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Associations between neighborhood vulnerabilities and neuropsychiatric outcomes during the COVID-19 pandemic among a diverse cohort of people aging with HIV

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Associations between neighborhood vulnerabilities and neuropsychiatric outcomes during the COVID-19 pandemic among a diverse cohort of people aging with HIV

A dissertation submitted in partial satisfaction of the requirements for the degree of Doctor of Philosophy

in

Clinical Psychology

by

Lily Kamalyan

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2024

The dissertation of Lily Kamalyan is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

Chair

University of California San Diego

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2024

DEDICATION

To my grandparents, who, either throughout long and complex lives or before an early and sorrowful passing, supported their family's needs during dark and trying times, expressed unwavering pride in their first grandchild's ambitions, grounded me in my lineage, and most of all, provided a sense of purpose and meaning to my work.

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ABSTRACT OF THE DISSERTATION

Associations between neighborhood vulnerabilities and neuropsychiatric outcomes during the COVID-19 pandemic among a diverse cohort of people aging with HIV

by

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Doctoral of Philosophy in Clinical Psychology

University of California, San Diego, 2024

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Rationale: Neighborhoods adversely impact neurocognitive impairment and depression among older adults without HIV. These associations are unknown among diverse older PWH, who have higher rates of neuropsychiatric outcomes. Negative repercussions of COVID-19 disproportionally impacted vulnerable communities. We aimed to 1) examine associations between neighborhood characteristics and neurocognitive decline and worsened mood during the COVID-19 pandemic among older PWH, and 2) determine if the neighborhood impact of COVID-19, as a severe community stressor, moderates these relationships.

Design: Participants were 180 PWH 50+ years, enrolled in observational studies at the HIV Neurobehavioral Research Center. Seventy-nine completed neuropsychiatric assessments at two time-points: (1) March 2019-March 2020; and (2) March 2021-June 2022. Negative change in global mean scaled scores (GSS) reflected neurocognitive decline. Negative change in the Medical Outcomes Study HIV Health Survey Mental Health Summary T-scores (MSS) indicated worsened mood. Exploratory factor analyses of publicly available census and satellite data created ‘Sociodemographic’ ‘Economic’ and ‘Undeveloped’ neighborhood factors. Cumulative COVID-19 cases rates per zip code reflected the neighborhood impact of COVID-19. Participant’s home addresses were geocoded and linked to neighborhood data. Multivariable linear regression models investigated whether neighborhood factors were related to changes in GSS and MSS, and the moderating effect of COVID-19 case rates.

Results: Average change in GSS was 0.05 (SD=0.99) scaled scores. Average MSS change was -1.76 (SD=6.91) T-scores. The average percent of COVID-19 cases was 23%. ‘Sociodemographic,’ ‘Economic,’ and ‘Undeveloped’ factors were not related to significantly greater neurocognitive decline or worsened mood over time (ps>.05). There was no significant moderating effect of COVID-19 cases on cognitive or emotional decline (ps>.05). Exploratory analyses suggested that living in neighborhoods with greater crowded households was significantly related to decline in MSS (b=-0.45, p=.04). Pooled estimates after multiple imputation procedures did not uphold this finding (b=-0.12, p=.49).

Conclusions: Neighborhood features did not relate to neurocognitive or emotional change among older diverse PWH during a historically stressful time. Lack of substantial change may have contributed to null findings. Additional work with larger samples