increased morbidity and mortality due to CVD (Baker et al., 2008; Kaplan et al., 2008; Modrich et al., 2010). These findings have consistently highlighted the importance of antiretroviral medications in preventing CVD among women with HIV.

Despite the significance of medication adherence in preventing the progression of HIV, certain medication regimens have been associated with elevated risk for CVD. In this conceptual model, HIV medication and side effects refer to the continued use and exposure to various antiretroviral agents and their interaction with immune, inflammatory cardiovascular, and metabolic functions. The specific cardiovascular impacts of various antiretroviral regimens are controversial. Certain antiretroviral medication regimens have been associated with elevated risk for CVD, and include nucleoside and non-nucleoside reverse-transcriptase inhibitors, and protease inhibitors (Alcaide et al., 2013; Carr & Cooper, 2000; Friis-Møller et al., 2003; Kaplan et al., 2012; Lekakis et al., 2008). These medications have been associated with dyslipidemia, insulin resistance, lipodystrophy,



endothelial tissue damage, and diastolic dysfunction (Butler et al., 2018; Carr & Cooper, 2000; Friis-Møller et al., 2003; Tien et al., 2010; Zanetti et al., 2018). Antiretroviral medications are necessary for the survival and wellness of women living with HIV and contribute to protect immune function yet can alter metabolic function (Carr & Cooper, 2000). More evidence is needed to examine the chronic effects of antiretroviral regimen on cardiovascular health among WLWH.

One commonly experienced effect of antiretroviral medications can occur as morphologic and cardiometabolic system changes that may predispose WLWH to CVD. For instance, body fat distribution changes that are associated with antiretroviral medication use include lipoatrophy of the face and limbs and lipohypertrophy of visceral, breast, cervical regions of the abdomen (Grunfeld et al., 2010; Hadigan, Liebau, Andersen, Holalkere, & Sahani, 2007; Jacobson et al., 2005; Torriani, Hadigan, Jensen, & Grinspoon, 2003). Similarly, cardiometabolic alterations associated with antiretroviral therapies that may predispose WLWH to CVD include dyslipidemia and glucose and insulin changes that may contribute to metabolic syndrome and CVD. For example, antiretroviral medications have been associated with hypertriglyceridemia, hypercholesterolemia, glucose intolerance, elevated fasting blood glucose, glucose intolerance, and insulin resistance (Behrens et al., 1999; Brown et al., 2004; Friis-Møller et al., 2003; Hadigan et al., 2001; Martínez, Conget, Lozano, Casamitjana, & Gatell, 1999). Continued investigations and interventions are needed to address morphologic and metabolic changes associated with antiretroviral medication use as WLWH age to promote cardiovascular health and disease prevention.

### *Stress and inflammation*

Stress and inflammation are the key processes that mediate general and HIV related risk factors that contribute to a cascade of process that cause CVD. Stress has been conceived in a variety of ways, incorporating multiple bodily systems and processes that often contribute to negative health outcomes. Selye (1959) defined stress as stress “a state manifested by a specific syndrome which consists of all the non-specifically induced changes in a biologic system”. Thus, stress is an individual’s psychological and biological responses to challenges and circumstances that are caused by stressors (Dimsdale, 2008). However, beyond defining stress as a response to stimuli, cognitive theory of stress and coping defines stress in relational and process-oriented terms. In this perspective, stress is relational regarding the individual and their environment, and the individual perceived aspects or situations in their environment as stressors. As a process, the individual stress experience is dynamic and bidirectional (Folkman, 1984). This conceptual framework recognizes that an individual’s experience is predicated on cognitive appraisal, is mediated by biological bodily responses, and is situated within a dynamic system between the individual and their environment.

One key mechanism by which stress impacts health outcomes is altered immune functioning. In a review of 30 years of research regarding the impact of stress on immune function, Segerstrom and Miller (2004) noted that chronic stress was consistently associated with suppression of both cellular and humoral immune function in a meta-analysis of over 300 peer-reviewed publications of stress and immune function. More specifically, chronic stress can suppress humoral and cellular immune function (e.g. decreased neutrophils, eosinophils, monocytes, cytotoxic T cells, natural killer cells) and

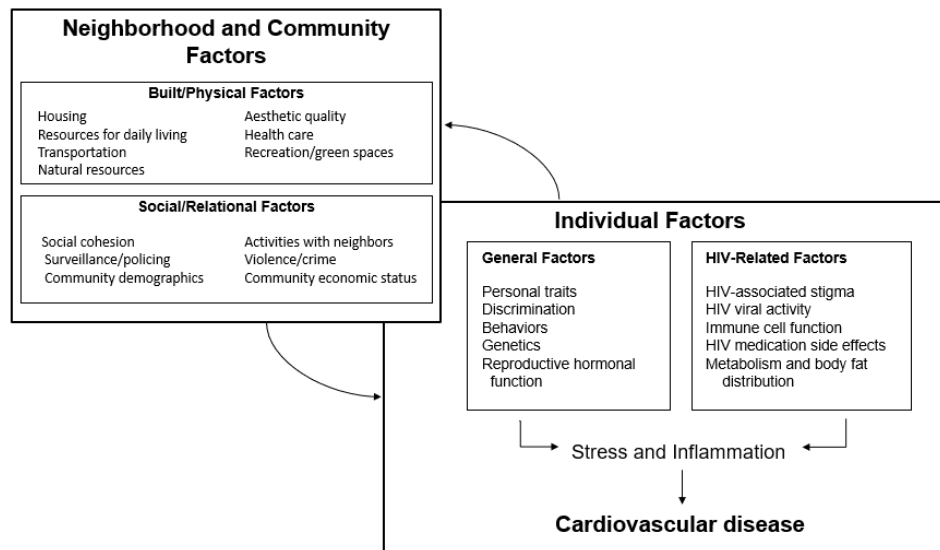
increase pro-inflammatory cytokines (Segerstrom & Miller, 2004), which increase an individual's susceptibility to illness and disease. Further, individuals with HIV have greater predisposition for illness as impacted by stress and HIV, as HIV infection directly impacts immune function and is associated with accelerated immunosenescence (Appay et al., 2011; Dock & Effros, 2011; Hearps et al., 2011; Napolitano et al., 2001). This body of evidence suggests that stress among WLWH can critically impact their immune system, which in addition to the impact of HIV itself, can contribute to cardiovascular disease. In this model, it is posited that women with HIV are exposed to a combination of a variety of factors (e.g. HIV management, stigma, SES, gender, and race/ethnicity) over time that reduce immune functioning capacity and contribute to the development of CVDs. More evidence is needed to specifically examine the extent to which stressors contribute to CVD among women with HIV.

Individual-level stressors are common among women with HIV, and can include unemployment (Brief et al., 2004) and low socioeconomic position (Machtiger, Wilson, Haberer, & Weiss, 2012) single-parent role (Georgina Spies et al., 2012), childhood trauma (Spies, Fennema-Notestine, Archibald, Cherner, & Seedat, 2012), physical and intimate partner violence (Palar et al., 2018), and HIV-associated stigma (Palar et al., 2018; Rice et al., 2018). In turn, the added effect of these chronic stressors contribute to reduced antiretroviral treatment adherence (Bottonari, Safren, McQuaid, Hsiao, & Roberts, 2010; L. Delahanty, M. Bogart, & L. Figler, 2004), increased inflammation, and increased morbidity and mortality due to CVD (Golbidi, Frisbee, & Laher, 2015). Chronic stress a process by which these neighborhood-level and individual-level stressors are internalized and impact individual health for women with HIV. As defined by

Segerstrom and Miller (2004), chronic stress is the continuation of an individual’s stress responses across the life course, and can be caused by a variety of circumstances that often influence individual behaviors, including neighborhood stressors. For instance, neighborhoods are the environments in which individuals are exposed to circumstantial and life stressors, such as violence and concentrated poverty, are a daily part of living and can be hard to avoid (Lederbogen et al., 2011; Matheson et al., 2006). Women with HIV tend to reside in neighborhoods that are impacted by segregation and disinvestment and exposed to violence, pollution, poverty, and other neighborhood-level stressors that may impact their lives daily (Brawner, 2014; White & Borrell, 2011). Therefore, these structural forces at the neighborhood level influence the chronic stress and perpetuate inequity in health outcomes of women with HIV across the life span (Geronimus, 2000; White & Borrell, 2011).

### Conceptual Model

*Figure 1: Conceptual model of neighborhood and individual factors associated with CVD among women with HIV*



This conceptual model (Figure 1) seeks to incorporate varying levels of factors that contribute to disparities in diagnosis of CVD among HIV-infected women. Focusing on the disease process of CVD in this model promotes a focus on various factors that intersect to contribute to or protect from CVD among women with HIV. The explicit focus on neighborhood and community influences and interactions on individual CVD incidence among women with HIV has been designated for a variety of reasons. First, neighborhoods and communities are widely regarded as the context for which people make health decisions, and that these environments are the foundation for which individual health develops from (Weiss, Ompad, Galea, & Vlahov, 2007). Further, neighborhoods across the United States are spatial units in which differential allocation of resources and freedoms manifest and have historically been influenced by racism, mass incarceration and concentrated policing, segregation, white supremacy, and the pursuit of capital. These forces continue to influence neighborhoods and perpetuate inequity and injustice (White & Borrell, 2011). By narrowing our attention to neighborhoods and communities, this conceptual model encourages the investigation of these forces in the setting in which women with HIV age. Evaluating neighborhoods and communities encourages healthcare providers, researchers, policy makers, and communities to collaboratively develop multilevel interventions to reduce health disparities in CVD incidence among HIV-infected women and promote healthy aging through a health-equity lens.

## **Discussion**

The purpose of this paper was to develop a conceptual framework of neighborhood and community factors that influence cardiovascular health and disease

among WLWH across the lifespan through a synthesis of existing research and theory. This framework integrates literature that suggests the contribution of various aspects of neighborhoods (e.g. social ecological theory, social learning theory, etc.) that are associated with health behaviors, stress, and inflammation among WLWH. The interaction between individual and neighborhood environment, over time, can contribute to individual cardiovascular health outcomes and disease risk.

There are a variety of theoretical models that have sought to describe salient factors associated with CVD among individuals with HIV. For instance, several frameworks have been proposed to describe the inflammatory mechanisms of CVD among individuals with HIV. Several of these conceptual models have illustrated immune activation and inflammatory activity among individuals with HIV. Specifically, many of these theories have focused on the relationship between vascular hyperinflammation and ischemic heart disease resulting from prolonged HIV infection and treatment (Beltrán et al., 2015; Cerrato et al., 2015; Stein, Currier, & Hsue, 2014; Vachiat, McCutcheon, Tsabedze, Zachariah, & Manga, 2017; Zanetti et al., 2018). Further, various theories of neighborhood and community influences on health, such as socioecological theory and social determinants of health, lack a disease-specific approach relative to their level of theoretical abstraction, and therefore do not connect salient constructs and their interrelations with disease-specific health outcomes. The conceptual framework presented here adds to the scientific literature by connecting varying levels of environmental factors, ranging from cities to cells, that contribute to CVD among WLWH.

This theoretical synthesis and description of a conceptual model of neighborhood and individual factors associated with CVD among WLWH is not without limitations. First, the literature review used to generate this theoretical synthesis was conducted via narrative review. This review strategy is difficult to reproduce and does not include a critical evaluation of the literature or analysis of evidence across studies (Green et al., 2006). This review method was selected due to the sparse literature regarding neighborhood and community associations with health outcomes among individuals living with HIV. As studies of neighborhood-level influences on health outcomes among persons with HIV emerge, further reviews of the literature are needed to evaluate the strength and quality of the evidence. Additionally, this conceptual model is a disease-specific model that focuses on risk related to stress as a mechanism of CVD. This model does not capture cognitive processes and factors that impact stress response, coping, and other mental health or mood disorders (e.g. depressive mood) in their relation to CVD among WLWH. Future iterations of this conceptual model will incorporate cognition and mood disorders and their influence on CVD among WLWH. Further, like many theories that focus on disease risk, many of the key concepts included in this theory are related to pathology and considered as deficits-focused (Aronowitz, 2015). Importantly, the lives and wellness of WLWH are complex, and they are often resilient to difficulties despite inequity and various health and life challenges (Dale et al., 2014). Continued research is needed to examine resiliency and strengths and their relationship to health outcomes among WLWH. Thereby, the strength and resilience of WLWH can be supported by clinical and policy interventions to promote cardiovascular health and wellness as defined by the women themselves.

## **Conclusion**

Women with HIV are vulnerable to CVD in a variety of ways, and their neighborhood and environment form the context in which they are exposed to circumstances that contribute to CVD. Since women with HIV are aging and women are contracting HIV at older ages, it is critical that we determine causal mechanisms that contribute to disparities in CVD disease incidence and outcomes. The development of interventions to reduce risk for CVD must take into account factors that are important with HIV disease management (e.g. medication management, elevating CD4 cell count) and general prevention of cardiovascular disease (e.g. lipid and blood pressure management, smoking cessation, diet and exercise behavior change) simultaneously among women aging with HIV. Furthermore, a health equity focus provided by this conceptual framework allows for the examination of differential allocation of resources in relation to HIV management and cardiovascular health can promote broad and sustainable interventions that can reduce inequality and injustice experienced by with HIV in the neighborhoods and communities in which they reside. Further research is needed to consider these factors to encourage cardiovascular health and wellness for women with HIV as they age.



## References

- Al-Kindi, S. G., ElAmm, C., Ginwalla, M., Mehanna, E., Zacharias, M., Benatti, R., . . . Longenecker, C. T. (2016). Heart failure in patients with human immunodeficiency virus infection: epidemiology and management disparities. *International journal of cardiology*, 218, 43-46.
- Alcaide, M. L., Parmigiani, A., Pallikkuth, S., Roach, M., Freguja, R., Della Negra, M., . . . Pahwa, S. (2013). Immune activation in HIV-infected aging women on antiretrovirals—implications for age-associated comorbidities: a cross-sectional pilot study. *PLoS One*, 8(5), e63804.
- Alinsky, S. (1972). *Rules for radicals: A political primer for practical radicals*: New York: Random House.
- Appay, V., Fastenackels, S., Katlama, C., Ait-Mohand, H., Schneider, L., Guihot, A., . . . Lambotte, O. (2011). Old age and anti-cytomegalovirus immunity are associated with altered T-cell reconstitution in HIV-1-infected patients. *Aids*, 25(15), 1813-1822.
- Armstead, C. A., Lawler, K. A., Gorden, G., Cross, J., & Gibbons, J. (1989). Relationship of racial stressors to blood pressure responses and anger expression in black college students. *Health Psychology*, 8(5), 541.
- Aronowitz, R. (2015). *Risky medicine: our quest to cure fear and uncertainty*: University of Chicago Press.
- Asuquo, E. F., Etowa, J. B., & Akpan, M. I. (2017). Assessing women caregiving role to people living with HIV/AIDS in Nigeria, West Africa. *SAGE Open*, 7(1), 2158244017692013.

- Baker, J. V., Peng, G., Rapkin, J., Krason, D., Reilly, C., Cavert, W. P., . . . Neaton, J. D. (2008). Poor initial CD4+ recovery with antiretroviral therapy prolongs immune depletion and increases risk for AIDS and non-AIDS diseases. *Journal of acquired immune deficiency syndromes (1999)*, *48*(5), 541.
- Bandura, A. (1978). The self system in reciprocal determinism. *American psychologist*, *33*(4), 344.
- Bandura, A. (1983). Temporal dynamics and decomposition of reciprocal determinism: A reply to Phillips and Orton.
- Behrens, G., Dejam, A., Schmidt, H., Balks, H.-J., Brabant, G., Körner, T., . . . Schmidt, R. E. (1999). Impaired glucose tolerance, beta cell function and lipid metabolism in HIV patients under treatment with protease inhibitors. *Aids*, *13*(10), F63-F70.
- Beltrán, L. M., Rubio-Navarro, A., Amaro-Villalobos, J. M., Egido, J., García-Puig, J., & Moreno, J. A. (2015). Influence of immune activation and inflammatory response on cardiovascular risk associated with the human immunodeficiency virus. *Vascular health and risk management*, *11*, 35.
- Bird, S. T., Bogart, L. M., & Delahanty, D. L. (2004). Health-related correlates of perceived discrimination in HIV care. *AIDS Patient care and STDs*, *18*(1), 19-26.
- Block, J. P., Scribner, R. A., & DeSalvo, K. B. (2004). Fast food, race/ethnicity, and income: a geographic analysis. *American journal of preventive medicine*, *27*(3), 211-217.
- Boarts, J. M., Bogart, L. M., Tabak, M. A., Armelie, A. P., & Delahanty, D. L. (2008). Relationship of race-, sexual orientation-, and HIV-related discrimination with

- adherence to HIV treatment: a pilot study. *Journal of behavioral medicine*, 31(5), 445-451.
- Bottonari, K. A., Safren, S. A., McQuaid, J. R., Hsiao, C.-B., & Roberts, J. E. (2010). A longitudinal investigation of the impact of life stress on HIV treatment adherence. *Journal of behavioral medicine*, 33(6), 486-495.
- Brawner, B. M. (2014). A multilevel understanding of HIV/AIDS disease burden among African American women. *Journal of Obstetric, Gynecologic & Neonatal Nursing*, 43(5), 633-643.
- Brawner, B. M., Reason, J. L., Goodman, B. A., Schensul, J. J., & Guthrie, B. (2015). Multilevel drivers of human immunodeficiency virus/acquired immune deficiency syndrome among Black Philadelphians: exploration using community ethnography and geographic information systems. *Nursing research*, 64(2), 100-110.
- Brief, D. J., Bollinger, A., Vielhauer, M., Berger-Greenstein, J., Morgan, E., Brady, S., . . . Group, C. S. (2004). Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*, 16(sup1), 97-120.
- Bronfenbrenner, U. (1977). Toward an experimental ecology of human development. *American psychologist*, 32(7), 513.
- Brown, T., Cole, S., Li, X., Kingsley, L., Palella, F., & Riddler, S. (2004). *Prevalence and incidence of pre-diabetes and diabetes in the Multicenter AIDS Cohort Study*. Paper presented at the Eleventh Conference on Retroviruses and Opportunistic Infections. San Francisco, CA.

- Butler, J., Kalogeropoulos, A. P., Anstrom, K. J., Hsue, P. Y., Kim, R. J., Scherzer, R., . . . Hernandez, A. F. (2018). Diastolic Dysfunction in Individuals With Human Immunodeficiency Virus Infection: Literature Review, Rationale and Design of the Characterizing Heart Function on Antiretroviral Therapy (CHART) Study. *Journal of cardiac failure, 24*(4), 255-265.
- Caiola, C., Barroso, J., & Docherty, S. L. (2017). Capturing the social location of African American mothers living with HIV: An inquiry into how social determinants of health are framed. *Nursing research, 66*(3), 209.
- Calvin, R., Winters, K., Wyatt, S. B., Williams, D. R., Henderson, F. C., & Walker, E. R. (2003). Racism and cardiovascular disease in African Americans. *The American journal of the medical sciences, 325*(6), 315-331.
- Carr, A., & Cooper, D. A. (2000). Adverse effects of antiretroviral therapy. *The Lancet, 356*(9239), 1423-1430.
- Center for Disease Control and Prevention. (2015). Heart Disease (CAD). Retrieved from [https://www.cdc.gov/heartdisease/coronary\\_ad.htm](https://www.cdc.gov/heartdisease/coronary_ad.htm)
- Center for Disease Control and Prevention. (2017a). Heart Disease Facts. Retrieved from <https://www.cdc.gov/heartdisease/facts.htm>
- Center for Disease Control and Prevention. (2017b). HIV among women. Retrieved from <https://www.cdc.gov/hiv/group/gender/women/index.html>.
- Centers for Disease Control and Prevention, & National Center for Health Statistics. (2017). *Underlying Cause of Death 1999-2015 on CDC WONDER Online Database, released December, 2016. Data are from the Multiple Cause of Death Files, 1999-2015, as compiled from data provided by the 57 vital statistics*

*jurisdictions through the Vital Statistics Cooperative Program*. Retrieved from:  
<https://wonder.cdc.gov/ucd-icd10.html>

Cerrato, E., Calcagno, A., D'ascenzo, F., Biondi-Zoccai, G., Mancone, M., Marra, W. G., . . . Bonora, S. (2015). Cardiovascular disease in HIV patients: from bench to bedside and backwards. *Open heart*, 2(1), e000174.

Chaix, B., Rosvall, M., & Merlo, J. (2007). Neighborhood socioeconomic deprivation and residential instability: effects on incidence of ischemic heart disease and survival after myocardial infarction. *Epidemiology*, 18(1), 104-111.

Chávez, V., Minkler, M., Wallerstein, N., & Spencer, M. S. (2007). Community organizing for health and social justice. *Prevention is primary: Strategies for community well-being*, 95-120.

Chitewere, T., Shim, J. K., Barker, J. C., & Yen, I. H. (2017). How Neighborhoods Influence Health: Lessons to be learned from the application of political ecology. *Health & place*, 45, 117-123.

Dale, S. K., Cohen, M. H., Kelso, G. A., Cruise, R. C., Weber, K. M., Watson, C., . . . Brody, L. R. (2014). Resilience among women with HIV: Impact of silencing the self and socioeconomic factors. *Sex roles*, 70(5-6), 221-231.

Day, R. A. (1998). How to write and publish scientific papers: SciELO Brasil.

Diez-Roux, A. V., & Mair, C. (2010). Neighborhoods and health. *Annals of the New York Academy of Sciences*, 1186(1), 125-145.

Diez-Roux, A. V., Merkin, S. S., Arnett, D., Chambless, L., Massing, M., Nieto, F. J., . . . Watson, R. L. (2001). Neighborhood of residence and incidence of coronary heart disease. *New England Journal of Medicine*, 345(2), 99-106.

- Diez-Roux, A. V., Nieto, F. J., Muntaner, C., Tyroler, H. A., Comstock, G. W., Shahar, E., . . . Szklo, M. (1997). Neighborhood environments and coronary heart disease: a multilevel analysis. *American journal of epidemiology*, *146*(1), 48-63.
- Dimsdale, J. E. (2008). Psychological stress and cardiovascular disease. *Journal of the American College of Cardiology*, *51*(13), 1237-1246.
- Dock, J. N., & Effros, R. B. (2011). Role of CD8 T cell replicative senescence in human aging and in HIV-mediated immunosenescence. *Aging and disease*, *2*(5), 382.
- Dubé, M. P., Stein, J. H., Aberg, J. A., Fichtenbaum, C. J., Gerber, J. G., Tashima, K. T., . . . Glesby, M. J. (2003). Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group. *Clinical infectious diseases*, *37*(5), 613-627.
- Duran, A., Almeida, L., Segurado, A., & Jaime, P. (2008). Diet quality of persons living with HIV/AIDS on highly active antiretroviral therapy. *Journal of human nutrition and dietetics*, *21*(4), 346-350.
- Echeverría, S., Diez-Roux, A. V., Shea, S., Borrell, L. N., & Jackson, S. (2008). Associations of neighborhood problems and neighborhood social cohesion with mental health and health behaviors: the Multi-Ethnic Study of Atherosclerosis. *Health & place*, *14*(4), 853-865.
- Evenson, K. R., Block, R., Roux, A. V. D., McGinn, A. P., Wen, F., & Rodríguez, D. A. (2012). Associations of adult physical activity with perceived safety and police-

- recorded crime: the Multi-ethnic Study of Atherosclerosis. *International journal of behavioral nutrition and physical activity*, 9(1), 146.
- Fan, M. D., Maslow, B.-S., Santoro, N., & Schoenbaum, E. (2008). HIV and the menopause. *Menopause International*, 14(4), 163-168.
- Fang, C. Y., & Myers, H. F. (2001). The effects of racial stressors and hostility on cardiovascular reactivity in African American and Caucasian men. *Health Psychology*, 20(1), 64.
- Fishbein, M., & Yzer, M. C. (2003). Using theory to design effective health behavior interventions. *Communication theory*, 13(2), 164-183.
- Fitch, K. V., Anderson, E. J., Hubbard, J. L., Carpenter, S. J., Waddell, W. R., Caliendo, A. M., & Grinspoon, S. K. (2006). Effects of a lifestyle modification program in HIV-infected patients with the metabolic syndrome. *Aids*, 20(14), 1843-1850.
- Folkman, S. (1984). Personal control and stress and coping processes: A theoretical analysis. *Journal of personality and social psychology*, 46(4), 839.
- Friis-Møller, N., Weber, R., Reiss, P., Thiébaud, R., Kirk, O., Monforte, A. d. A., . . . Law, M. (2003). Cardiovascular disease risk factors in HIV patients—association with antiretroviral therapy. Results from the DAD study. *Aids*, 17(8), 1179-1193.
- Geronimus, A. T. (2000). To mitigate, resist, or undo: addressing structural influences on the health of urban populations. *American journal of public health*, 90(6), 867.
- Glanz, K., Rimer, B., & Viswanath, K. (2008). *Health Behavior and Education: Theory, Research and Practice* (4th ed.): San Francisco, CA: Jossey-Bass.
- Goffman, E. (2009). *Stigma: Notes on the management of spoiled identity*: Simon and Schuster.

- Golbidi, S., Frisbee, J. C., & Laher, I. (2015). Chronic stress impacts the cardiovascular system: animal models and clinical outcomes. *American Journal of Physiology-Heart and Circulatory Physiology*, 308(12), H1476-H1498.
- Green, B. N., Johnson, C. D., & Adams, A. (2006). Writing narrative literature reviews for peer-reviewed journals: secrets of the trade. *Journal of chiropractic medicine*, 5(3), 101-117.
- Grunfeld, C., Michael, S., Cofrancesco Jr, J., Lewis, C. E., Kronmal, R., Heymsfield, S., . . . Scherzer, R. (2010). Regional adipose tissue measured by MRI over five years in HIV-infected and control subjects indicates persistence of HIV-associated lipodystrophy. *AIDS (London, England)*, 24(11), 1717.
- Hadigan, C., Liebaw, J., Andersen, R., Holalkere, N.-S., & Sahani, D. V. (2007). Magnetic resonance spectroscopy of hepatic lipid content and associated risk factors in HIV infection. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 46(3), 312-317.
- Hadigan, C., Meigs, J. B., Corcoran, C., Rietschel, P., Piecuch, S., Basgoz, N., . . . Wilson, P. W. (2001). Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. *Clinical infectious diseases*, 32(1), 130-139.
- Hearps, A. C., Angelovich, T. A., Jaworowski, A., Mills, J., Landay, A. L., & Crowe, S. M. (2011). HIV infection and aging of the innate immune system. *Sexual health*, 8(4), 453-464.
- Herbert, S. (2001). Policing the contemporary city: fixing broken windows or shoring up neo-liberalism? *Theoretical criminology*, 5(4), 445-466.



- Hessol, N. A., Ameli, N., Cohen, M. H., Urwin, S., Weber, K. M., & Tien, P. C. (2013). The association between diet and physical activity on insulin resistance in the Women's Interagency HIV Study. *Journal of acquired immune deficiency syndromes (1999)*, *62*(1), 74.
- Hessol, N. A., Weber, K. M., D'Souza, G., Burton, D., Young, M., Milam, J., . . . Cohen, M. H. (2014). Smoking cessation and recidivism in the women's interagency human immunodeficiency virus study. *American journal of preventive medicine*, *47*(1), 53-69.
- High, K. P., Brennan-Ing, M., Clifford, D. B., Cohen, M. H., Currier, J., Deeks, S. G., . . . Goronzy, J. J. (2012). HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. *Journal of acquired immune deficiency syndromes (1999)*, *60*(Suppl 1), S1-18.
- Hipp, J. R. (2010). A dynamic view of neighborhoods: The reciprocal relationship between crime and neighborhood structural characteristics. *Social Problems*, *57*(2), 205-230.
- Jackson, G. (1994). Coronary artery disease and women. *BMJ: British Medical Journal*, *309*(6954), 555.
- Jacobson, D. L., Knox, T., Spiegelman, D., Skinner, S., Gorbach, S., & Wanke, C. (2005). Prevalence of, evolution of, and risk factors for fat atrophy and fat deposition in a cohort of HIV-infected men and women. *Clinical infectious diseases*, *40*(12), 1837-1845.

- Kamalu, N. C., & Onyeozili, E. C. (2018). A Critical Analysis of the 'Broken Windows' Policing in New York City and Its Impact: Implications for the Criminal Justice System and the African American Community. *African Journal of Criminology & Justice Studies, 11*(1).
- Kaplan, R. C., Kingsley, L. A., Gange, S. J., Benning, L., Jacobson, L. P., Lazar, J., . . . Hodis, H. N. (2008). Low CD4+ T cell count as a major atherosclerosis risk factor in HIV-infected women and men. *AIDS (London, England), 22*(13), 1615.
- Kaplan, R. C., Landay, A. L., Hodis, H. N., Gange, S. J., Norris, P. J., Young, M., . . . Lazar, J. (2012). Potential cardiovascular disease risk markers among HIV-infected women initiating antiretroviral treatment. *Journal of acquired immune deficiency syndromes (1999), 60*(4), 359.
- Kathiresan, S., & Srivastava, D. (2012). Genetics of human cardiovascular disease. *Cell, 148*(6), 1242-1257.
- Kelling, G. L., & Wilson, J. Q. (1982). Broken windows. *Atlantic monthly, 249*(3), 29-38.
- Kelso, G. A., Cohen, M. H., Weber, K. M., Dale, S. K., Cruise, R. C., & Brody, L. R. (2014). Critical consciousness, racial and gender discrimination, and HIV disease markers in African American women with HIV. *AIDS and Behavior, 18*(7), 1237-1246.
- Khera, A. V., & Kathiresan, S. (2017). Genetics of coronary artery disease: discovery, biology and clinical translation. *Nature Reviews Genetics, 18*(6), 331.
- Kim, D., Diez Roux, A. V., Kiefe, C. I., Kawachi, I., & Liu, K. (2010). Do neighborhood socioeconomic deprivation and low social cohesion predict coronary

- calcification? The CARDIA study. *American journal of epidemiology*, 172(3), 288-298.
- Klijs, B., de Leon, C. F. M., Kibele, E. U., & Smidt, N. (2017). Do social relations buffer the effect of neighborhood deprivation on health-related quality of life? Results from the LifeLines Cohort Study. *Health & place*, 44, 43-51.
- Klonoff, E. A., Landrine, H., & Ullman, J. B. (1999). Racial discrimination and psychiatric symptoms among Blacks. *Cultural Diversity and Ethnic Minority Psychology*, 5(4), 329.
- Koczor, C. A., Fields, E., Jedrzejczak, M. J., Jiao, Z., Ludaway, T., Russ, R., . . . Lewis, W. (2015). Methamphetamine and HIV-Tat alter murine cardiac DNA methylation and gene expression. *Toxicology and applied pharmacology*, 288(3), 409-419.
- L. Delahanty, D., M. Bogart, L., & L. Figler, J. (2004). Posttraumatic stress disorder symptoms, salivary cortisol, medication adherence, and CD4 levels in HIV-positive individuals. *AIDS care*, 16(2), 247-260.
- Lai, H., Moore, R., Celentano, D. D., Gerstenblith, G., Treisman, G., Keruly, J. C., . . . Lai, S. (2016). HIV infection itself may not be associated with subclinical coronary artery disease among African Americans without cardiovascular symptoms. *Journal of the American Heart Association*, 5(3), e002529.
- LaVeist, T. A., Nickerson, K. J., & Bowie, J. V. (2000). Attitudes about racism, medical mistrust, and satisfaction with care among African American and white cardiac patients. *Medical Care Research and Review*, 57(1\_suppl), 146-161.

- Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., . . . Deuschle, M. (2011). City living and urban upbringing affect neural social stress processing in humans. *Nature*, *474*(7352), 498.
- Lee, H., Wildeman, C., Wang, E. A., Matusko, N., & Jackson, J. S. (2014). A heavy burden: the cardiovascular health consequences of having a family member incarcerated. *American journal of public health*, *104*(3), 421-427.
- Lekakis, J., Tsiodras, S., Ikonomidis, I., Palios, J., Poulakou, G., Rallidis, L., . . . Giamarellou, H. (2008). HIV-positive patients treated with protease inhibitors have vascular changes resembling those observed in atherosclerotic cardiovascular disease. *Clinical science*, *115*(6), 189-196.
- Lugalia-Hollon, R., & Cooper, D. (2018). *The War on Neighborhoods: Policing, Prison, and Punishment in a Divided City*: Beacon Press.
- Machtiger, E., Wilson, T., Haberer, J. E., & Weiss, D. (2012). Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS and Behavior*, *16*(8), 2091-2100.
- Macintyre, S., Ellaway, A., & Cummins, S. (2002). Place effects on health: how can we conceptualise, operationalise and measure them? *Social science & medicine*, *55*(1), 125-139.
- Martínez, E., Conget, I., Lozano, L., Casamitjana, R., & Gatell, J. M. (1999). Reversion of metabolic abnormalities after switching from HIV-1 protease inhibitors to nevirapine. *Aids*, *13*(7), 805-810.

- Matheson, F. I., Moineddin, R., Dunn, J. R., Creatore, M. I., Gozdyra, P., & Glazier, R. H. (2006). Urban neighborhoods, chronic stress, gender and depression. *Social science & medicine*, 63(10), 2604-2616.
- Meleis, A., & Im, E. (2001). From fragmentation to integration: Situation specific theories. *The Nursing Profession: Tomorrow's Vision*. Thousands Oaks, CA: Sage Publications.
- Meleis, A. I. (1997). Theoretical nursing. *Development and progress*. New York: Lippincott.
- Meleis, A. I. (1998). A passion for making a difference: ReVisions for empowerment. *Sch Inq Nurs Pract*, 12, 87-94.
- Mesch, V., Siseles, N., Maidana, P., Boero, L., Sayegh, F., Prada, M., . . . Berg, G. (2008). Androgens in relationship to cardiovascular risk factors in the menopausal transition. *Climacteric*, 11(6), 509-517.
- Modrich, L., Scherzer, R., Zolopa, A., Rimland, D., Lewis, C. E., Bacchetti, P., . . . Tien, P. C. (2010). Association of HIV infection, demographic and cardiovascular risk factors with all-cause mortality in the recent HAART era. *Journal of acquired immune deficiency syndromes (1999)*, 53(1), 102.
- Napolitano, L. A., Grant, R. M., Deeks, S. G., Schmidt, D., De Rosa, S. C., Herzenberg, L. A., . . . McCune, J. M. (2001). Increased production of IL-7 accompanies HIV-1-mediated T-cell depletion: implications for T-cell homeostasis. *Nature medicine*, 7(1), 73.

- National Cancer Institute. (n.d.). NCI Dictionary of Cancer Terms. Retrieved from <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/reproductive-hormone>
- Nazmi, A., Roux, A. D., Ranjit, N., Seeman, T. E., & Jenny, N. S. (2010). Cross-sectional and longitudinal associations of neighborhood characteristics with inflammatory markers: findings from the multi-ethnic study of atherosclerosis. *Health & place, 16*(6), 1104-1112.
- Nazmi, A., & Victora, C. G. (2007). Socioeconomic and racial/ethnic differentials of C-reactive protein levels: a systematic review of population-based studies. *BMC public health, 7*(1), 212.
- Newman, P. A., Williams, C. C., Massaquoi, N., Brown, M., & Logie, C. (2008). HIV prevention for Black women: structural barriers and opportunities. *Journal of health care for the poor and underserved, 19*(3), 829-841.
- Okafor, C. N., Cook, R. L., Chen, X., Surkan, P. J., Becker, J. T., Shoptaw, S., . . . Plankey, M. W. (2017). Trajectories of marijuana use among HIV-seropositive and HIV-seronegative MSM in the Multicenter AIDS Cohort Study (MACS), 1984–2013. *AIDS and Behavior, 21*(4), 1091-1104.
- Palar, K., Frongillo, E. A., Escobar, J., Sheira, L. A., Wilson, T. E., Adedimeji, A., . . . Adimora, A. A. (2018). Food Insecurity, Internalized Stigma, and Depressive Symptoms Among Women Living with HIV in the United States. *AIDS and Behavior, 1-10*.
- Paradies, Y. (2006). A systematic review of empirical research on self-reported racism and health. *International journal of epidemiology, 35*(4), 888-901.

- Patterson, S., Cescon, A., Samji, H., Chan, K., Zhang, W., Raboud, J., . . . Rourke, S. B. (2015). Life expectancy of HIV-positive individuals on combination antiretroviral therapy in Canada. *BMC infectious diseases*, *15*(1), 274.
- Petoumenos, K., & Law, M. G. (2016). Smoking, alcohol and illicit drug use effects on survival in HIV-positive persons. *Current Opinion in HIV and AIDS*, *11*(5), 514-520.
- Reece, A. S., Norman, A., & Hulse, G. K. (2016). Cannabis exposure as an interactive cardiovascular risk factor and accelerant of organismal ageing: a longitudinal study. *BMJ open*, *6*(11), e011891.
- Rice, W. S., Logie, C. H., Napoles, T. M., Walcott, M., Batchelder, A. W., Kempf, M.-C., . . . Wilson, T. E. (2018). Perceptions of intersectional stigma among diverse women living with HIV in the United States. *Social science & medicine*, *208*, 9-17.
- Rivera, F. G., & Erlich, J. L. (2001). An option assessment framework for organizing in emerging minority communities. *JE Tropman, JL Erlich & J. Rothman, Tactics and techniques of community intervention (pp169-177)*. Itasca, IL: FE Peacock Publishers.
- Sallis, J. F., Floyd, M. F., Rodríguez, D. A., & Saelens, B. E. (2012). Role of built environments in physical activity, obesity, and cardiovascular disease. *Circulation*, *125*(5), 729-737.
- Sampson, R. J., & Raudenbush, S. W. (2004). Seeing disorder: Neighborhood stigma and the social construction of “broken windows”. *Social psychology quarterly*, *67*(4), 319-342.

- Schoenbaum, E. E., Hartel, D., Lo, Y., Howard, A. A., Floris-Moore, M., Arnsten, J. H., & Santoro, N. (2005). HIV infection, drug use, and onset of natural menopause. *Clinical infectious diseases, 41*(10), 1517-1524.
- Segerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychological bulletin, 130*(4), 601.
- Selye, H. (1959). Perspectives in stress research. *Perspectives in biology and medicine, 2*(4), 403-416.
- Sen, R. (2003). *Stir it up: Lessons in community organizing and advocacy* (Vol. 16): John Wiley & Sons.
- Shacham, E., Lian, M., Önen, N., Donovan, M., & Overton, E. (2013). Are neighborhood conditions associated with HIV management? *HIV medicine, 14*(10), 624-632.
- Simbayi, L. C., Kalichman, S., Strebel, A., Cloete, A., Henda, N., & Mqeketo, A. (2007). Internalized stigma, discrimination, and depression among men and women living with HIV/AIDS in Cape Town, South Africa. *Social science & medicine, 64*(9), 1823-1831.
- Slavin, R. E. (1995). Best evidence synthesis: an intelligent alternative to meta-analysis. *Journal of clinical epidemiology, 48*(1), 9-18.
- Spies, G., Afifi, T. O., Archibald, S. L., Fennema-Notestine, C., Sareen, J., & Seedat, S. (2012). Mental health outcomes in HIV and childhood maltreatment: a systematic review. *Systematic reviews, 1*(1), 30.



- Spies, G., Fennema-Notestine, C., Archibald, S., Cherner, M., & Seedat, S. (2012). Neurocognitive deficits in HIV-infected women and victims of childhood trauma. *AIDS care*, 24(9), 1126-1135.
- Stein, J. H., Currier, J. S., & Hsue, P. Y. (2014). Arterial Disease in Patients With Human Immunodeficiency Virus Infection. *What Has Imaging Taught Us?*, 7(5), 515-525. doi:10.1016/j.jcmg.2013.08.019
- Stradling, C., Chen, Y.-F., Russell, T., Connock, M., Thomas, G. N., & Taheri, S. (2012). The effects of dietary intervention on HIV dyslipidaemia: a systematic review and meta-analysis. *PLoS One*, 7(6), e38121.
- Strong, L. L., Reitzel, L. R., Wetter, D. W., & McNeill, L. H. (2013). Associations of perceived neighborhood physical and social environments with physical activity and television viewing in African-American men and women. *American journal of health promotion*, 27(6), 401-409.
- Suttles, G. D. (1972). *The social construction of communities*: University of Chicago Press.
- Tien, P. C., Schneider, M. F., Cox, C., Cohen, M., Karim, R., Lazar, J., . . . Glesby, M. J. (2010). HIV, Highly Active Antiretroviral Therapy and Lipoprotein Particle Concentrations in the Women's Interagency HIV Study. *AIDS (London, England)*, 24(18), 2809.
- Torpy, J. M., Burke, A. E., & Glass, R. M. (2009). Coronary heart disease risk factors. *Jama*, 302(21), 2388-2388.
- Torriani, M., Hadigan, C., Jensen, M. E., & Grinspoon, S. (2003). Psoas muscle attenuation measurement with computed tomography indicates intramuscular fat

- accumulation in patients with the HIV-lipodystrophy syndrome. *Journal of applied physiology*, 95(3), 1005-1010.
- Vachiat, A., McCutcheon, K., Tsabedze, N., Zachariah, D., & Manga, P. (2017). HIV and ischemic heart disease. *Journal of the American College of Cardiology*, 69(1), 73-82.
- Vallecillo, G., Mojal, S., Roquer, A., Martinez, D., Rossi, P., Fonseca, F., . . . Torrens, M. (2013). Risk of QTc prolongation in a cohort of opioid-dependent HIV-infected patients on methadone maintenance therapy. *Clinical infectious diseases*, 57(8), 1189-1194.
- Walker, L. O., & Avant, K. C. (2005). Strategies for theory construction in nursing.
- Webel, A. R., Barkley, J., Longenecker, C. T., Mittelsteadt, A., Gripshover, B., & Salata, R. A. (2015). A cross-sectional description of age and gender differences in exercise patterns in adults living with HIV. *Journal of the Association of Nurses in AIDS Care*, 26(2), 176-186.
- Weiss, L., Ompad, D., Galea, S., & Vlahov, D. (2007). Defining neighborhood boundaries for urban health research. *American journal of preventive medicine*, 32(6), S154-S159.
- White, K., & Borrell, L. N. (2011). Racial/ethnic residential segregation: framing the context of health risk and health disparities. *Health & place*, 17(2), 438-448.
- Wildeman, C., & Wang, E. A. (2017). Mass incarceration, public health, and widening inequality in the USA. *The Lancet*, 389(10077), 1464-1474.
- Zanetti, H. R., Mendes, E. L., Chagas, A. C. P., Douglas, M. O. G., Lopes, L. T. P., Roever, L., . . . Resende, E. S. (2018). Triad of the Ischemic Cardiovascular

Disease in People Living with HIV? Association Between Risk Factors, HIV Infection, and Use of Antiretroviral Therapy. *Current atherosclerosis reports*, 20(6), 30.

## **CHAPTER 3**

### **Associations of neighborhood perception and chronic stress among women with HIV**

## Abstract

Women living with HIV (WLWH) are susceptible to chronic stress throughout their lifespan. Their perception of neighborhood environment- such as perceived violence, aesthetic quality, and diminished access to affordable healthy food- likely increase the susceptibility to elevated stress and deleterious health outcomes. Preliminary evidence suggests that perceived neighborhood environmental factors likely influence the perceived stress experienced by WLWH. Additionally, the hypothalamic pituitary adrenal (HPA) axis- a major biologic pathway for individual stress response- changes in association with neighborhood environmental factors. Despite existing evidence, direct examinations of these associations are needed among WLWH. Therefore, the purpose of this study was to examine the associations between perception of neighborhood environment and perceived chronic stress. This study was a secondary analysis of data from the Chicago Women's Interagency HIV Study (WIHS) collected in 2012. A total of 147 HIV-positive women were included in this study. The Perception of Neighborhood Environments Scale (PNES) was used as a measure for perceived neighborhood environment. We conducted a multivariable linear regression analysis to explore the associations between neighborhood perception and chronic stress. We did not observe significant associations between chronic stress measures and neighborhood perception, yet we noted the consistent association between depression, income, and Black race with increased chronic stress. The results from this study can inform future neighborhood-level interventions that can reduce chronic stress experienced by WLWH as they age.

Keywords: *HIV, women, chronic stress, cortisol, neighborhood environment*

## Introduction

Neighborhoods influence the health of women living with HIV (WLWH) as they age (Burke-Miller et al., 2016; Burke-Miller et al., 2017). WLWH tend to reside in poor, segregated neighborhoods of urbanized areas of the United States (AIDSvu, 2016). After adjusting for individual factors, several studies have demonstrated the lasting effect of neighborhood segregation and poverty on HIV outcomes, including reduced medication adherence, elevated viral load, and lower CD4 cell counts when compared to less segregated and impoverished areas (Castel et al., 2012; Shacham, Lian, Önen, Donovan, & Overton, 2013; Surratt, O'Grady, Levi-Minzi, & Kurtz, 2015). This can contribute to AIDS and non-AIDS associated diseases and comorbidities among WLWH, such as neurocognitive disorders, cardiovascular diseases, cancers, and renal disease (Schouten et al., 2014). Neighborhood environments also may expose WLWH to other deleterious health contexts, such as violence, access to affordable food, and reduced access to health promoting resources such as spaces for physical activity (Burke-Miller et al., 2016).

One key mechanism for which neighborhood environment factors impact health among WLWH is chronic stress, which manifests through psychological and biological mechanisms (Segerstrom & Miller, 2004). For example, the psychological experiences of chronic stress among WLWH is influenced by a variety of intersecting circumstances, ranging from individual-level experiences to neighborhood-level factors (Diez-Roux & Mair, 2010; Fishbein & Yzer, 2003). The biologically mediated pathway, the hypothalamic pituitary adrenal (HPA) axis, among individuals with HIV undergoes a variety of changes in the biologic human stress response cascade. Hypercortisolism and glucocorticoid resistance are defining HPA axis changes associated with HIV infection

(Chrousos & Zapanti, 2014; McEwen, 2004; Zapanti, Terzidis, & Chrousos, 2008), which can contribute chronic illnesses such as cardiovascular disease and diabetes (Chiodini et al., 2007; Golbidi, Frisbee, & Laher, 2015). In total, WLWH encounter stressors in the context of their neighborhoods, and with stressful life experiences and altered HPA axis activity, can be linked to poor health outcomes (Bottonari, Safren, McQuaid, Hsiao, & Roberts, 2010; Brief et al., 2004).

Chronic stress is widely considered a contributor to morbidity and mortality (Segerstrom & Miller, 2004). Since the biologic mechanisms of stress can contribute to elevated inflammation (e.g. cortisol, pro-inflammatory cytokines, histamine, etc.) individuals with chronic stress are predisposed to hypertension, diabetes, CVDs, cancers, and other illnesses (Monnier et al., 2006; Reiche, Nunes, & Morimoto, 2004; Spruill, 2010; Thaker, Lutgendorf, & Sood, 2007) that are the greatest contributors to mortality in the United States (Murphy, 2018). Further, WLWH may experience significant chronic stress related to chronic HIV management and HIV-associated stigma (Hatzenbuehler, Phelan, & Link, 2013). Additional circumstances that can contribute to stress across the lifespan among WLWH include the lasting effects of living with low income, unemployment, incarceration, substance abuse, single parenthood, childhood trauma, and intimate partner violence (Brief et al., 2004; Campbell et al., 2008; Dunkle et al., 2004; Lee, Wildeman, Wang, Matusko, & Jackson, 2014; Machtiger, Wilson, Haberer, & Weiss, 2012; Spies et al., 2012; Teitelman, Ratcliffe, Dichter, & Sullivan, 2008).

Currently, the associations between specific aspects of neighborhood environment and chronic stress among WLWH are unclear. Certain features of neighborhoods, which include access to food, walkability, aesthetic qualities, have been examined in association

with health outcomes (e.g. hypertension, atherosclerosis). Stress, in turn, is often examined as the mechanism for which neighborhood characteristics are internalized to contribute to health outcomes (Aneshensel, 2008). Studies that have examine neighborhood environment often utilize aggregate measures, such as census tract data, to explore associations between neighborhood environment and HIV outcomes among WLWH (Burke-Miller et al., 2017). Despite the utility and availability of census data, these measures serve as proxy measures (e.g. census tract-level data for poverty, education, crime, etc.) of neighborhood environment that are not directly evaluated by individuals who reside in these neighborhoods (Echeverria, Diez-Roux, & Link, 2004). An individual's perception of their neighborhood, however, may be more closely linked to stress experience, as individuals appraise their environment as a part of their stress experience. Several domains of neighborhoods-including aesthetic quality, walkability, access to affordable food, violence, safety, social cohesion, and activities with neighbors-shape an individual's neighborhood perception (Echeverria et al., 2004). These aspects of neighborhoods have been linked to increased risk for chronic illness and mortality (Boardman, 2004; Brenner, Zimmerman, Bauermeister, & Caldwell, 2013; Elliott, 2000; Smith et al., 2017), yet have not been examined in the context of WLWH. Therefore, the purpose of this study is to examine the associations between perception of neighborhood and environment, and chronic stress among WLWH. We hypothesize that decreased (poor) perception of neighborhood environment will be associated with increased chronic stress.



## **Methods**

### ***Design***

This study was completed utilizing a secondary analysis of data from the Women's Interagency HIV Study (WIHS). This longitudinal, prospective, multi-site study of women with HIV has examined the natural history and progression of HIV since its initiation in 1993. WIHS is at the forefront of investigation into reproductive health, clinical outcomes (such as cardiovascular disease, diabetes, and neurocognitive disorders), and the efficacy of antiretroviral therapies (WIHS Data Management and Analysis Center, 2017). Specifically, we utilized data collected from the psychoneuroimmunology and hair cortisol sub studies at Chicago site of WIHS that were exclusively conducted at the Chicago WIHS location. Within the larger framework of WIHS, these sub studies seek to better understand the stress response and experience of WLWH, and the utility of hair cortisol as a biomarker among WLWH. In addition, we also included data collected during WIHS clinical examinations and study visits to achieve the study aims. Women were included in this study if they had a HIV-positive status, residence in the Chicago area, and participation in the previously mentioned Chicago WIHS sub studies in 2012 (visit 36). This study received a waiver of review from the University of Pennsylvania Institutional Review Board (IRB) related to our use of de-identified data from Chicago WIHS.

### **Measures**

#### **Predictor variables**

The Perception of Neighborhood Environments Scale (PNES) was used to characterize how WLWH perceive their neighborhood environment. The PNES is a 36-

item measure of perceived neighborhood environment with seven subscales, including: aesthetic quality; physical activity/walking environment; availability of healthy food; safety; violence; social cohesion; and activities with neighbors (Echeverria et al., 2004). The PNES includes Likert scale responses to statements that evaluate neighborhood environment, such as “There is a lot of trash and litter on the street in my neighborhood”, “A large selection of fresh fruits and vegetables is available in my neighborhood”, and “People in my neighborhood generally get along with each other”. We found that the total scale of the PNES had a Cronbach’s alpha of 0.85, with PNES subscales ranging from 0.87-0.81. The PNES subscales were highly correlated, with the aesthetic quality subscale having a strong Pearson’s correlation with the walkability (0.77), social cohesion (0.62). Further, the safety subscale of the PNES was highly correlated with the walkability (0.6562), violence (0.67), and social cohesion (0.59) subscales (see Table \_). Our findings our consistent with previous WIHS studies demonstrate findings regarding the psychometric properties of the PNES and subscales within this sample (Burke-Miller et al., 2016). In a previous WIHS study, the PNES had strong reliability across subscales, with a Cronbach’s alpha of 0.94 for the total scale reliability, with Cronbach’s alphas ranging from 0.72-0.89 across PNES subscales (Burke-Miller et al., 2017). Therefore, the PNES was selected as measure for examining neighborhood environment in this study.

### *Correlates*

We selected variables associated with the predictor and outcome variables for this study from the Chicago WIHS database relative to the scientific literature. Briefly, variables examined for bivariate linear regression analysis included demographic variables (age, race/ethnicity, income, education, employment, housing, and incarceration

history), general factors associated with CVD risk among women (alcohol use, drug use, cigarette smoking, menopause, inflammatory markers), and HIV-associated risk factors (CD4 count, viral load). Additional total scale values were examined for bivariate associations with predictor and outcome variables and include depression (CES-D) and physical activity. We also created dichotomous variables for education (1=more than high school, 0=high school or less), income (1=annual income greater than \$12,000, 0= annual income equal to or less than \$12,000), and race (1= Black race, 0= other race). These variables were examined in bivariate analyses with our primary outcome variable.

### *Outcome variables*

We utilized two measures of chronic stress in this study. First, as a measure of psychological stress, we used the Perceived Stress Scale (PSS), which is a general measure of perceived stress. The PSS is a self-reported, 10-item Likert scale measure (Cohen, Kamarck, & Mermelstein, 1994). The PSS assesses perceived stress over the course of one month with a five-point scale (0 = never; 1 = almost never; 2 = sometimes; 3 = fairly often; and 4 = very often). Sample items for the PSS include “In the last month, how often have you felt nervous and ‘stressed’?” and “In the last month, how often have you been upset because of something that happened unexpectedly?”. The PNES Further, the PSS has been associated with several health outcomes among women.

Additionally, we utilized hair cortisol concentration (HCC) as a biological stress measure of aggregate HPA axis activity among WLWH in the Chicago WIHS sample. HCC is as a cumulative measure of cortisol over an extended period, typically used to measure one to three months of cortisol expression. Hair cortisol was collected in 2012 by Chicago WIHS personnel after participants provided informed consent. Hair sample

collection protocol was established in Chicago WIHS similarly as described by Wennig (2000). About six centimeters of hair was cut nearest to the scalp in two, three-centimeter segments. Hair samples were stored at room temperature prior to cortisol extraction. As outlined by Stalder et al. (2012) and Steudte et al. (2013), extracted hair was washed with 1800  $\mu$ L methanol for 18 hours at 45°C. To analyze HCC via liquid chromatography tandem mass spectrometry (LC-MS/MS), 50  $\mu$ L of the sample cortisol solution was incubated with methanol until evaporation. After methanol evaporation, the sample was reconstituted with 250  $\mu$ L double distilled water. We utilized unadjusted and log-transformed HCC values in study analyses as the distribution for hair cortisol within this sample was not normally distributed (skewness: 4.03; kurtosis: 18.65; normality test findings: skewness:  $p < 0.001$ , kurtosis  $p < 0.001$ ;  $\chi^2 = 57.01$ ,  $p < 0.001$ ).

### ***Main Analyses***

WIHS data were used to examine the relationship between perception of neighborhood environment and chronic stress among women with HIV in Chicago WIHS. Descriptive statistics of demographic and health data were completed to observe trends within this sample. We developed a dichotomous measure of PSS values to explore differences in demographic, health, and neighborhood characteristics by level of PSS. This dichotomous variable was developed utilizing the mean PSS value (16.14) from a representative sample of United States women in 2009 (Cohen & Janicki-Deverts, 2012). Women in this sample were dichotomized as either low perceived stress ( $PSS < 16.14$ ) or high perceived stress ( $PSS > 16.14$ ). Other dichotomous variables were developed for race (Black v other race) and income (high v low income). Additionally, we completed bivariate analyses between demographic and health variables and both the predictor

variables- as measured PNES total score and subscales- and the outcome variable- chronic stress as measured by PSS and HCC scores. We evaluated bivariate relationships via bivariate regression and specified that significance of  $p \leq 0.20$  was used to select covariates for multivariable linear regression. We completed multivariable linear regression models with the PNES total score specified as a predictor (independent) variable and the PSS scores and HCC values as outcome (dependent) variables. A stepwise approach was used for development of regression models, and similar results were found with both forwards and backwards stepwise regression. The PNES subscales were also examined in separate regression models as predictor (independent) variables. All statistical analyses were conducted utilizing Stata 15 software (StataCorp, 2017).

### ***Effect Size Calculation***

The total number of participants eligible for this study from the Chicago WIHS sample includes 147 HIV-positive women. The total number of Chicago WIHS women that provided hair cortisol samples is 55 HIV-positive women. For the main study analyses with the seven PNES subscales as independent variables, we calculated an effect size  $f^2$  of 0.057 with a sample size of 147, power calculated at 0.80, and alpha at 0.05. For the analyses with hair cortisol concentration with the seven PNES subscales also as independent variables, we calculated an effect size  $f^2$  of 0.177, with a sample size of 55, power calculated at 0.80, and an alpha of 0.05. Effect size was calculated using PASS software (Hintze, 2004).

## Results

### *Sample characteristics*

Demographic and clinical characteristics of the women included in this study are described in Table 3.1. A total of 147 HIV-positive women with complete data were included in this sample that were obtained from the Chicago WIHS study data collected in 2012. Based on previous population-level assessment of stress with the PSS, 31 (21.1%) women in this study were dichotomized as low stress ( $PSS \leq 16.14$ ) and 116 (78.9%) women in this sample were dichotomized in the high stress as measured by the PSS. The mean age of the sample was 47.1 (95% CI: 45.7-48.5), 76.9% were African American, Non-Hispanic, and 15.0% were White, Non-Hispanic. A notable proportion of the women in this sample received at most a high school education (57.8%), were not employed at the time of this study (70.8%) and had previous history of incarceration in their lifetime (40.8%).

The overall mean values of the PSS for this sample is 18.9 (95% CI: 18.1 - 19.8). With the potential response values ranging from 0-40 on the PSS, this mean value indicates that women in this study perceived notable amounts of stress over the course of the month prior to data collection. We observed a statistically significant difference ( $p < 0.0001$ ,  $t = 6.45$ ) between the mean PSS values in this sample relative to the mean values of PSS (16.1, SD 7.56) representative sample of women in the United States in 2009 (Cohen & Janicki-Deverts, 2012). Additionally, the HCC values of this sample are, on average, 370.02 pg/mg (95% CI: 48.0-649.0 pg/mg). The HCC values in this sample were not normally distributed as HCC values ranged from 8.1 pg/mg- 7713.6 pg/mg. Further, HCC values were positively skewed (4.69) and demonstrated marked kurtosis

(24.56). Log-transformed HCC values demonstrated less skewness (1.13) and kurtosis (4.36) than unadjusted HCC values.

Table 3.2 contains the health and neighborhood characteristics of the Chicago WIHS women included in this study. Women in this study had, on average, a viral load of 17592.2 copies/mL (95% CI: 2326.0-32858.3 copies/mL), a CD4 cell count of 591.1 cells/mm<sup>3</sup> (95% CI: 539.2-643.0 cells/mm<sup>3</sup>) and 89.8% reported use of antiretroviral medications at the study visit in 2012. Additional health data of women in this study indicate that they had a mean systolic blood pressure of 118.6 mmHg (95% CI: 115.7-121.6 mmHg), total cholesterol of 178.4 mg/dL (95% CI: 172.1-184.8 mg/dL), and HDL cholesterol of 55.0 mg/dL (95% CI: 51.9-58.1 mg/dL). Further, the majority of this sample reported cigarette smoking (70.8%), and a notable proportion injection drug use within the past five years (24.1%).

Of the demographic and health data examined, we observed differences in level of perceived stress and CD4 cell percent, with women with high perceived stress having significantly greater CD4 cell percentiles 32.9%, 95% CI: 30.8-34.9%) as compared to women in the low stress group (27.3%, 95% CI: 23.2-31.5%), and this difference was statistically significant (p=0.0145). We did not observe any other significant differences in various health characteristics based on high or low chronic stress (PSS) values among WLWH. However, we observed significant differences in perceived stress and levels of reported social cohesion among WLWH in this study. Women with greater chronic stress (PSS) reported decreased social cohesion (17.3, 95% CI:16.6-18.0) in comparison to women with lower stress (18.9, 95% CI:17.6-20.3, p=0.0364). Women perceived various aspects of their neighborhoods as positive, with participants reporting an mostly that they

“agree” in response to items regarding positive aspects of aesthetic quality (mean= 21.4, 95% CI: 20.5-22.2), walking environment and physical activity (35.2, 95% CI: 34.2-36.3), and social cohesion (13.5, 95% CI: 12.9-14.1). For other subscales of the PNEs, participants responded on average “neutral” to items in the availability of healthy food (mean= 12.4, 95% CI: 11.9-12.9), safety (9.0, 95% CI: 8.5-9.5). Participants also, on average, reported that violence as “rare” (12.1, 95% CI: 11.5-12.7) and activities with neighbors happening “often” or “sometimes” (17.6, 95% CI: 17.0-18.3). We observed significant differences ( $p=0.0364$ ) in perceived activities with neighbors based on level of stress, with women in the low stress group reporting greater activities with neighbors (18.9, 95% CI: 17.6-20.3) than women in the high stress group (17.3, 95% CI: 16.6-18.0).

Of note, there were many fewer women in the WIHS sample that provided hair cortisol samples ( $n=55$ ). All the HIV-positive women in the Chicago WIHS sample who provided HCC samples also completed the PSS. In comparison between participants who provided both HCC and PSS values versus PSS only, women with both HCC and PSS data reported greater unemployment (80.0%,  $p=0.057$ ), higher previous incarceration (55.6 %,  $p=0.009$ ), lower educational attainment (74.5% had completed high school or less,  $p=0.002$ ) greater reported drug use (34.6%,  $p=0.007$ ) and poverty (71.2% below annual household income of \$12,000,  $p=0.059$ ) than the women that only provided data for the PSS measure (unemployment: 65.2%; incarceration history: 32.6%; education: 47.8% had completed high school or less; drug use: 15.2%; poverty: 44.9% had below an annual household income of \$12,000). Further, a higher proportion of the women who provided both PSS and HCC values identified as African American (89.1%) than did women with only PSS values (69.6% African American,  $p=0.014$ ). Further, women with



both PSS and HCC data demonstrated lower LDL cholesterol levels (91.47 mg/dL; 95% CI: 82.24- 100.70 mg/dL,  $p=0.0524$ ) and lower CD4 cell percent (33.1%, 95% CI: 31.0-35.3% ,  $p=0.0487$ ), when compared to participants who provided PSS data only (LDL cholesterol: 102.6 mg/dL, 95% CI: 95.8 -109.4 mg/dL; CD4 cell percent: 29.3% (95% CI: 26.0-33.0%).

Table 3.3 displays bivariate correlations between study variables. Of note, we observed a strong positive correlation between PSS values and depression ( $r^2= 0.637$ ). Additionally, CD4 cell count and CD4 cell percent values demonstrated a strong positive correlation ( $r^2= 0.725$ ). Age was weakly negatively correlated with HDL cholesterol ( $r^2= 0.316$ ) and viral load ( $r^2= - 0.346$ ). Additionally, we observed a moderate positive correlation between total cholesterol and HDL cholesterol ( $r^2= 0.531$ ).

### ***Bivariate analyses***

We completed bivariate regression analyses to select covariates to complete multivariable linear regression models for neighborhood perception and PSS values. We observed significant associations between PSS values and depression (coef: 0.08, SE: 0.04,  $p=0.049$ ), systolic blood pressure (coef: -0.03 , SE: 0.02,  $p=0.168$ ), Black v other race (coef: -1.33, SE: 1.04,  $p=0.202$ ), and high v low income (coef: 2.03, SE: 0.87,  $p=0.022$ ). In bivariate regression analyses for covariate selection for analyses with log-transformed HCC values, we observed associations between log-transformed HCC values and age (coef: -0.03, SE: 0.02,  $p=0.182$ ), HDL cholesterol (coef: -0.02, SE: 0.01,  $p=0.023$ ), CD4 cell count (coeff-0.001,SE: 0.001,  $p=0.188$ ), menopause (coef: -0.72, SE: 0.47,  $p=0.131$ ), and incarceration history (coef: 0.63, SE: 0.39,  $p=0.108$ ). Additionally, we observed significant bivariate associations with based on Black vs other race (coef:

1.26, SE: 0.61,  $p=0.043$ ). These variables were selected as covariates for multivariable regression models examining the associations between neighborhood perception and stress as measured by either PSS or log-transformed HCC.

### ***Linear regression***

We report findings from linear regression models in Tables 3.4-3.5. Models developed in this study did not demonstrate notable collinearity as indicated by the variance inflation factor (VIF) which values ranged from 1.02-1.70. When analyzing the associations between aspects of neighborhood and chronic stress, we examined the extent to which the PNES was associated with PSS values with depression (CES-D), Black v other race, systolic blood pressure (SBP), and high v low income. Results for the full regression models are displayed in Table 3.4. We did not observe statistically significant associations between PNES and subscales and PSS scores in these analyses. However, we observed a consistent significant association of depression, and high v low income with PSS scores across all regression models. For the total PNES score, for every unit increase in depression as measured by the CES-D, there was a 0.10 increase in PSS, and this was statistically significant ( $p=0.011$ ). Additionally, women with high income demonstrated 2.71 units greater perceived stress than women with low income ( $p=0.005$ ) in our model assessing the association of total PNES score and PSS values. These findings were consistent across PNES subscales.

Table 3.5 contain results from multivariable linear regression models for chronic stress as measured by log-transformed HCC. We observed a statistically significant association between perception of activities with neighbors and HCC levels among WLWH in Chicago WIHS. For every one unity increase of perceived activities with

neighbors, there was a 0.72 unit increase in HCC levels (SE: 1.18,  $p=0.050$ ). Of covariates included in study models, Black v other race was significantly associated with log-transformed HCC levels in models of social cohesion and activities with neighbors subscales of the PNES. For instance, women who identified as Black race had a 22.03 unit increase in HCC levels when compared to women of other races (SE: 4.12,  $p=0.035$ ) in a model examining the associations of social cohesion and HCC levels. Additionally, Black women had a 26.92 unit increase in HCC levels when compared to women of other races (SE: 4.14,  $p= 0.026$ ). in our model examining the association between activities with neighbors and HCC levels

### **Discussion**

The purpose of this study was to examine the associations of neighborhood environment and chronic stress among WLWH. The findings from this study did not support our hypothesis that reduced perception of neighborhood environment would be associated with increased chronic stress. This study highlights the importance for research and interventions that address poverty, cigarette smoking, and depression among WLWH and their associations with chronic stress. Further, this study demonstrates the need for care models that support the health needs of WLWH who have been incarcerated or unemployed.

Few studies have examined the associations of neighborhood environment with stress and health outcomes among WLWH. In previous WIHS studies, the PNES subscales were significantly associated with census measures of neighborhood disorder ( $p>0.01$ ), such as concentrated poverty ( $\geq 25\%$  below the federal poverty line) and racial segregation ( $\geq 50\%$  Black/non-Hispanic residents) (Burke-Miller et al., 2016).

Importantly, the Chicago WIHS participants reside in a total of 81 community areas in the Chicago area, with roughly 70% of the sample residing in Chicago versus neighboring suburban residence. Further, the WIHS sample serves as a representative sample of the geographic distribution of WLWH in Chicago. Additionally, US Census data from 2012 indicated that the median values of the community area percent of individuals below the federal poverty line was about 17% (IQR 8.95-28.42%), with a maximum of 52% of persons below the federal poverty line the community area (Burke-Miller et al., 2016). Additionally, WLWH in this study often perceived aspects of their neighborhoods as positive as measured by the PNES. Several studies have demonstrated the internal and test-retest of the PNES, noting that individual perceptions of neighborhood closely relate to aggregate measures of neighborhoods (Echeverria et al., 2004; Ross, Mirowsky, & Pribesh, 2001). However, Suttles (1972) notes that individuals in deprived neighborhoods may minimize the as a means of coping, or that residents “know” the resources or risks in their neighborhood, and thereby feel safe and secure.

Depression and income were consistently associated with stress among WLWH in Chicago WIHS. Several studies of individuals with HIV have noted increased depression symptomology in this population when compared to HIV-negative individuals (Nanni, Caruso, Mitchell, Meggiolaro, & Grassi, 2015). A review of the literature by Leserman (2003) notes that across a variety of studies, depression is associated with HIV disease progression, yet the mechanisms for how depression contributes to these outcomes is poorly understood. Given that depression and stress were highly correlated with one another and depression associated with stress in multivariable regression models in this

study, future studies must explore these relationships in relation to neighborhood environment.

This study has several noteworthy features, including the use of innovative measures, and examination of within-population associations of stress and neighborhoods among WLWH. First, this study utilized innovative measures of neighborhood environment (PNES) and chronic stress (HCC). The use of these measures adds to the scientific literature by examining the associations of modifiable characteristics of neighborhood environment as they are evaluated by the individuals that reside in these neighborhoods. Further, this study connects these modifiable aspects of neighborhood environment with HCC, which is a relatively new measure of chronic stress, and has seldom been used in human subjects research. Hair samples for cortisol studies are cheap to collect and store and can serve as an aggregate stress measure for 1-3 months (Sauvé, Koren, Walsh, Tokmakejian, & Van Uum, 2007). This measure can prove to be a useful tool in studies of chronic stress and health outcomes in future studies of WLWH. Additionally, this study promotes health equity among WLWH by directly examine salient demographic, health, and neighborhood characteristics associated with chronic stress. While a vast number of studies focus on disparities, this study adds to the scientific literature by directly examining within-population associations of neighborhood environment and chronic stress.

This study has several limitations. First, the cross-sectional data for this study were collected in 2012, and it is possible that neighborhood perceptions and characteristics have changed in the time since data collection. Further, we analyzed data collected at one cross-section. Since the effects of neighborhood environments are

cumulative, we were unable to examine the chronicity of neighborhood environment associations with stress. Additionally, there was a considerable difference between the number of women that provided PSS responses (n=147) to women that provided HCC samples (n=55). Hair can be a source of pride, identity, and cultural expression among women. Barriers to hair sample collection includes use of wigs and extensions, religious ties to hair covering, or other reasons for refusal. We believe that specific examinations of the barriers to hair cortisol sample collections among women are needed to determine best practices for HCC use in studies among women.

### **Conclusions**

This study examined the associations of specific aspects of neighborhood environment with chronic stress as experienced by WLWH. By directly examining neighborhood-level characteristics as evaluated by WLWH, this study contributes to a broader focus of health research that highlights the importance of neighborhood environment in the health and wellness of WLWH as they age. Future research is needed to explore the specific experiences and perspectives of WLWH regarding their neighborhood, stress experience, and HIV. Future studies of stress and aging among WLWH must incorporate the neighborhood context in which they live. Additionally, smoking cessation and depression treatment are needed among WLWH to promote health and wellness as they age.

## References

- AIDSvu. (2016). Rates of Females Living with Diagnosed HIV, 2014. Retrieved from <https://map.aidsvu.org/map>
- Aneshensel, C. S. (2008). Neighborhood as a social context of the stress process *Advances in the Conceptualization of the Stress Process* (pp. 35-52): Springer.
- Boardman, J. D. (2004). Stress and physical health: the role of neighborhoods as mediating and moderating mechanisms. *Social science & medicine*, 58(12), 2473-2483.
- Bottonari, K. A., Safren, S. A., McQuaid, J. R., Hsiao, C.-B., & Roberts, J. E. (2010). A longitudinal investigation of the impact of life stress on HIV treatment adherence. *Journal of behavioral medicine*, 33(6), 486-495.
- Brenner, A. B., Zimmerman, M. A., Bauermeister, J. A., & Caldwell, C. H. (2013). Neighborhood context and perceptions of stress over time: an ecological model of neighborhood stressors and intrapersonal and interpersonal resources. *American Journal of Community Psychology*, 51(3-4), 544-556.
- Brief, D. J., Bollinger, A., Vielhauer, M., Berger-Greenstein, J., Morgan, E., Brady, S., . . . Group, C. S. (2004). Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*, 16(sup1), 97-120.
- Burke-Miller, J. K., Weber, K., Cohn, S. E., Hershov, R. C., Sha, B. E., French, A. L., & Cohen, M. H. (2016). Neighborhood community characteristics associated with HIV disease outcomes in a cohort of urban women living with HIV. *AIDS care*, 28(10), 1274-1279.

- Burke-Miller, J. K., Weber, K. M., Cohn, S. E., Hershow, R. C., Sha, B., French, A. L., & Cohen, M. H. (2017). Measurement of Neighborhood Context in an Urban Cohort of HIV-infected or at risk Low-Income Women. *Journal of poverty, 21*(1), 80-96.
- Campbell, J. C., Baty, M., Ghandour, R. M., Stockman, J. K., Francisco, L., & Wagman, J. (2008). The intersection of intimate partner violence against women and HIV/AIDS: a review. *International journal of injury control and safety promotion, 15*(4), 221-231.
- Castel, A. D., Befus, M., Willis, S., Griffin, A., West, T., Hader, S., & Greenberg, A. E. (2012). Use of the community viral load as a population-based biomarker of HIV burden. *Aids, 26*(3), 345-353.
- Chiodini, I., Adda, G., Scillitani, A., Coletti, F., Morelli, V., Di Lembo, S., . . . Orsi, E. (2007). Cortisol secretion in patients with type 2 diabetes: relationship with chronic complications. *Diabetes Care, 30*(1), 83-88.
- Chrousos, G. P., & Zapanti, E. D. (2014). Hypothalamic-pituitary-adrenal axis in HIV infection and disease. *Endocrinology and Metabolism Clinics, 43*(3), 791-806.
- Cohen, S., & Janicki-Deverts, D. (2012). Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009 1. *Journal of applied social psychology, 42*(6), 1320-1334.
- Cohen, S., Kamarck, T., & Mermelstein, R. (1994). Perceived stress scale. *Measuring stress: A guide for health and social scientists, 235-283*.
- Diez-Roux, A. V., & Mair, C. (2010). Neighborhoods and health. *Annals of the New York Academy of Sciences, 1186*(1), 125-145.



- Dunkle, K. L., Jewkes, R. K., Brown, H. C., Gray, G. E., McIntyre, J. A., & Harlow, S. D. (2004). Gender-based violence, relationship power, and risk of HIV infection in women attending antenatal clinics in South Africa. *The Lancet*, *363*(9419), 1415-1421.
- Echeverria, S. E., Diez-Roux, A. V., & Link, B. G. (2004). Reliability of self-reported neighborhood characteristics. *Journal of Urban Health*, *81*(4), 682-701.
- Elliott, M. (2000). The stress process in neighborhood context. *Health & place*, *6*(4), 287-299.
- Fishbein, M., & Yzer, M. C. (2003). Using theory to design effective health behavior interventions. *Communication theory*, *13*(2), 164-183.
- Golbidi, S., Frisbee, J. C., & Laher, I. (2015). Chronic stress impacts the cardiovascular system: animal models and clinical outcomes. *American Journal of Physiology-Heart and Circulatory Physiology*, *308*(12), H1476-H1498.
- Hatzenbuehler, M. L., Phelan, J. C., & Link, B. G. (2013). Stigma as a fundamental cause of population health inequalities. *American journal of public health*, *103*(5), 813-821.
- Hintze, J. (2004). NCSS and PASS software. *Kaysville, UT: Number Cruncher Statistical Systems*.
- Lee, H., Wildeman, C., Wang, E. A., Matusko, N., & Jackson, J. S. (2014). A heavy burden: the cardiovascular health consequences of having a family member incarcerated. *American journal of public health*, *104*(3), 421-427.
- Leserman, J. (2003). HIV disease progression: depression, stress, and possible mechanisms. *Biological psychiatry*, *54*(3), 295-306.

- Machtiger, E., Wilson, T., Haberer, J. E., & Weiss, D. (2012). Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS and Behavior*, *16*(8), 2091-2100.
- McEwen, B. S. (2004). Protection and damage from acute and chronic stress: allostasis and allostatic overload and relevance to the pathophysiology of psychiatric disorders. *Annals of the New York Academy of Sciences*, *1032*(1), 1-7.
- Monnier, L., Mas, E., Ginet, C., Michel, F., Villon, L., Cristol, J.-P., & Colette, C. (2006). Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. *Jama*, *295*(14), 1681-1687.
- Murphy, S. L., Xu, J. Q., Kochanek, K. D., & Arias E. (2018). *Mortality in the United States, 2017*. Retrieved from
- Nanni, M. G., Caruso, R., Mitchell, A. J., Meggiolaro, E., & Grassi, L. (2015). Depression in HIV infected patients: a review. *Current psychiatry reports*, *17*(1), 530.
- Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement*, *1*(3), 385-401.
- Reiche, E. M. V., Nunes, S. O. V., & Morimoto, H. K. (2004). Stress, depression, the immune system, and cancer. *The lancet oncology*, *5*(10), 617-625.
- Ross, C. E., Mirowsky, J., & Pribesh, S. (2001). Powerlessness and the amplification of threat: Neighborhood disadvantage, disorder, and mistrust. *American sociological review*, *66*(4), 568.

- Sauvé, B., Koren, G., Walsh, G., Tokmakejian, S., & Van Uum, S. H. (2007). Measurement of cortisol in human hair as a biomarker of systemic exposure. *Clinical & Investigative Medicine*, 30(5), 183-191.
- Schouten, J., Wit, F. W., Stolte, I. G., Kootstra, N. A., van der Valk, M., Geerlings, S. E., . . . Reiss, P. (2014). Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEHIV cohort study. *Clinical Infectious Diseases*, 59(12), 1787-1797.
- Seegerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychological bulletin*, 130(4), 601.
- Shacham, E., Lian, M., Önen, N., Donovan, M., & Overton, E. (2013). Are neighborhood conditions associated with HIV management? *HIV medicine*, 14(10), 624-632.
- Smith, J. A., Zhao, W., Wang, X., Ratliff, S. M., Mukherjee, B., Kardia, S. L., . . . Needham, B. L. (2017). Neighborhood characteristics influence DNA methylation of genes involved in stress response and inflammation: The Multi-Ethnic Study of Atherosclerosis. *Epigenetics*, 12(8), 662-673.
- Spies, G., Afifi, T. O., Archibald, S. L., Fennema-Notestine, C., Sareen, J., & Seedat, S. (2012). Mental health outcomes in HIV and childhood maltreatment: a systematic review. *Systematic reviews*, 1(1), 30.
- Spruill, T. M. (2010). Chronic psychosocial stress and hypertension. *Current hypertension reports*, 12(1), 10-16.

- Stalder, T., Steudte, S., Miller, R., Skoluda, N., Dettenborn, L., & Kirschbaum, C. (2012). Intraindividual stability of hair cortisol concentrations. *Psychoneuroendocrinology*, *37*(5), 602-610.
- StataCorp. (2017). Stata Statistical Software. College Station, TX: StataCorp LLC.
- Steudte, S., Kirschbaum, C., Gao, W., Alexander, N., Schönfeld, S., Hoyer, J., & Stalder, T. (2013). Hair cortisol as a biomarker of traumatization in healthy individuals and posttraumatic stress disorder patients. *Biological psychiatry*, *74*(9), 639-646.
- Surratt, H. L., O'Grady, C. L., Levi-Minzi, M. A., & Kurtz, S. P. (2015). Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. *AIDS care*, *27*(3), 307-314.
- Suttles, G. D. (1972). *The social construction of communities*: University of Chicago Press.
- Teitelman, A. M., Ratcliffe, S. J., Dichter, M. E., & Sullivan, C. M. (2008). Recent and past intimate partner abuse and HIV risk among young women. *Journal of Obstetric, Gynecologic & Neonatal Nursing*, *37*(2), 219-227.
- Thaker, P. H., Lutgendorf, S. K., & Sood, A. K. (2007). The neuroendocrine impact of chronic stress on cancer. *Cell Cycle*, *6*(4), 430-433.
- Wennig, R. (2000). Potential problems with the interpretation of hair analysis results. *Forensic science international*, *107*(1-3), 5-12.
- WIHS Data Management and Analysis Center. (2017). Our Study: The Women's Interagency HIV Study. Retrieved from <https://statepi.jhsph.edu/wihs/wordpress/>

Zapanti, E., Terzidis, K., & Chrousos, G. (2008). Dysfunction of the hypothalamic-pituitary-adrenal axis in HIV infection and disease. *Hormones (Athens)*, 7(3), 205-216.

## Appendices

*Table 3.1: Sample Demographic Characteristics*

Characteristic (n, %)	Overall N=147	Low Stress n=31 (21.1%)	High Stress n=116 (78.9%)	P-value
<i>Age (Mean, 95% CI)</i>	47.1 (45.7-48.5)	46.6 (43.6-49.6)	47.3 (45.7-48.9)	0.6831
<i>Race/Ethnicity</i>				0.115
White, Non-Hispanic	22 (15.0%)	1 (3.2%)	21 (18.1%)	
White, Hispanic	4 (2.7%)	0 (0%)	4 (3.5%)	
African American, Non- Hispanic	113 (76.9%)	30 (96.8%)	83 (71.6%)	
African American, Hispanic	1 (0.7%)	0 (0%)	1 (0.9%)	
Other Hispanic	6 (4.1%)	0 (0%)	6 (5.2%)	
Native American/Alaskan	1 (0.7%)	0 (0%)	1 (0.9%)	
<i>Education</i>				0.593
Grades 1-6	2 (1.4%)	1 (3.2%)	1 (0.9%)	
Grades 7-11	49 (33.3%)	13 (41.9%)	36 (31.0%)	
Completed high school	34 (23.1%)	7 (22.6%)	27 (23.3%)	
Some college	41 (27.9%)	8 (25.8%)	33 (28.5%)	
Completed 4 years of college	13 (8.8%)	1 (3.2%)	12 (10.3%)	
Attended/completed graduate school	8 (5.4%)	1 (3.2%)	7 (6.0%)	
<i>Average household income/year</i>				0.131
\$6000 or less	22 (15.6%)	6 (20.0%)	16 (14.4%)	
\$6001-\$12000	55 (39.0%)	17 (56.7%)	38 (34.2%)	
\$12001-\$18000	12 (8.5%)	3 (10.0%)	9 (8.1%)	
\$18001-\$24000	11 (7.8%)	2 (6.7%)	9 (8.1%)	
\$24001-\$30000	6 (4.3%)	1 (3.3%)	5 (4.5%)	
\$30001-\$36000	7 (5.0%)	0 (0%)	7 (7.1%)	
\$36001-\$75000	16 (11.4%)	0 (0%)	16 (14.4%)	
>\$75000	12 (8.5%)	1 (3.3%)	11 (9.9%)	
<i>Residence</i>				0.568
Own house/apartment	124 (84.4%)	29 (93.6%)	95 (81.9%)	
Parent's house	9 (6.1%)	0 (0%)	9 (7.8%)	
Someone else's house or apartment	10 (6.8%)	2 (6.5%)	8 (6.9%)	
Rooming/boardng/halfway house	1 (0.7%)	0 (0%)	1 (0.9%)	
Residential drug/alcohol treatment facility	2 (1.4%)	0 (0%)	2 (1.7%)	
Other	1 (0.7%)	0 (0%)	1 (0.9%)	
<i>Employment</i>				0.071
Unemployed	104 (70.8%)	26 (83.9%)	78 (67.2%)	
Employed	43 (29.3%)	5 (16.1%)	38 (32.8%)	
<i>Ever incarcerated</i>				0.334
Yes	60 (40.8%)	15 (48.4%)	45 (38.8%)	
No	87 (59.2%)	156 (51.6%)	71 (61.3%)	

Table 3.1 contains two-tailed t-test for comparison of means for continuous variables, and chi-squared test for comparison of proportions of categorical variables by low (PSS<16.14) versus high (PSS>16.14) chronic stress. Exact p-values are reported and considered statistically significant if beyond p <0.05.

Table 3.2 Neighborhood and Health Characteristics

Characteristic (mean, 95% CI)	Overall N=147	Low Stress n=31 (21.1%)	High Stress n=116 (78.9%)	P-value
<i>Stress</i>				
Perceived Stress Scale (PSS)	18.9 (18.0-19.8)	10.8 (9.0-12.6)	21.1 (20.6-21.5)	<0.0001
Hair cortisol (pg/mg) * n=55	307.0 (48.0-692.0)	183.9 (24.7-343.1)	563.0 (-86.5-1212.5)	0.2415
Log of hair cortisol (pg/mg) *	4.3 (3.9-4.7)	4.2 (3.7-4.7)	4.5 (3.9-5.1)	0.4120
<i>Metabolic characteristics</i>				
Body mass index (BMI)	29.9 (28.5-31.4)	31.3 (28.0-34.5)	29.6 (28.0-31.2)	0.3503
Systolic blood pressure (mmHg)	118.6 (115.7-121.6)	122.9 (115.6-130.2)	117.5 (114.3-120.7)	0.1364
Cholesterol (mg/dL)	178.4 (172.1-184.8)	173.6 (156.6-190.7)	179.7 (173.0-186.5)	0.4420
HDL cholesterol (mg/dL)	55.0 (51.9-58.1)	52.4 (43.2-61.5)	55.7 (52.6-58.9)	0.3841
LDL cholesterol (mg/dL)	98.4 (92.9-103.9)	94.6 (80.9-108.4)	99.4 (93.4-105.4)	0.4830
<i>Diabetes</i>				
Yes	34 (23.1%)	8 (25.8%)	26 (22.4%)	0.691
No	113 (76.9%)	23 (74.2%)	90 (77.6%)	
<i>HIV management</i>				
Viral load (copies/mL) n=144	17592.2 (2326.0-32858.3)	25316.1 (7044.6-43587.7)	15473.1 (-3425.7-34372.0)	0.6021
CD4 cell count (cells/mm <sup>3</sup> ) n=144	591.1 (539.2-643.0)	527.8 (401.4-654.2)	608.5 (551.4-665.5)	0.2081
CD4 cell percent n=145	31.7 (29.8-33.5)	27.3 (23.2-31.5)	32.9 (30.8-34.9)	<b>0.0145</b>
<i>Antiretroviral medication use (n, %)</i>				
Yes	132 (89.8%)	28 (90.3%)	104 (89.3%)	0.913
No	15 (10.2%)	3 (9.7%)	12 (10.3%)	
<i>Treatment for hypertension (n, %)</i>				
Yes	57 (38.8%)	12 (38.7%)	45 (38.8%)	0.993
No	90 (61.2%)	19 (61.3%)	71 (61.2%)	
<i>Cigarette smoking history (n, %)</i>				
Yes	104 (70.8%)	24 (77.4%)	80 (69.0%)	0.358
No	43 (29.3%)	7 (22.6%)	36 (31.0%)	
<i>Drank alcohol since last visit</i>				
Yes	63 (42.9%)	11 (35.5%)	52 (44.8%)	0.350
No	84 (57.1%)	20 (64.5%)	64 (45.2%)	
<i>Injection drug use in the past 5 years</i>				
Yes	33 (22.5%)	8 (25.8%)	25 (21.6%)	0.614
No	114 (77.6%)	23 (74.2%)	91 (78.4%)	
<i>Menopause (Y/N) n=131</i>				
Yes	43 (32.8%)	7 (28.0%)	36 (34.0%)	0.568
No	88 (67.2%)	18 (72.0%)	70 (66.0%)	
<i>Depression (CES-D)</i>				
13.9 (12.1-15.8)	13.9 (12.1-15.8)	11.8 (7.7-15.9)	14.5 (12.4-16.6)	0.2451
<i>Neighborhood perception (PNES)</i>				
Aesthetic quality (6 items)	21.4 (20.5-22.2)	21.8 (20.1-23.5)	21.3 (20.3-22.2)	0.5986
Walking environment/physical activity (10 items)	35.2 (34.2-36.3)	35.8 (33.3-38.2)	35.1 (33.9-36.3)	0.6004
Availability of healthy food (4 items)	12.4 (11.9-12.9)	13.1 (11.9-14.2)	12.2 (11.6-12.8)	0.1754
Safety (3 items)	9.0 (8.5-9.5)	8.9 (7.9-9.9)	9.1 (8.5-9.6)	0.8014
Violence (4 items)	12.1 (11.5-12.7)	11.5 (10.3-12.7)	12.3 (11.7-13.0)	0.2446
Social cohesion (4 items)	13.5 (12.9-14.1)	14.1 (13.0-15.3)	13.4 (12.7-14.0)	0.2859
Activities with neighbors (5 items)	17.6 (17.0-18.3)	18.9 (17.6-20.3)	17.3 (16.6-18.0)	<b>0.0364</b>
<b>Total score (36-items)</b>	121.3 (117.8-124.8)	124.1 (117.0-131.3)	120.6 (116.5-124.6)	0.4143

Table 3.2 contains two-tailed t-test for comparison of means for continuous variables, and chi-squared test for comparison of proportions of categorical variables by low (PSS<16.14) versus high (PSS>16.14) stress. Exact p-values are reported and considered statistically significant if beyond p <0.05.

Table 3.3: Bivariate correlations between study variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12
1. PSS	1.000											
2. log HCC	0.043	1.000										
3. Age	-0.041	-0.183	1.000									
4. CES-D	<b>0.637</b>	0.002	-0.148	1.000								
5. BMI	-0.105	0.026	-0.156	-0.215	1.000							
6. SBP	-0.134	0.022	0.118	-0.124	0.290	1.000						
7. Diabetes	-0.056	-0.065	0.168	-0.019	0.198	0.104	1.000					
8. Chol	-0.006	-0.098	0.242	-0.125	-0.089	0.106	0.195	1.000				
9. HDL	0.007	-0.315	0.316	-0.051	-0.272	0.030	-0.015	<b>0.531</b>	1.000			
10. Viral load	-0.154	0.024	-0.346	0.174	-0.116	-0.122	-0.149	-0.204	-0.213	1.000		
11. CD 4 cell count	-0.061	-0.174	0.264	-0.045	0.134	-0.056	0.173	-0.187	0.010	-0.250	1.000	
12. CD 4 cell percent	-0.051	-0.176	0.095	0.047	0.135	-0.002	0.001	-0.210	0.069	0.284	<b>0.725</b>	1.000

Table 3.3 contains correlation coefficients of all continuous study variables. Strong correlations ( $r^2$  0.5-1.0 or -1.0- 0.5) are bolded.



Table 3.4: Multivariable linear regression models of neighborhood perception on chronic stress (PSS)

Model 1						Model 2					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
PNES total	-0.03	0.02	-1.46	0.146	1.11	Aesthetic quality	-0.06	0.09	-0.65	0.518	1.10
CES-D	0.10	0.04	2.59	<b>0.011</b>	1.11	CES-D	0.11	0.04	2.68	<b>0.008</b>	1.12
Black v other race	-0.82	1.10	-0.75	0.457	1.13	Black v other race	-0.74	1.10	-0.67	0.505	1.12
SBP	-0.04	0.02	1.43	0.156	1.05	SBP	-0.03	0.02	-1.31	0.193	1.05
High v low income	2.71	0.96	2.84	<b>0.005</b>	1.23	High v low income	2.57	0.96	2.68	<b>&gt;0.001</b>	1.22
Model 3						Model 4					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Walkability	-0.09	0.07	-1.25	0.212	1.07	Access to affordable food	-0.25	0.14	-1.82	0.071	1.06
CES-D	0.10	0.04	2.62	<b>0.010</b>	1.11	CES-D	0.11	0.04	2.77	<b>0.006</b>	1.09
Black v other race	-0.75	1.10	-0.68	0.495	1.12	Black v other race	-1.07	1.11	-0.97	0.335	1.16
SBP	-0.03	0.02	-1.33	0.186	1.04	SBP	-0.03	0.02	-1.33	0.184	1.03
High v low income	2.65	0.95	2.78	<b>0.006</b>	1.22	High v low income	2.61	0.94	2.77	<b>0.006</b>	1.20
Model 5						Model 6					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Safety	-0.11	0.14	-0.80	0.427	1.07	Violence	-0.003	0.13	-0.03	0.977	1.14
CES-D	0.11	0.04	2.76	<b>0.007</b>	1.10	CES-D	0.11	0.04	2.78	<b>0.006</b>	1.11
Black v other race	-0.70	1.01	-0.64	0.524	1.12	Black v other race	-0.71	1.10	-0.64	0.522	<b>1.13</b>
SBP	-0.03	0.02	-1.30	0.196	1.04	SBP	-0.03	0.03	-1.22	0.226	1.06
High v low income	2.62	0.96	2.72	<b>0.007</b>	1.23	High v low income	2.48	0.97	2.56	<b>0.012</b>	1.25
Model 7						Model 8					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Social Cohesion	-0.20	0.12	-1.67	0.097	1.07	Interactions with neighbors	-0.15	0.11	-1.33	1.84	1.01
CES-D	0.10	0.04	2.59	<b>0.011</b>	1.11	CES-D	0.11	0.04	2.78	<b>0.006</b>	1.09
Black v other race	-0.76	1.09	-0.70	0.488	1.12	Black v other race	-0.75	1.10	-0.68	0.497	1.12
SBP	-0.03	0.02	-1.32	0.190	1.04	SBP	-0.03	0.02	-1.36	0.177	1.04
High v low income	2.70	3.92	6.04	<b>0.005</b>	1.21	High v low income	2.44	0.94	2.59	<b>0.011</b>	1.19

Table 3.4 contains regression models of chronic stress (PSS) and PNES and subscales. Bolded values are considered statistically significant at a p<0.05.

Table 3.5: Multivariable linear regression models of neighborhood perception on chronic stress (log HCC)

Model 1						Model 2					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
PNES total	0.77	1.29	-1.05	0.302	1.12	Aesthetic quality	0.21	1.11	-1.54	0.131	1.17
Age	1.02	1.08	0.32	0.754	1.68	Age	1.03	1.08	0.42	0.679	1.69
HDL	0.96	1.03			1.22	HDL	0.96	1.03	-1.44	0.158	1.21
CD 4 cell count	1.00	1.00	-0.67	0.506	1.30	CD 4 cell count	1.00	1.00	-0.43	0.671	1.36
Black v other race	16.0	4.22	1.93	0.061	1.08	Black v other race	16.55	4.12	1.98	0.055	1.08
Menopause	0.10	3.45	-1.87	0.069	1.57	Menopause	0.09	3.39	-1.96	0.057	1.57
Incarceration history	5.31	2.75	1.65	0.010	1.21	Incarceration history	5.66	2.70	1.74	0.089	1.21
Model 3						Model 4					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Walkability	1.00	1.09	0.11	0.911	1.14	Access to affordable food	0.11	1.17	-1.37	0.178	1.03
Age	1.02	1.08	0.25	0.800	1.68	Age	1.05	1.07	0.33	0.741	1.68
HDL	0.97	1.03	-1.37	0.179	1.25	HDL	0.96	1.03	-1.50	0.141	1.21
CD 4 cell count	1.00	1.00	-0.97	0.337	1.30	CD 4 cell count	1.00	1.00	-0.89	0.378	1.22
Black v other race	14.51	4.29	1.84	0.074	1.08	Black v other race	12.18	1.15	1.75	0.088	1.02
Menopause	0.12	3.50	-1.71	0.095	1.56	Menopause	0.12	3.38	-1.72	0.094	1.55
Incarceration history	5.51	2.78	1.67	0.103	1.21	Incarceration history	5.87	2.72	1.77	0.085	1.21
Model 5						Model 6					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Safety	1.00	1.19	0.04	0.968	1.10	Violence	2.11	1.17	0.47	0.644	1.25
Age	1.02	1.08	0.26	0.795	1.68	Age	1.02	1.08	0.28	0.780	1.68
HDL	0.96	1.03	-1.40	0.168		HDL	0.97	1.03	-1.37	0.178	1.22
CD 4 cell count	1.00	1.00	-0.97	0.337	1.23	CD 4 cell count	0.95	1.02	-1.08	0.286	1.39
Black v other race	14.58	4.29	1.84	0.073	1.07	Black v other race	14.82	4.27	1.86	0.071	1.08
Menopause	0.12	3.58	-1.68	0.101	1.62	Menopause	0.13	3.52	-1.64	0.109	1.58
Incarceration history	5.54	2.79	1.67	0.103	1.22	Incarceration history	5.81	2.79	1.71	0.094	1.22
Model 7						Model 8					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Social cohesion	0.75	1.17	-1.83	0.074	1.06	Activities with neighbors	0.72	1.18	-2.02	<b>0.050</b>	1.10
Age	1.03	1.08	0.44	0.664	1.69	Age	1.00	1.08	0.02	0.980	1.70
HDL	0.96	1.02	-1.47	0.149	1.21	HDL	0.96	1.02	-1.37	0.178	1.22
CD 4 cell count	1.00	1.00	-0.75	0.456	1.23	CD 4 cell count	1.00	1.00	-1.14	0.261	1.21
Black v other race	22.03	4.12	2.18	<b>0.035</b>	1.10	Black v other race	26.92	4.14	2.32	<b>0.026</b>	1.13
Menopause	0.09	3.33	-1.98	0.055	1.56	Menopause	0.14	3.28	-1.68	0.100	1.55
Incarceration history	4.78	2.68	1.59	0.120	1.22	Incarceration history	4.51	2.66	1.54	0.132	1.22

Table 3.5 displays full regression models of the PNES and subscales and covariates. Beta coefficient values were log-transformed to the original scale for interpretation. Variables were considered statistically significant at  $p < 0.05$ .

*Measure 3.1: Perceptions of Neighborhood Environment Scale domains and items (Echeverria et al., 2004)*

**Perception of Neighborhood Environment Scale**

*Scale and subscale score ranges are described below. Response scores in which the scoring is reversed are indicated with an (R). Possible range of scores is 36 to 171, with the higher scores indicating positive perception of neighborhood.*

Aesthetic quality

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

- A1. There is a lot of trash and litter on the street in my neighborhood
- A2. There is a lot of noise in my neighborhood
- A3. In my neighborhood the buildings and homes are well-maintained (Reversed (R))
- A4. The buildings and houses in my neighborhood are interesting (R)
- A5. My neighborhood is attractive (R)
- A6. There are interesting things to do in my neighborhood (R)

Walking environment/Physical activity

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

- B1. My neighborhood offers many opportunities to be physically active (R)
- B2. Local sports clubs and other facilities in my neighborhood offer many opportunities to get exercise (R)
- B3. It is pleasant to walk in my neighborhood (R)
- B4. The trees in my neighborhood provide enough shade (R)
- B5. In my neighborhood it is easy to walk places (R)
- B6. I often see other people walking in my neighborhood (R)

B7. I often see other people exercising (for example, jogging, bicycling, and playing sports) in my neighborhood (R)

B8. My neighborhood has heavy traffic

B9. There are busy roads to cross when out for walks in my neighborhood

B10. In my neighborhood, the streets and sidewalks are in good condition (R)

#### Availability of healthy food

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

C1. A large selection of fresh fruits and vegetables is available in my neighborhood (R)

C2. The fresh fruits and vegetables in my neighborhood are of high quality (R)

C3. A large selection of low-fat products is available in my neighborhood (R)

C4. There are many opportunities to purchase fast foods in my neighborhood

#### Safety

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

D1. I feel safe walking in my neighborhood, day or night (R)

D2. Violence is not a problem in my neighborhood (R)

D3. My neighborhood is safe from crime (R)

#### Violence

*Scale is 1-4, often to never, with 4 being most positive perception.*

E1. During the past 6 months, how often was there a fight in your neighborhood in which a weapon was used?

E2. During the past 6 months, how often were there gang fights in your neighborhood?

E3. During the past 6 months, how often was there a sexual assault or rape in your neighborhood?

E4. During the past 6 months, how often was there a robbery or mugging in your neighborhood?

Social cohesion

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

F1. People around here are willing to help their neighbors (R)

F2. People in my neighborhood generally get along with each other (R)

F3. People in my neighborhood can be trusted (R)

F4. People in my neighborhood share the same values (R)

Activities with Neighbors

*Scale is 1-4, often to never, with 4 being most positive perception.*

G1. About how often do you and people in your neighborhood do favors for each other?

By favors, we mean such things as watching each other's children, helping with shopping, lending garden or house tools, and other small acts of kindness (R)

G2. When a neighbor is not at home or on vacation, how often do you and other neighbors watch over their property? (R)

G3. How often do you and other people in the neighborhood ask each other for advice about personal things such as child-rearing or job openings? (R)

G4. How often do you and people in your neighborhood have parties or other get-togethers where other people in the neighborhood are invited? (R)

G5. How often do you and other people in your neighborhood visit in each other's homes or speak with each other on the street? (R)

*Measure 3.2: Perceived Stress Scale (Cohen et al., 1994)*

**Perceived Stress Scale**

*Scale is 0-4. Responses to stress over a one-month period include a score of zero if “never”, score of one if “almost never”, a score of two if “sometimes”, a score of three if “fairly often”, and a score of four if “very often” per question. The range of scores is zero to 40, with the higher scores indicating the presence of more symptomatology*

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

1. In the last month, how often have you been upset because of something that happened unexpectedly?
2. In the last month, how often have you felt that you were unable to control the important things in your life?
3. In the last month, how often have you felt nervous and “stressed”?
4. In the last month, how often have you felt confident about your ability to handle your personal problems?
5. In the last month, how often have you felt that things were going your way?
6. In the last month, how often have you found that you could not cope with all the things that you had to do?
7. In the last month, how often have you been able to control irritations in your life?
8. In the last month, how often have you felt that you were on top of things?

9. In the last month, how often have you been angered because of things that were outside of your control?

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

*Measure 3.3: Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977)*

**Center for Epidemiologic Studies Depression Scale (CES-D), NIMH**

*Scale is 0-3. Responses include a score of zero if rarely or none of the time (less than 1 day), a score of one if some or a little of the time (1-2 days), a score of two if occasionally or a moderate amount of time (3-4 days), and a score of three if most or all of the time (5-7 days) per question. The scoring of positive items is reversed. Possible range of scores is zero to 60, with the higher scores indicating the presence of more symptomatology.*

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

1. I was bothered by things that usually don't bother me.
2. I did not feel like eating; my appetite was poor.
3. I felt that I could not shake off the blues even with help from my family or friends.
4. I felt I was just as good as other people. (R)
5. I had trouble keeping my mind on what I was doing.
6. I felt depressed.
7. I felt that everything I did was an effort.
8. I felt hopeful about the future. (R)
9. I thought my life had been a failure.
10. I felt fearful.



11. My sleep was restless.
12. I was happy. (R)
13. I talked less than usual.
14. I felt lonely.
15. People were unfriendly.
16. I enjoyed life. (R)
17. I had crying spells.
18. I felt sad.
19. I felt that people dislike me.
20. I could not get “going.”

## **CHAPTER 4**

### **The associations between neighborhood environment and CVD risk among women living with HIV**

## Abstract

Women living with HIV (WLWH) are uniquely at risk for developing cardiovascular disease (CVD) as they age in their neighborhood environments. Neighborhood conditions can increase the susceptibility for CVD as WLWH age, related to violence, pollution, and diminished access to affordable healthy food and spaces for physical activity. Chronic stress, both psychologically and biologically, is a major process in which neighborhood environmental features impact cardiovascular health among WLWH. Despite the existing evidence of neighborhood impacts on chronic stress and CVD risk, direct examination of these associations among WLWH is lacking. Therefore, the purpose of this study was to examine the associations between neighborhood environmental factors and risk for CVD. We completed this study through a secondary analysis of data from the Chicago Women's Interagency HIV Study (WIHS). Data for this study was collected in 2012. A total of 147 HIV-positive cisgender women were included in this study. We used the Perception of Neighborhood Environments Scale (PNES) as a measure for neighborhood environmental factors, and calculated CVD risk utilizing the Framingham Risk Score (FRS) algorithm. We conducted a multivariable linear regression analysis to explore the associations between neighborhood perception and CVD risk. The results from this study can inform future neighborhood-level interventions that promote cardiovascular health among WLWH as they age.

*Keywords: HIV, women, cardiovascular disease, neighborhood environment*

## Introduction

Women living with HIV/AIDS (WLWH) are uniquely at risk for developing cardiovascular disease (CVD) as they age in their neighborhood environments. For instance, WLWH are often exposed to neighborhood segregation and poverty (Burke-Miller et al., 2016; Haley et al., 2018), and these circumstances are associated with deleterious HIV outcomes, such as decreased medication adherence elevated viral load, and lower CD4 cell counts (Castel et al., 2012; Shacham, Lian, Önen, Donovan, & Overton, 2013; Surratt, Kurtz, Levi-Minzi, & Chen, 2015). In turn, these neighborhood conditions can increase the susceptibility for CVD as WLWH age related to reduced medication adherence, elevated viral load, and low CD4 cell counts, which have been associated with increased risk for CVD (Castel et al., 2012; Shacham et al., 2013; Surratt et al., 2015). WLWH may also be exposed to other factors that are damaging to the cardiovascular health, and can include violence, pollution, and diminished access to affordable healthy food and spaces for physical activity (Burke-Miller et al., 2016).

Despite the existing evidence of neighborhood impacts on chronic stress and CVD risk, direct examination of these associations among WLWH is lacking. Studies that have examined neighborhood environment often utilize aggregate measures, such as census tract data, to explore associations between neighborhood environment and HIV outcomes among WLWH (Echeverria, Diez-Roux, & Link, 2004). Despite the utility and availability of census data, these measures serve as proxy measures (e.g. census tract-level measures for population, income, crime, etc.) and often do not serve to directly depict the characteristics of neighborhoods that are associated with individual health outcomes, such as accessibility to affordable nutritious food, walkability, violence, and

other aspects of neighborhood environment (Diez-Roux et al., 1997; Echeverria et al., 2004). Therefore, the purpose of this study is to examine the associations to between perception of neighborhood environment are associated with CVD risk among WLWH. In this study, we examined aspects of neighborhood environment that have been linked to CVD. Therefore, this study examined whether the associations between these aspects of neighborhoods are linked to CVD risk among WLWH.

## **Methods**

### ***Design***

This study was secondary analysis of data collected from the Chicago Women's Interagency HIV Study (WIHS). This longitudinal, prospective, multi-site study of women began in 1993 and has examined the natural history of HIV among women. Key areas of investigation within the WIHS study include reproductive health, clinical outcomes (such as cardiovascular disease, diabetes, and neurocognitive disorders), and the efficacy of antiretroviral therapies (WIHS Data Management and Analysis Center, 2017). This study utilized data collected from the cardiovascular disease and neighborhood environment sub studies. These studies, within the larger framework of WIHS, sought to better understand cardiovascular function and the associations of neighborhood environment with health outcomes among WLWH. This study incorporated data from WIHS clinical examinations and data from Chicago WIHS sub studies to examine the study aims. Inclusion criteria for this study included HIV-positive status, residence in the Chicago area, and participation in the previously mentioned Chicago WIHS sub studies. Given that this study utilized de-identified data, this study received a waiver of review from the University of Pennsylvania Institutional Review Board (IRB)

prior to data transfer from Chicago WIHS. A total of 147 Chicago WIHS participants met these criteria and were included study. The data used for this study were collected during 2012. After transfer from the Chicago WIHS team, the data were cleaned and recoded as necessary to prepare the data for study analyses. All statistical analyses were conducted utilizing Stata 15 software (StataCorp, 2017).

## ***Measures***

### *Predictor variables*

The PNES was used to characterize how WLWH evaluate the quality of their neighborhood environment and is included as Measure 1. The PNES is a 36-item measure of perceived neighborhood environment with six subscales, including: aesthetic quality, physical activity/walking environment, availability of healthy food, safety, violence, social cohesion, and activities with neighbors (Echeverria et al., 2004). Among WIHS participants, The PNES has strong reliability across subscales, with a Cronbach's alpha of 0.94 for the total scale reliability. The PNES subscales also demonstrated good reliability, with Cronbach's alphas ranging from 0.72-0.89 (Burke-Miller et al., 2017). Further, the PNES subscales are significantly associated with census measures of neighborhood disorder ( $p > 0.01$ ), such as concentrated poverty ( $\geq 25\%$  below the federal poverty line) and racial segregation ( $\geq 50\%$  Black/non-Hispanic residents) (Burke-Miller et al., 2016). The PNES total score and scores of sub scales were used in the study analyses.

### *Correlates*

Variables that may be associated with the predictor and outcome variables for this study were selected from the Chicago WIHS database relative to the scientific literature and are listed in Table 1. Briefly, variables that were examined for bivariate analysis

include demographic variables (age, race/ethnicity, income, education, monthly income, employment, housing, and incarceration history), general factors associated with CVD risk among women (alcohol use, drug use, cigarette smoking, menopause, inflammatory markers), and HIV-associated risk factors (CD4 count, viral load). Additional total scale values were examined for bivariate associations with predictor and outcome variables and include depression (CES-D) and physical activity. We developed additional binary measures for education (1=more than high school, 0=high school or less), income (1=annual income greater than \$12,000, 0= annual income equal to or less than \$12,000), and race (1= Black race, 0= other race). These variables were examined in bivariate analyses with our primary outcome variable.

#### *Outcome variable*

The primary outcome of interest was CVD risk, which was evaluated with the Framingham Risk Score (FRS) 10-year risk algorithm as described in D'Agostino et al. (2008). Briefly, the FRS was developed based on the Framingham Heart Study, in which a variety of risk factors were identified as associated with increased risk for cardiovascular events (Wilson et al., 1998). Variables included in the 10-year risk algorithm include age, cholesterol, HDL, systolic blood pressure, diabetes diagnosis, current cigarette smoking status, and antihypertensive medication use. Measure 4.4 displays algorithms used for FRS variable generation. Since this sample is one sex, the female FRS algorithm coefficients were used. Values generated utilizing the algorithms in Measure 4.4 were checked with an online FRS-10 calculator for accuracy. For comparison of study characteristics by CVD risk, we created two CVD risk categorizations for this sample: low (FRS <10%) and intermediate/high risk ( $\geq 10\%$ ).

These bins have been used in previous studies of CVD risk using the FRS, and have been used to examine CVD risk in women (De Socio et al., 2008; Jahangiry, Farhangi, & Rezaei, 2017; Michos et al., 2005).

### ***Analysis Plan***

We examined univariate, descriptive statistics of demographic and health data to observe trends of each study variable. Bivariate regression analyses between continuous and binary demographic and health variables and CVD risk, the primary outcome variable to select covariates for multivariable regression models examining the association between neighborhood perception and CVD risk. Covariates were selected for multivariable linear regression analyses that had a significance of  $\leq 0.20$ . We completed a multivariable linear regression to examine the association between neighborhood environment (predictor variable) and CVD risk (outcome variable). All analyses were completed in StataIC 15 Statistical Software (StataCorp, 2017). A stepwise approach to model development was used to examine model performance with selected covariates. Similar findings were obtained in regression models with both forward and backward stepwise approaches.

### ***Effect Size Calculation***

The total number of HIV-positive women eligible for this study from the Chicago WIHS sample includes 147 HIV-positive women. To achieve the study aims, we calculated for effect size by specifying the effect size calculation of multiple linear regressions for our analysis of CVD risk as measured by the FRS (dependent variable) regressed on neighborhood perception as measured by the PNES and subscales. We were able to detect an effect size ( $f^2$ ) of 0.057 with a sample size of 147, power at 0.80, and



alpha at 0.05. All power calculations were calculated in PASS 2019 software (Hintze, 2004).

## **Results**

### ***Sample characteristics***

Demographic and clinical characteristics of the WLWH included in this study are described in Table 4.1. We included a total of 147 WLWH with complete data from the Chicago WIHS study data collected in 2012. The mean age of the sample was 47.2 (95% CI: 45.8-48.6), 76.9% were African American, and 15.0% were White, Non-Hispanic. A meaningful proportion of the WLWH included in this study received at most a high school education (57.8%), were not employed at the time of this study (70.8%) and had previous history of incarceration in their lifetime (40.8%). The overall mean CVD risk as measured by the FRS for this sample is 7.56% (95% CI: 6.23%- 8.89%, range: 0.34%-49.89%). A total of 113 (76.9%) women were categorized as “low” risk and 31 (21.08%) were categorized as “intermediate/high” risk based on the FRS algorithm. We observed a disproportionate number of White, Non-Hispanic women with intermediate/high FRS (n=9, 28.1%) relative to their overall representation in this sample (n=22, 15.0%), and this proportion was statistically significant (p=0.019). Despite this, African American women represented the largest racial/ethnic group in this study (n=113, 76.9%) and in the intermediate/high risk categorization (n=20, 62.5%). Further, women within intermediate/high FRS categorization had a statistically significant greater proportion of women who had experienced menopause (61.5%) than women within the low FRS risk category (25.7%, p>0.001). Upon further examination of the association between menopause and CVD risk, we found that the association between menopausal status and

CVD risk was no longer statistically significant after controlling for age (coeff. =1.63, SE=1.74,  $t= 0.93$ ,  $p=0.352$ ).

Table 4.2 contains health and neighborhood characteristics of WLWH included in this study. Participants had a mean viral load of 17592.2 copies/mL (95% CI: 2326.0-32858.3 copies/mL), a CD4 cell count of 591.1 cells/mm<sup>3</sup> (95% CI: 539.2-643.0 cells/mm<sup>3</sup>) and 89.8% reported antiretroviral medication use time if this study. Further, WLWH in this study had a mean systolic blood pressure of 118.6 mmHg (95% CI: 115.7-121.6 mmHg), total cholesterol of 178.4 mg/dL (95% CI: 172.1-184.8 mg/dL), and HDL cholesterol of 55.0 mg/dL (95% CI: 51.9-58.1 mg/dL). Importantly, most women in sample reported cigarette smoking (70.8%), and a notable proportion injection drug use within the past five years (24.1%).

We observed significant differences in reported alcohol consumption and FRS score among WLWH in Chicago WIHS. Women categorized in the intermediate/high FRS group reported alcohol significantly less consumption ( $n=7$ , 21.9%) than women in the low FRS group ( $n=56$ , 48.7%,  $p=0.007$ ). We did not observe any other differences in demographic, health, or neighborhood measures among low or intermediate/high FRS groups.

### ***Bivariate analyses***

In bivariate regression analyses for covariate selection, we observe associations between CD4 cell count (coef: 0.003, SE: 0.002,  $p= 0.135$ ), Black v other race (coef: -5.02, SE: 1.56,  $p= 0.002$ ), alcohol consumption (coef: -3.45, SE: 1.33,  $p= 0.011$ ), and illicit drug use in the past five years (coef: -2.92, SE: 1.60,  $p= 0.071$ ). These variables

were selected as covariates for multivariable regression models examining the associations between neighborhood perception and CVD risk as measured by the FRS.

### ***Linear regression***

We report findings from full linear regression models in Table 4.3. We examined the associations between the PNES and subscales with CVD risk as measured by the FRS 10-year algorithm. In the full regression models, we did not observe statistically significant associations between the PNES and subscales and FRS among women in the Chicago WIHS sample. Across multivariable regression models, Black v other race was significantly associated with FRS in models with the PNES and subscales. Our model examining the association of PNES total score and FRS, women with Black race demonstrated a 4.69 unit decrease in FRS when compared to women of other races (SE: 1.61,  $p=0.004$ ). Similar findings were observed in models of PNES subscales. Additionally, reported alcohol consumption was significantly associated with FRS in linear regression analyses. In our model examining associations of PNES total score and FRS, women who reported alcohol consumption since their last visit had a 4.03 unit decrease in FRS as compared to women who did not report alcohol consumption (SE: 1.31,  $p=0.003$ ). Again, these findings were consistent across regression analyses of PNES subscales and FRS in WLWH in Chicago WIHS.

### **Discussion**

The purpose of this study was to examine the associations between various aspects of neighborhood environment with CVD risk among WLWH. We hypothesized that decreased (poorer) perception of neighborhood environment would be associated with increased CVD risk. Although this study did not provide evidence to support the

hypothesized associations between neighborhood environment and CVD risk, this study demonstrated the persistent disparities in CVD risk that occur in HIV-positive women in connection to their perception of neighborhood. The findings from this study underscore the importance of race as a determinant of cardiovascular risk. Among studies of WLWH, African American women demonstrate the greatest burden of CVD morbidity and mortality. As African American women disproportionately are impacted by HIV and/or CVDs, it is critical that interventions tailored to the needs and perspectives of African American women.

Studies that have examined the associations of neighborhood environment and CVD risk among WLWH are lacking, yet there is a broad body of research that has examined neighborhood environment and CVD risk in the general population. Consistently, studies have demonstrated the consistent associations of CVD risk and neighborhood deprivation, low social cohesion, decreased safety, and residential instability (Chaix, Lindström, Rosvall, & Merlo, 2008; Chaix, Rosvall, & Merlo, 2007; Echeverría, Diez-Roux, Shea, Borrell, & Jackson, 2008; Kim, Diez Roux, Kiefe, Kawachi, & Liu, 2010). These aspects of neighborhoods have been linked to a variety of individual factors that are associated with CVD, such as cigarette smoking, depression, and reduced physical activity (Diez-Roux & Mair, 2010; Evenson et al., 2012; Matheson et al., 2006; Strong, Reitzel, Wetter, & McNeill, 2013).

Notably, this study illustrated a disproportionate CVD risk among White, Non-Hispanic women relative to other racial/ethnic groups in the Chicago WIHS sample. This sample had a low proportion of women with intermediate/high CVD risk (n=31, 21.08%), and while White, Non-Hispanic women demonstrated disproportionate CVD risk, African

American, Non-Hispanic women represented the majority of participants within the intermediate/high CVD risk category as calculated by the FRS. Importantly, White, Non-Hispanic women in this sample may have increased risk for CVD related to increased age, injection drug use, and history of incarceration relative to African American WLWH in the WIHS sample.

This study has several limitations. First, the data for this study were collected in 2012. Given the complexity and dynamic nature of neighborhoods as well as assessment of CVD risk, these associations may not be consistent with the passage of time. Additionally, the Chicago WIHS sample is largely African American/Black. While this is representative of the local HIV prevalence to Chicago, comparisons by race/ethnicity may be impacted by the homogeneity of the sample. Examinations of the associations of CVD risk and race/ethnicity revealed a meaningful proportion of White/Non-Hispanic women demonstrated elevated risk for CVD. While White/Non-Hispanic women represented a small proportion of participants relative to other racial/ethnic groups, it is critical that behavioral and circumstantial factors (injection drug use, incarceration history, etc.) that are associated with elevated risk of CVD are considered in developing CVD prevention strategies for WLWH. Further, this study utilized the FRS 10-year algorithm as a measure of CVD risk. The HIV-positive women in this study were young, with a mean age of 47.2 (IQR: 41.5-53.4). Typically, risk factors for CVD that are included in the FRS, such as elevated blood pressure, cholesterol, and diabetes increase in prevalence as individuals age, particularly beyond age 50 (Lloyd-Jones et al., 2006). Therefore, it is likely that WLWH in this sample would have increased risk attributed to the onset of CVD comorbidities and increased age over time. While the FRS is widely

used in research and clinical practice to characterize CVD risk, several studies have noted that the FRS underestimated CVD risk in women and among HIV-positive persons regardless of sex/gender (Cook et al., 2012; Schwartz et al., 2012; Serrano-Villar et al., 2014). Future studies are needed to compare the calibration of alternative CVD risk algorithms, such as the Reynold's Risk Score and the DAD Score (Ridker, Buring, Rifai, & Cook, 2007; Serrano-Villar et al., 2014).

### **Conclusions**

WLWH disproportionately are impacted by CVDs as they age. The purpose of this study was to examine the associations of CVD risk and neighborhood environment among WLWH to explore specific aspects of neighborhood environment as perceived by HIV-positive women that may be associated with CVD. We hypothesized that decreased perception of neighborhood would be associated with increased CVD risk in our sample. We did not observe significant associations between perception of neighborhood and CVD risk among WLWH in the Chicago WIHS study. Despite this, our study highlights the importance of disparity of CVD risk that impacts African American WLWH relative to other racial and ethnic groups. This study supports the development of individual, neighborhood, and policy interventions that can support WLWH and encourage cardiovascular health and wellness as they age.

## References

- Burke-Miller, J. K., Weber, K., Cohn, S. E., Hershov, R. C., Sha, B. E., French, A. L., & Cohen, M. H. (2016). Neighborhood community characteristics associated with HIV disease outcomes in a cohort of urban women living with HIV. *AIDS care*, 28(10), 1274-1279.
- Burke-Miller, J. K., Weber, K. M., Cohn, S. E., Hershov, R. C., Sha, B., French, A. L., & Cohen, M. H. (2017). Measurement of Neighborhood Context in an Urban Cohort of HIV-infected or at risk Low-Income Women. *Journal of poverty*, 21(1), 80-96.
- Castel, A. D., Befus, M., Willis, S., Griffin, A., West, T., Hader, S., & Greenberg, A. E. (2012). Use of the community viral load as a population-based biomarker of HIV burden. *Aids*, 26(3), 345-353.
- Chaix, B., Lindström, M., Rosvall, M., & Merlo, J. (2008). Neighbourhood social interactions and risk of acute myocardial infarction. *Journal of Epidemiology & Community Health*, 62(1), 62-68.
- Chaix, B., Rosvall, M., & Merlo, J. (2007). Neighborhood socioeconomic deprivation and residential instability: effects on incidence of ischemic heart disease and survival after myocardial infarction. *Epidemiology*, 18(1), 104-111.
- Cohen, S., Kamarck, T., & Mermelstein, R. (1994). Perceived stress scale. *Measuring stress: A guide for health and social scientists*, 235-283.
- Cook, N. R., Paynter, N. P., Eaton, C. B., Manson, J. E., Martin, L. W., Robinson, J. G., . . . Ridker, P. M. (2012). Comparison of the Framingham and Reynolds Risk scores for global cardiovascular risk prediction in the multiethnic Women's Health Initiative. *Circulation*, 125(14), 1748-1756.

- D'Agostino, R. B., Sr., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*, *117*(6), 743-753.  
doi:10.1161/circulationaha.107.699579
- De Socio, G. V. L., Parruti, G., Quirino, T., Ricci, E., Schillaci, G., Adriani, B., . . . Vichi, F. (2008). Identifying HIV patients with an unfavorable cardiovascular risk profile in the clinical practice: results from the SIMONE study. *Journal of Infection*, *57*(1), 33-40.
- Diez-Roux, A. V., & Mair, C. (2010). Neighborhoods and health. *Annals of the New York Academy of Sciences*, *1186*(1), 125-145.
- Diez-Roux, A. V., Nieto, F. J., Muntaner, C., Tyroler, H. A., Comstock, G. W., Shahar, E., . . . Szklo, M. (1997). Neighborhood environments and coronary heart disease: a multilevel analysis. *American journal of epidemiology*, *146*(1), 48-63.
- Echeverría, S., Diez-Roux, A. V., Shea, S., Borrell, L. N., & Jackson, S. (2008). Associations of neighborhood problems and neighborhood social cohesion with mental health and health behaviors: the Multi-Ethnic Study of Atherosclerosis. *Health & place*, *14*(4), 853-865.
- Echeverria, S. E., Diez-Roux, A. V., & Link, B. G. (2004). Reliability of self-reported neighborhood characteristics. *Journal of Urban Health*, *81*(4), 682-701.
- Evenson, K. R., Block, R., Roux, A. V. D., McGinn, A. P., Wen, F., & Rodríguez, D. A. (2012). Associations of adult physical activity with perceived safety and police-recorded crime: the Multi-ethnic Study of Atherosclerosis. *International journal of behavioral nutrition and physical activity*, *9*(1), 146.



- Haley, D. F., Wingood, G. M., Kramer, M. R., Haardörfer, R., Adimora, A. A., Rubtsova, A., . . . Hickson, D. A. (2018). Associations Between Neighborhood Characteristics, Social Cohesion, and Perceived Sex Partner Risk and Non-Monogamy Among HIV-Seropositive and HIV-Seronegative Women in the Southern US. *Archives of sexual behavior*, 1-13.
- Hintze, J. (2004). NCSS and PASS software. *Kaysville, UT: Number Cruncher Statistical Systems*.
- Jahangiry, L., Farhangi, M. A., & Rezaei, F. (2017). Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *Journal of Health, Population and Nutrition*, 36(1), 36.
- Kim, D., Diez Roux, A. V., Kiefe, C. I., Kawachi, I., & Liu, K. (2010). Do neighborhood socioeconomic deprivation and low social cohesion predict coronary calcification? The CARDIA study. *American journal of epidemiology*, 172(3), 288-298.
- Lloyd-Jones, D. M., Leip, E. P., Larson, M. G., d'Agostino, R. B., Beiser, A., Wilson, P., . . . Levy, D. (2006). Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation*, 113(6), 791-798.
- Matheson, F. I., Moineddin, R., Dunn, J. R., Creatore, M. I., Gozdyra, P., & Glazier, R. H. (2006). Urban neighborhoods, chronic stress, gender and depression. *Social science & medicine*, 63(10), 2604-2616.
- Michos, E. D., Vasamreddy, C. R., Becker, D. M., Yanek, L. R., Moy, T. F., Fishman, E. K., . . . Blumenthal, R. S. (2005). Women with a low Framingham risk score and

- a family history of premature coronary heart disease have a high prevalence of subclinical coronary atherosclerosis. *American heart journal*, 150(6), 1276-1281.
- Ridker, P. M., Buring, J. E., Rifai, N., & Cook, N. R. (2007). Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. *Jama*, 297(6), 611-619.
- Schwartz, R. M., Mansoor, A., Wilson, T. E., Anastos, K., Everson-Rose, S. A., Golub, E. T., . . . Lazar, J. (2012). Chronic depressive symptoms and Framingham coronary risk in HIV-infected and HIV-uninfected women. *AIDS care*, 24(3), 394-403.
- Serrano-Villar, S., Estrada, V., Gomez-Garre, D., Ávila, M., Fuentes-Ferrer, M., San, R. J., . . . Fernández-Cruz, A. (2014). Diagnosis of subclinical atherosclerosis in HIV-infected patients: higher accuracy of the D: A: D risk equation over Framingham and SCORE algorithms. *European journal of preventive cardiology*, 21(6), 739-748.
- Shacham, E., Lian, M., Önen, N., Donovan, M., & Overton, E. (2013). Are neighborhood conditions associated with HIV management? *HIV medicine*, 14(10), 624-632.
- StataCorp. (2017). Stata Statistical Software. College Station, TX: StataCorp LLC.
- Strong, L. L., Reitzel, L. R., Wetter, D. W., & McNeill, L. H. (2013). Associations of perceived neighborhood physical and social environments with physical activity and television viewing in African-American men and women. *American journal of health promotion*, 27(6), 401-409.

Surratt, H. L., Kurtz, S. P., Levi-Minzi, M. A., & Chen, M. (2015). Environmental influences on HIV medication adherence: The role of neighborhood disorder.

*American journal of public health, 105*(8), 1660-1666.

WIHS Data Management and Analysis Center. (2017). Our Study: The Women's

Interagency HIV Study. Retrieved from <https://statepi.jhsph.edu/wihs/wordpress/>

Wilson, P. W., D'Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel,

W. B. (1998). Prediction of coronary heart disease using risk factor categories.

*Circulation, 97*(18), 1837-1847.

## Appendices

*Table 4.1: Demographic Characteristics*

Characteristic (n,%)	Overall N=147	Low FRS n= 113 (76.87%)	Med/ High FRS n= 31 (21.08%)	P-value
<i>Age (Mean, 95% CI) †</i>	47.2 (45.8-48.6)	45.0 (43.5-46.4)	55.0 (52.5-57.5)	<b>&lt;0.0001</b>
<i>Race/Ethnicity</i>				<b>0.067</b>
White, Non-Hispanic	22 (15.0%)	13 (11.3%)	9 (28.1%)	
White, Hispanic	4 (2.7%)	4 (3.48%)	0 (0%)	
African American, Non- Hispanic	113 (76.9%)	93 (80.9%)	20 (62.5%)	
African American, Hispanic	1 (0.7%)	1 (0.9%)	0 (0%)	
Other (Hispanic)	6 (4.1%)	3 (2.6%)	3 (9.4%)	
Native American/Alaskan	1 (0.7%)	1 (0.9%)	0 (0%)	
<i>Education</i>				0.494
Grades 1-6	2 (1.4%)	2 (1.7%)	0 (0%)	
Grades 7-11	49 (33.3%)	36 (31.3%)	13 (40.6%)	
Completed high school	34 (23.1%)	28 (24.4%)	6 (18.8%)	
Some college	41 (27.9%)	32 (27.8%)	9 (28.1%)	
Completed 4 years of college	13 (8.8%)	9 (7.8%)	4 (12.5%)	
Attended/completed graduate school	8 (5.4%)	8 (7.0%)	0 (0%)	
<i>Average household income/year</i>				0.187
\$6000 or less	22 (15.6%)	18 (16.2%)	4 (13.3%)	
\$6001-\$12000	55 (39.0%)	40 (36.0%)	15 (50.0%)	
\$12001-\$18000	12 (8.5%)	11 (9.9%)	1 (3.3%)	
\$18001-\$24000	11 (7.8%)	10 (9.0%)	1 (3.3%)	
\$24001-\$30000	6 (2.3%)	3 (2.7%)	3 (10.0%)	
\$30001-\$36000	7 (5.0%)	5 (4.5%)	2 (6.7%)	
\$36001-\$75000	16 (11.4%)	12 (10.8%)	4 (13.3%)	
>\$75000	12 (8.5%)	12 (10.8%)	0 (0%)	
<i>Residence</i>				0.860
Own house/apartment	124 (84.4%)	95 (82.6%)	29 (90.6%)	
Parent's house	9 (6.1%)	8 (7.0%)	1 (3.1%)	
Someone else's house/apartment	10 (6.8%)	8 (7.0%)	2 (6.3%)	
Rooming/boarding/halfway house	1 (0.7%)	1 (0.9%)	0 (0%)	
Residential drug/alcohol treatment facility	2 (1.4%)	2 (1.7%)	0 (0%)	
Other	1 (1.4%)	1 (0.9%)	0 (0%)	
<i>Employment</i>				0.300
Unemployed	104 (70.8%)	79 (68.7%)	25 (78.1%)	
Employed	43 (29.3%)	36 (31.3%)	7 (21.9%)	
<i>Ever incarcerated</i>				0.980
Yes	60 (40.8%)	47 (40.9%)	13 (40.6%)	
No	87 (59.2%)	68 (59.1%)	19 (59.4%)	

Table 4.1 contains two-tailed t-test for comparison of means for continuous variables, and chi-squared test for comparison of proportions of categorical variables.

†- Variable included in FRS algorithm

Table 4.2: Neighborhood and Health Characteristics

Characteristic (mean, 95% CI)	Overall N=147	Low FRS n=113 (76.87%)	Med/High FRS n=31 (21.08%)	P-value
<i>Metabolic characteristics</i>				
Body mass index (BMI)	29.9 (28.5-31.4)	29.7 (28.0-31.4)	30.8 (27.9-33.8)	0.5274
Systolic blood pressure (mmHg) †	118.6 (115.7-121.6)	114.3 (111.3-117.2)	134.4 (128.7-140.1)	>0.001
Cholesterol (mg/dL) †	178.4 (172.1-184.8)	174.0 (167.0-181.0)	194.4 (180.1-208.7)	<b>0.0086</b>
HDL cholesterol (mg/dL) †	55.6 (51.9-58.1)	56.2 (52.6-59.9)	50.6 (45.2-56.0)	0.01389
LDL cholesterol (mg/dL) †	98.4 (92.9-103.9)	95.8 (89.8-101.8)	107.8 (94.8-120.9)	0.0735
<i>Diabetes (n, %) †</i>				
Yes	34 (23.1%)	12 (10.4%)	22 (68.8%)	>0.001
No	113 (76.9%)	103 (89.6%)	10 (31.3%)	
<i>Treatment for hypertension (n, %) †</i>				
Yes	57 (38.8%)	33 (28.7%)	24 (75.0%)	>0.001
No	90 (61.2%)	82 (71.3%)	8 (25.0%)	
<i>Menopause (n, %)</i>				
<i>n=131</i>				
Yes	43 (32.8%)	27 (25.7%)	16 (61.5%)	>0.001
No	88 (67.2%)	78 (74.3%)	10 (38.5%)	
<i>Cigarette smoking history (n, %) †</i>				
Yes	104 (70.8%)	76 (66.1%)	28 (87.5%)	<b>0.019</b>
No	43 (29.3%)	39 (33.9%)	4 (12.5%)	
<i>Drank alcohol since last visit (n, %)</i>				
Yes	63 (42.9%)	56 (48.7%)	7 (21.9%)	<b>0.007</b>
No	84 (57.1%)	59 (51.3%)	25 (78.1%)	
<i>Injection drug use in past 5 yrs (n, %)</i>				
Yes	33 (22.5%)	29 (25.2%)	4 (12.5%)	0.127
No	114 (77.6%)	86 (74.8%)	28 (87.5%)	
<i>HIV management</i>				
Viral load (copies/mL)	17592.2 (2326.0-32858.3)	21901.3 (2470/3-41332.2)	1884.6 (-532.2-4301.5)	0.2883
CD4 cell count (cells/mm <sup>3</sup> )	591.1 (539.2-643.3)	578.2 (521.3-635.0)	638.2 (509.4-767.0)	0.3491
CD4 cell percent	31.7 (29.8-33.1)	31.8 (29.7-33.9)	31.2 (27.3-35.1)	0.7928
<i>Antiretroviral use (n, %)</i>				
Yes	132 (89.8%)	103 (89.6%)	29 (90.6%)	0.861
No	15 (10.2%)	12 (10.4%)	3 (9.4%)	
<i>Depression (CES-D)</i>				
	13.9 (12.1-15.8)	14.0 (11.8-16.1)	13.7 (9.8-17.7)	0.9086
<i>Neighborhood perception (PNES)</i>				
Aesthetic quality	21.4 (20.6-22.2)	21.4 (20.5-22.4)	21.1 (19.4-22.8)	0.7170
Walking environment	35.2 (34.2-36.3)	35.1 (33.9-36.3)	35.8 (33.5-38.3)	0.5464
Availability of healthy food	12.4 (11.9-12.9)	12.6 (12.0-13.2)	11.7 (10.4-13.0)	0.1477
Safety	9.0 (8.5-9.5)	9.2 (8.6-9.8)	8.4 (7.4-9.4)	0.1974
Violence	12.1 (11.6-12.7)	12.2 (11.6-12.9)	11.8 (10.5-13.1)	0.5227
Social cohesion	13.5 (12.9-14.1)	13.4 (12.8-14.1)	13.8 (12.5-15.1)	0.5996
Activities with neighbors	17.6 (17.0-18.3)	17.7 (16.9-18.4)	17.6 (16.2-18.9)	0.9092
<b>Total PNES score</b>	<b>121.3 (117.8-124.8)</b>	<b>121.6 (117.7-125.6)</b>	<b>120.2 (112.5-127.9)</b>	<b>0.7352</b>

Table 4.2 contains two-tailed t-test for comparison of means for continuous variables, and chi-squared test for comparison of proportions of categorical variables. Bolded p-values are statistically significant.

† Variable included in FRS algorithm.

Table 4.3: Multivariable linear regression models of neighborhood perception on CVD risk

Model 1						Model 2					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
PNES total	-0.01	0.03	-0.43	0.665	1.04	Aesthetic quality	-0.07	0.13	-0.50	0.621	1.09
CD4 cell count	0.003	0.002	1.47	0.145	1.05	CD4 cell count	0.003	0.002	1.50	0.135	1.11
Black v other race	-4.69	1.61	-1.01	<b>0.004</b>	1.05	Black v other race	-4.69	1.61	-2.92	<b>0.004</b>	1.05
Alcohol use	-4.03	1.31	-3.08	<b>0.003</b>	1.01	Alcohol use	-4.00	1.31	-3.05	<b>0.003</b>	1.02
Drug use	-1.62	1.61	-1.01	0.315	1.08	Drug use	-1.61	1.61	-1.01	0.316	1.08
Model 3						Model 4					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Walkability	0.01	0.10	0.11	0.911	1.05	Access to affordable food	-0.26	0.20	-1.29	0.198	1.03
CD4 cell count	0.003	0.002	1.40	0.164	1.05	CD4 cell count	0.003	0.002	1.42	0.156	1.04
Black v other race	-4.63	1.61	-2.89	<b>0.004</b>	1.05	Black v other race	-5.00	1.62	-3.09	<b>0.002</b>	1.08
Alcohol use	-4.14	1.31	-3.09	<b>0.002</b>	1.01	Alcohol use	-4.07	1.30	-3.12	<b>0.002</b>	1.01
Drug use	-1.53	1.62	-0.94	0.346	1.09	Drug use	-1.60	1.60	-1.01	0.316	1.07
Model 5						Model 6					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Safety	-0.30	0.21	-1.42	0.157	1.00	Violence	-0.15	0.19	-0.80	0.426	1.05
CD4 cell count	0.003	0.002	1.38	0.170	1.04	CD4 cell count	0.003	0.002	1.52	0.130	1.06
Black v other race	-4.76	1.60	-2.98	<b>0.003</b>	1.05	Black v other race	-4.76	1.61	-2.96	<b>0.004</b>	1.06
Alcohol use	-4.06	1.30	-3.12	<b>0.002</b>	1.01	Alcohol use	-4.00	1.31	-3.05	<b>0.003</b>	1.02
Drug use	-1.53	1.59	-0.96	0.338	1.07	Drug use	-1.65	1.61	-1.03	0.304	1.08
Model 7						Model 8					
Variable	Coef.	SE	t	P-value	VIF	Variable	Coef.	SE	t	P-value	VIF
Social cohesion	0.10	0.18	0.57	0.570	1.03	Activities with neighbors	0.07	0.17	0.40	0.690	1.00
CD4 cell count	0.003	0.002	1.38	0.169	1.04	CD4 cell count	0.003	0.002	1.44	0.151	1.04
Black v other race	-4.59	1.61	-2.86	<b>0.005</b>	1.05	Black v other race	-4.62	1.60	-2.88	<b>0.005</b>	1.05
Alcohol use	-4.02	1.31	-3.07	<b>0.003</b>	1.01	Alcohol use	-4.04	1.31	-3.08	<b>0.002</b>	1.01
Drug use	-1.46	1.61	-0.91	0.367	1.08	Drug use	-1.56	1.60	-0.97	0.333	1.07

Table 4.3 contains full linear regression models for the PNES and subscales with the FRS.

*Measure 4.1: Perceptions of Neighborhood Environment Scale domains and items  
(Echeverria et al., 2004)*

### **Perception of Neighborhood Environments Scale**

*Scale and subscale score ranges are described below. Response scores in which the scoring is reversed are indicated with an (R). Possible range of scores is 36 to 156, with the higher scores indicating positive perception of neighborhood.*

#### Aesthetic quality

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

- A1. There is a lot of trash and litter on the street in my neighborhood
- A2. There is a lot of noise in my neighborhood
- A3. In my neighborhood the buildings and homes are well-maintained (Reversed (R))
- A4. The buildings and houses in my neighborhood are interesting (R)
- A5. My neighborhood is attractive (R)
- A6. There are interesting things to do in my neighborhood (R)

#### Walking environment/Physical activity

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

- B1. My neighborhood offers many opportunities to be physically active (R)
- B2. Local sports clubs and other facilities in my neighborhood offer many opportunities to get exercise (R)
- B3. It is pleasant to walk in my neighborhood (R)
- B4. The trees in my neighborhood provide enough shade (R)
- B5. In my neighborhood it is easy to walk places (R)
- B6. I often see other people walking in my neighborhood (R)

B7. I often see other people exercising (for example, jogging, bicycling, and playing sports) in my neighborhood (R)

B8. My neighborhood has heavy traffic

B9. There are busy roads to cross when out for walks in my neighborhood

B10. In my neighborhood, the streets and sidewalks are in good condition (R)

#### Availability of healthy food

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

C1. A large selection of fresh fruits and vegetables is available in my neighborhood (R)

C2. The fresh fruits and vegetables in my neighborhood are of high quality (R)

C3. A large selection of low-fat products is available in my neighborhood (R)

C4. There are many opportunities to purchase fast foods in my neighborhood

#### Safety

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

D1. I feel safe walking in my neighborhood, day or night (R)

D2. Violence is not a problem in my neighborhood (R)

D3. My neighborhood is safe from crime (R)

#### Violence

*Scale is 1-4, often to never, with 4 being most positive perception.*

E1. During the past 6 months, how often was there a fight in your neighborhood in which a weapon was used?

E2. During the past 6 months, how often were there gang fights in your neighborhood?

E3. During the past 6 months, how often was there a sexual assault or rape in your neighborhood?



E4. During the past 6 months, how often was there a robbery or mugging in your neighborhood?

Social cohesion

*Scale is 1-5, strongly agree to strongly disagree with 5 being most positive perception.*

F1. People around here are willing to help their neighbors (R)

F2. People in my neighborhood generally get along with each other (R)

F3. People in my neighborhood can be trusted (R)

F4. People in my neighborhood share the same values (R)

Activities with Neighbors

*Scale is 1-4, often to never, with 4 being most positive perception.*

G1. About how often do you and people in your neighborhood do favors for each other?

By favors, we mean such things as watching each other's children, helping with shopping, lending garden or house tools, and other small acts of kindness (R)

G2. When a neighbor is not at home or on vacation, how often do you and other neighbors watch over their property? (R)

G3. How often do you and other people in the neighborhood ask each other for advice about personal things such as child-rearing or job openings? (R)

G4. How often do you and people in your neighborhood have parties or other get-togethers where other people in the neighborhood are invited? (R)

G5. How often do you and other people in your neighborhood visit in each other's homes or speak with each other on the street? (R)

*Measure 4.2: Center for Epidemiological Studies Depression Scale (CES-D)*  
**Center for Epidemiologic Studies Depression Scale (CES-D), NIMH**

*Scale is 0-3. Responses include a score of zero if rarely or none of the time (less than 1 day), a score of one if some or a little of the time (1-2 days), a score of two if occasionally or a moderate amount of time (3-4 days), and a score of three if most or all of the time (5-7 days) per question. The scoring of positive items is reversed. Possible range of scores is zero to 60, with the higher scores indicating the presence of more symptomatology.*

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

1. I was bothered by things that usually don't bother me.
2. I did not feel like eating; my appetite was poor.
3. I felt that I could not shake off the blues even with help from my family or friends.
4. I felt I was just as good as other people. (R)
5. I had trouble keeping my mind on what I was doing.
6. I felt depressed.
7. I felt that everything I did was an effort.
8. I felt hopeful about the future. (R)
9. I thought my life had been a failure.
10. I felt fearful.

11. My sleep was restless.
12. I was happy. (R)
13. I talked less than usual.
14. I felt lonely.
15. People were unfriendly.
16. I enjoyed life. (R)
17. I had crying spells.
18. I felt sad.
19. I felt that people dislike me.
20. I could not get “going.”

*Measure 4.3: Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1994)*

### **Perceived Stress Scale**

*Scale is 0-4. Responses to stress over a one-month period include a score of zero if “never”, score of one if “almost never”, a score of two if “sometimes”, a score of three if “fairly often”, and a score of four if “very often” per question. The range of scores is zero to 40, with the higher scores indicating the presence of more symptomatology*

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

1. In the last month, how often have you been upset because of something that happened unexpectedly?
2. In the last month, how often have you felt that you were unable to control the important things in your life?
3. In the last month, how often have you felt nervous and “stressed”?
4. In the last month, how often have you felt confident about your ability to handle your personal problems?
5. In the last month, how often have you felt that things were going your way?
6. In the last month, how often have you found that you could not cope with all the things that you had to do?
7. In the last month, how often have you been able to control irritations in your life?
8. In the last month, how often have you felt that you were on top of things?

9. In the last month, how often have you been angered because of things that were outside of your control?

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

*Measure 4.4: Framingham Risk Score (FRS) 10-year risk calculation (D'Agostino et al., 2008)*

Calculation for risk points:

$$\text{Riskfactors}^1 = (\ln(\text{age}) * 2.32888) + (\ln(\text{total cholesterol}) * 1.20904) - (\ln(\text{HDL cholesterol}) * 0.70833) + (\ln(\text{systolic BP}) * 2.76157) + (\text{cigarette smoking} * 0.52873) + (\text{diabetes} * 0.6915)$$

$$\text{Riskfactors}^2 = (\ln(\text{age}) * 2.32888) + (\ln(\text{total cholesterol}) * 1.20904) - (\ln(\text{HDL cholesterol}) * 0.70833) + (\ln(\text{systolic BP}) * 2.82263) + (\text{cigarette smoking} * 0.52873) + (\text{diabetes} * 0.6915)$$

Calculation for risk percentage:

$$\text{Risk} = 100 * (1 - 0.95012^{e(\text{Riskfactors} - 26.1931)})$$

<sup>1</sup>-Untreated for hypertension or does not take antihypertensive medications

<sup>2</sup>-Treated for hypertension or takes antihypertensive medications

## CHAPTER 5

### Summary of Findings, Integration, and Discussion

The purpose of this dissertation study was to examine the relationships between neighborhood environment, chronic stress, and CVD risk among WLWH. First, I developed a conceptual framework of CVD risk as it is associated with neighborhood environments among WLWH. Based on the narrative review of the literature provided in this chapter, it became clear that direct examination of specific attributes of neighborhood environments must be examined in their associations with chronic stress. Therefore, I examined the associations between neighborhood environment and chronic stress among WLWH via secondary analysis of data collected in the Chicago WIHS study in 2012. I did not observe significant associations between perception of neighborhood environment and chronic stress measures. I also examined the associations between neighborhood environment and CVD risk among WLWH in this sample. We sought to further explore the mediating relationship of chronic stress on the relationship between neighborhood perception and CVD risk among WLWH in support of our conceptual framework. For this chapter of this dissertation study, the following section provides a summary of the major findings of each of these sections and contextualize these findings in relation to clinical practice, policy, and research.

### Major Findings

#### *Chapter 2: A conceptual model of neighborhood factors associated with chronic stress and CVD among women living with HIV*

The purpose of this chapter was to describe and provide scientific evidence for a conceptual framework of neighborhood and community factors that contribute to CVD

among women aging with HIV and fulfilled the first aim of this dissertation. The conceptual framework that I developed is situation-specific theory and was designed to specifically focus on the neighborhood contextual factors that influence cardiovascular health of WLWH. In order to describe the posited relationships between constructs of this conceptual model, I completed a synthesis of existing theory and research. Via narrative review, this conceptual framework integrated literature that has suggested the associations of aspects of neighborhoods that are associated with health behaviors, stress, and inflammation among WLWH related to a theory overall posits that the interaction between individual and neighborhood environment, over time, can contribute to individual cardiovascular health outcomes and disease risk.

My conceptualization of neighborhood and community in this model recognizes specific aspects of physical space, location, and meaning of neighborhoods as dynamic and defined by individuals. I characterized the aspects of neighborhood environments associated with CVD among WLWH as either built and physical factors of neighborhoods or social and relational factors of neighborhoods. Built and physical factors of neighborhoods associated with CVD include the structures and objects that influence health and wellness (Macintyre, Ellaway, & Cummins, 2002). Resources and services allocated to neighborhoods that individuals utilize for daily living (e.g. food, water, utilities) that are embedded in the physical and build neighborhood environment have been linked to CVD. I further conceptualized as social systems as adaptive to the needs of the community (Alinsky, 1972), have specific functions, including political, economic, and relational functions. Neighborhood social and relational functions meet the demands of their residents in reaction to issues that impact them in a specific time and



place (Alinsky, 1972; Sen, 2003). Lastly, I described that the racial and ethnic background of inhabitants is linked to the social and relational functions and dynamics of neighborhoods. Various non-White communities are impacted by systems of oppression (e.g. racism, sexism, etc.), and these systems influence relationships and social interactions of residents within their neighborhoods (Chávez, Minkler, Wallerstein, & Spencer, 2007; Rivera & Erlich, 2001).

I defined health resources and services as the resources for daily living, health maintenance, and variety of services that are associated with cardiovascular functioning. I later described the influence of neighborhood environmental context on HIV-positive women related to CVD risk. Within this conceptual framework, I argued that decreased health resources and services, negative or reduced social interactions and networks, and limited transportation and movement options at the neighborhood level, can separately or in combination, contribute to CVD as these aspects of neighborhood environments influence health behaviors. I further argued that individuals in neighborhoods with neighborhood socioeconomic deprivation, concentrated incarceration, increased crime and violence, fewer health care services, reduced transportation options, less affordable food options, less walkable neighborhoods have an increased risk for CVD (Diez-Roux et al., 2001; Diez-Roux et al., 1997; Kim et al., 2010; Lee et al., 2014; Lugalia-Hollon & Cooper, 2018; Nazmi et al., 2010; Nazmi & Victora, 2007; Wildeman & Wang, 2017).

Further, I discussed individual factors that contribute to CVD pathogenesis include a variety of characteristics that uniquely contribute to CVD among WLWH. Within this model, I described two categorizations of individual factors that are associated with chronic stress and CVDs among WLWH. First, I discussed general

factors, which include behaviors, personal characteristics, and experiences that are commonly regarded as factors for CVD within HIV-negative persons. Secondly, I described various HIV-related factors associated with CVDs, which include specific aspects of HIV that influence CVD. Within individuals, general and HIV-related risk factors contribute to increased stress and inflammation that, in turn, advances aging. These processes, over time, contribute to chronic stress, inflammation, and thereby CVD and associated health problems among women with HIV. The presented conceptual framework sought to promote investigation into causal mechanisms that contribute to CVD incidence among HIV-positive women such that interventions can be developed to reduce health disparities and promote health equity.

### ***Chapter 3: Associations of neighborhood perception and chronic stress among women with HIV***

The purpose of this chapter was to examine the associations between perception of neighborhood and environment, and chronic stress among WLWH in fulfillment of our second aim of this dissertation study. I hypothesize that decreased (poor) perception of neighborhood environment will be associated with increased chronic stress.

To achieve this aim, I conducted a secondary analysis of data from the Women's Interagency HIV Study (WIHS). This longitudinal, prospective, multisite study has examined the natural progression of HIV among women since its initiation in 1993. The WIHS study also serves as a leading source of investigation into reproductive health, clinical outcomes (such as cardiovascular disease, diabetes, and neurocognitive disorders), and the efficacy of antiretroviral therapies (WIHS Data Management and Analysis Center, 2017). I utilized data from several WIHS sub studies that were

conducted exclusively at the Chicago WIHS, including the psychoneuroimmunology and hair cortisol sub studies. I utilized the Perceived Stress Scale (PSS) 10-item measure and hair cortisol concentration (HCC) as measures of chronic stress (dependent variable). Additionally, I utilized the Perception of Neighborhood Environments Scale (PNES) and subscales as measures of neighborhood environment.

In total, 147 HIV-positive women in the Chicago WIHS were included in this study from study visits in 2012. A distinct proportion of the women in this sample received at most a high school education (57.8%), were not employed at the time of this study (70.8%) and had previous lifetime history of incarceration (40.8%). Most of women in this sample also reported cigarette smoking (70.8%), and a notable proportion injection drug use within the past five years (24.1%). We observed statistically significant differences ( $p=0.0145$ ) in level of perceived stress and CD4 cell percent, with HIV-positive women with high perceived stress having significantly greater CD4 cell percentiles 32.9%, 95% CI: 30.8-34.9%) as compared to HIV-positive women in the low stress group (27.3%, 95% CI: 23.2-31.5%). I did not observe any other significant differences in various health characteristics based on high or low chronic stress (PSS) values among WLWH. I also did not observe statistically significant associations between PNES and subscales and both PSS and HCC scores in these analyses when testing our hypotheses. However, we observed a consistent significant association of depression, and high v low income with PSS scores across all regression models. In models examining the associations between neighborhood perception and HCC levels, Black v other race was significantly associated with log-transformed HCC levels in models of two neighborhood perception subscales- social cohesion and activities with neighbors

subscales. I found that in a model examining associations between social cohesion and HCC, women who identified as Black race had a 22.03 unit increase in HCC levels when compared to women of other races (SE: 4.12,  $p=0.035$ ). This study contributes to a broader focus of health research that highlights the importance of neighborhood environment in the health and wellness of WLWH as they age by directly examining neighborhood-level characteristics as evaluated by WLWH. Future studies must explore the specific experiences and perspectives of WLWH regarding their neighborhood, stress experience, and HIV.

#### ***Chapter 4: The associations between neighborhood environment and CVD risk among women living with HIV***

To achieve the third aim of this study, the purpose of this chapter was to examine the associations between various aspects of neighborhood environment with CVD risk among WLWH. I hypothesized that decreased (poorer) perception of neighborhood environment would be associated with increased CVD risk. This study also utilized data collected from Chicago WIHS and completed a secondary analysis of data collected in 2012. This study utilized data collected from the cardiovascular disease and neighborhood environment sub studies. A total of 147 Chicago WIHS participants met these criteria and were included study.

As similarly reported in chapter 3, the mean age of the sample was 47.2 (95% CI: 45.8-48.6), 76.9% were African American, and 15.0% were White, Non-Hispanic. Many WLWH included in this study received at most a high school education (57.8%), were not employed at the time of this study (70.8%) and had previous history of incarceration in their lifetime (40.8%). CVD risk as measured by the FRS for this sample is 7.56%

(95% CI: 6.23%- 8.89%, range: 0.34%-49.89%). A total of 113 (76.9%) WLWH in Chicago WIHS were categorized as “low” CVD risk and 31 (21.1%) were categorized as “intermediate/high” CVD risk. I observed a disproportionate number of White, Non-Hispanic women with intermediate/high FRS (n=9, 28.1%) relative to their overall representation in this sample (n=22, 15.0%), and this proportion was statistically significant (p=0.019). However, African American women represented the largest racial/ethnic group in this study (n=113, 76.9%) and in the intermediate/high risk categorization (n=20, 62.5%). I observed significant differences in reported alcohol consumption and FRS score, as women categorized in the intermediate/high FRS group reported alcohol significantly less consumption (n=7, 21.9%) than women in the low FRS group (n=56, 48.7%, p=0.007). I did not observe any other differences in demographic, health, or neighborhood measures among low or intermediate/high FRS groups.

. In the regression models developed in this analysis, I did not observe significant differences in reported aspects of neighborhood environment of the PNES total scale and subscales among WLWH in this study. Across multivariable regression models, Black v other race was significantly associated with FRS in models with the PNES and subscales. My model examining the association of PNES total score and FRS, individuals with Black race demonstrated a 4.69 unit decrease in FRS when compared to individuals of other races (SE: 1.61, p=0.004). Additionally, reported alcohol consumption was significantly associated with FRS in linear regression analyses, as women who reported alcohol consumption since their last WIHS visit had a 4.03 unit decrease in FRS as compared to women who did not report alcohol consumption (SE: 1.31, p=0.003). I did not observe significant associations between perception of neighborhood and CVD risk

among WLWH in the Chicago WIHS study. Given the lack of significant associations between either CVD risk or chronic stress and neighborhood perception, I did not meet the criteria to conduct a mediation test to examine the extent to which chronic stress mediates the relationship between neighborhood perception and CVD risk. Despite this, my study highlights the importance of disparity of CVD risk that impacts African American WLWH relative to other racial and ethnic groups. This study supports the development of individual, neighborhood, and policy interventions that can support WLWH and encourage cardiovascular health and wellness as they age.

### **Study Limitations**

There were several limitations in Chapter 2, which discussed development of the conceptual framework of neighborhood and individual factors associated with CVD among WLWH. First, I conducted a narrative review of the literature review used to synthesize theory and research for the conceptual model. By design, narrative review strategy is difficult to reproduce and does not critically evaluate the literature or analyze evidence across studies (Green et al., 2006). I selected this review method due to the sparse literature regarding the direct examination neighborhood and community associations with health outcomes among individuals living with HIV. Therefore, further reviews of the literature are needed to evaluate the strength and quality of the evidence that are reproducible and have transparent search strategies. Additionally, this conceptual model is a disease-specific model that focuses on risk. Like many theories that focus on disease risk, many of the key concepts included in this theory are related to pathology and considered as deficits-focused (Aronowitz, 2015). Importantly, the lives and wellness of WLWH are complex, and they are often resilient to difficulties despite inequity and

various health and life challenges (Dale et al., 2014). Continued research is needed to examine resiliency and strengths and their relationship to health outcomes among WLWH. Thereby, the strength and resilience of WLWH can be supported by clinical and policy interventions to promote cardiovascular health and wellness as defined by the women themselves.

For Chapter 3 of this dissertation, in which I assessed the associations between chronic stress and neighborhood environment, there are several limitations. First, data for this study were collected in 2012, and it is possible that neighborhood perceptions and characteristics have changed in the time since data collection. Further, the data collected within WIHS were analyzed at one cross-section. Since the effects of neighborhood environments are cumulative, I was unable to examine the chronicity of neighborhood environment associations with stress. Additionally, there was a considerable difference between the number of individuals that provided PSS responses (n=147) to individuals that provided HCC samples (n=55), making it difficult to compare stress between measures. Hair can be a source of pride, identity, and cultural expression among women. Barriers to hair sample collection includes use of wigs and extensions, religious ties to hair covering, or other reasons for refusal. I believe that specific examinations of the barriers to hair cortisol sample collections among women are needed to determine best practices for HCC use in studies among women.

Lastly the analyses conducted in Chapter 4 include notable limitations. First, the data for this study were also collected in 2012. Given the complexity and dynamic nature of neighborhoods as well as assessment of CVD risk, these associations may not be consistent with the passage of time. Additionally, the Chicago WIHS sample is largely

African American/Black. While this is representative of the local HIV prevalence to Chicago, comparisons by race/ethnicity may be impacted by the homogeneity of the sample. Additionally, this study utilized the FRS 10-year algorithm as a measure of CVD risk. The HIV-positive women in this study were young, with a mean age of 47.2 (IQR: 41.5-53.4). Typically, risk factors for CVD that are included in the FRS, such as elevated blood pressure, cholesterol, and diabetes increase in prevalence as individuals age, particularly beyond age 50 (Lloyd-Jones et al., 2006). Therefore, it is likely that WLWH in this sample would have increased risk attributed to the onset of CVD comorbidities and increased age over time. While the FRS is widely used in research and clinical practice to characterize CVD risk, several studies have noted that the FRS underestimated CVD risk in women and among individuals with HIV regardless of sex/gender identity (Cook et al., 2012; Schwartz et al., 2012; Serrano-Villar et al., 2014). Future studies are needed to compare the calibration of alternative CVD risk algorithms, such as the Reynold's Risk Score and the DAD Score (Ridker et al., 2007; Serrano-Villar et al., 2014).

### **Implications**

This study informs several areas of clinical practice. First, this study underscores the importance of providing primary care for individuals with HIV for the prevention of CVD and other diseases associated with aging. Given that HIV is now managed as a chronic illness with the advancement of HIV treatment modalities, healthcare professionals, researchers, and policy makers have begun to shift interventions for HIV management to focus on the development of CVD and other chronic non-communicable illnesses in this population. Therefore, it is critical that individuals with HIV receive



support and have access to interventions that promote cardiovascular health, including smoking cessation, blood pressure and blood glucose management, statin therapy, depression treatment, and other healthcare services.

As this study focuses on neighborhoods, this research can inform several policy and global health interventions. First and foremost, this study underscores the need for policy interventions that address neighborhood deprivation and poverty among WLWH. Importantly, successful policy interventions must be designed in order to empower WLWH within their communities. Given the high prevalence of incarceration among WLWH in this study, our studies support the need for policy interventions to reduce concentrated punishment, mass incarceration, and criminalization of HIV. Furthermore, investments in neighborhoods and communities, such as community health promotion programs, urban greening, and public space maintenance, can be implemented to impact WLWH and their entire communities. Further, federal and state level policies, such as increased funding for Supplemental Nutrition Assistance Programs (SNAP), increased funding for housing choice vouchers, and other interventions targeted at addressing poverty.

Globally, women disproportionately are impacted by HIV. As of 2017, an estimated 18.2 million women over 15 years-old around the world are living with HIV (UNAIDS, 2018). In sub-Saharan Africa, the region that is most impacted by HIV globally, women account for a quarter of HIV infections despite account for only 10% of the population (UNAIDS, 2018). As women with HIV age globally, it is critical to examine the associations with a variety of contextual and behavioral factors with CVD. For instance, neighborhood and community factors vary widely, and the aspects of

neighborhood environments that are salient in the United States may not be as important in rural settings. Exploring the distinct environments in relation to CVD among WLWH can support the development of clinical and policy interventions to prevent CVD globally.

Finally, this study can inform various programs of research. First, this study highlights the continued need for adequate representation of women in CVD and HIV research. Exploring within-population correlates with health outcomes is critical to developing health interventions that are focused on the unique needs of WLWH. Secondly, this study utilized hair cortisol as a measure of chronic stress. As this tool is relatively new in regard to human subjects research, examinations into the barriers and facilitators of hair sampling are needed when studying diverse populations.

As previously stated, we did not observe significant associations between perception of neighborhood, stress, and CVD risk as posited in the theoretical framework (Chapter 2). Study limitations, which include cross-sectional analysis, lack of heterogeneity in the data reduce the ability to support the theoretical relationships posited in the conceptual framework. More research is needed to examine these associations longitudinally and in varying samples to explore the associations between neighborhood environment, stress, and CVD in women with HIV.

Furthermore, conceptual relationships posited by the framework (Chapter 2) do not describe the affective, mood, and cognitive factors that influence neighborhood environment appraisal, stress, and health behaviors. Therefore, future research will be conducted with a modified conceptual model (Figure 1) to examine the associations between neighborhood environment, stress, and CVD among WLWH. In short, I intend

to further develop a conceptual model of CVD among WLWH as it relates to their neighborhood environment by better describing individual factors that may contribute to CVD over time. As described in Figure 1, these will include background factors (e.g. HIV, demographics, health history, mental health), perceptions (e.g. neighborhood perception, depression, stress and anxiety, internalized stigma), health behaviors (e.g. diet, exercise, medication use, cigarette smoking), and cardiovascular health indicators (e.g. metabolic function, physical assessment, HIV progression, and inflammation).

As this study did not demonstrate associations between neighborhood environment, stress, and CVD risk, further research is needed to examine the processes by which neighborhood environment influences CVD among WLWH. As this study noted, depression was associated with chronic stress among women in the WIHS study. I believe that further investigations are needed to examine the relationship between neighborhood perception, depression, and CVD risk. It is possible that depression serves to mediate the relationship between neighborhood perception and CVD risk, and therefore depression could serve as a target for health interventions that could reduce CVD risk.

Additionally, this study investigated CVD risk using the FRS 10-year algorithm among WLWH. As this algorithm for CVD risk is widely used, it is one of many CVD risk algorithms. Therefore, further research studies must examine the calibration of various CVD risk algorithms for their effectiveness of predicting outcomes among WLWH. Overall, these areas of research are important for investigating the associations of neighborhood environment and health outcomes among WLWH. As these women

continue to age in place, future studies must continue to explore geospatial determinants of health in this population as a means of promoting health equity.

### **Conclusion**

This dissertation study sought to examine the relationships between neighborhood environment, chronic stress, and CVD risk as they impact HIV-positive women in support of a conceptual framework of CVD risk among WLWH as related to neighborhood environments. We did not observe significant associations between neighborhood perception, stress, and CVD risk in this study. Despite this, our findings underscore the importance of depression, poverty, and race among HIV-positive women and their experience of stress and CVD risk. We believe that these findings can inform future research, policies, and healthcare interventions of neighborhood environments and chronic stress to promote cardiovascular health among WLWH.

## References

- Alinsky, S. (1972). *Rules for radicals: A political primer for practical radicals*: New York: Random House.
- Aronowitz, R. (2015). *Risky medicine: our quest to cure fear and uncertainty*: University of Chicago Press.
- Chávez, V., Minkler, M., Wallerstein, N., & Spencer, M. S. (2007). Community organizing for health and social justice. *Prevention is primary: Strategies for community well-being*, 95-120.
- Cook, N. R., Paynter, N. P., Eaton, C. B., Manson, J. E., Martin, L. W., Robinson, J. G., . . . Ridker, P. M. (2012). Comparison of the Framingham and Reynolds Risk scores for global cardiovascular risk prediction in the multiethnic Women's Health Initiative. *Circulation*, 125(14), 1748-1756.
- Dale, S. K., Cohen, M. H., Kelso, G. A., Cruise, R. C., Weber, K. M., Watson, C., . . . Brody, L. R. (2014). Resilience among women with HIV: Impact of silencing the self and socioeconomic factors. *Sex roles*, 70(5-6), 221-231.
- Diez-Roux, A. V., Merkin, S. S., Arnett, D., Chambless, L., Massing, M., Nieto, F. J., . . . Watson, R. L. (2001). Neighborhood of residence and incidence of coronary heart disease. *New England Journal of Medicine*, 345(2), 99-106.
- Diez-Roux, A. V., Nieto, F. J., Muntaner, C., Tyroler, H. A., Comstock, G. W., Shahar, E., . . . Szklo, M. (1997). Neighborhood environments and coronary heart disease: a multilevel analysis. *American journal of epidemiology*, 146(1), 48-63.

- Green, B. N., Johnson, C. D., & Adams, A. (2006). Writing narrative literature reviews for peer-reviewed journals: secrets of the trade. *Journal of chiropractic medicine*, 5(3), 101-117.
- Kim, D., Diez Roux, A. V., Kiefe, C. I., Kawachi, I., & Liu, K. (2010). Do neighborhood socioeconomic deprivation and low social cohesion predict coronary calcification? The CARDIA study. *American journal of epidemiology*, 172(3), 288-298.
- Lee, H., Wildeman, C., Wang, E. A., Matusko, N., & Jackson, J. S. (2014). A heavy burden: the cardiovascular health consequences of having a family member incarcerated. *American journal of public health*, 104(3), 421-427.
- Lloyd-Jones, D. M., Leip, E. P., Larson, M. G., d'Agostino, R. B., Beiser, A., Wilson, P., . . . Levy, D. (2006). Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation*, 113(6), 791-798.
- Lugalia-Hollon, R., & Cooper, D. (2018). *The War on Neighborhoods: Policing, Prison, and Punishment in a Divided City*: Beacon Press.
- Macintyre, S., Ellaway, A., & Cummins, S. (2002). Place effects on health: how can we conceptualise, operationalise and measure them? *Social science & medicine*, 55(1), 125-139.
- Nazmi, A., Roux, A. D., Ranjit, N., Seeman, T. E., & Jenny, N. S. (2010). Cross-sectional and longitudinal associations of neighborhood characteristics with inflammatory markers: findings from the multi-ethnic study of atherosclerosis. *Health & place*, 16(6), 1104-1112.

- Nazmi, A., & Victora, C. G. (2007). Socioeconomic and racial/ethnic differentials of C-reactive protein levels: a systematic review of population-based studies. *BMC public health*, 7(1), 212.
- Ridker, P. M., Buring, J. E., Rifai, N., & Cook, N. R. (2007). Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. *Jama*, 297(6), 611-619.
- Rivera, F. G., & Erlich, J. L. (2001). An option assessment framework for organizing in emerging minority communities. *JE Tropman, JL Erlich & J. Rothman, Tactics and techniques of community intervention (pp169-177)*. Itasca, IL: FE Peacock Publishers.
- Schwartz, R. M., Mansoor, A., Wilson, T. E., Anastos, K., Everson-Rose, S. A., Golub, E. T., . . . Lazar, J. (2012). Chronic depressive symptoms and Framingham coronary risk in HIV-infected and HIV-uninfected women. *AIDS care*, 24(3), 394-403.
- Sen, R. (2003). *Stir it up: Lessons in community organizing and advocacy* (Vol. 16): John Wiley & Sons.
- Serrano-Villar, S., Estrada, V., Gomez-Garre, D., Ávila, M., Fuentes-Ferrer, M., San, R. J., . . . Fernández-Cruz, A. (2014). Diagnosis of subclinical atherosclerosis in HIV-infected patients: higher accuracy of the D: A: D risk equation over Framingham and SCORE algorithms. *European journal of preventive cardiology*, 21(6), 739-748.
- WIHS Data Management and Analysis Center. (2017). Our Study: The Women's Interagency HIV Study. Retrieved from <https://statepi.jhsph.edu/wihs/wordpress/>

Wildeman, C., & Wang, E. A. (2017). Mass incarceration, public health, and widening inequality in the USA. *The Lancet*, 389(10077), 1464-1474.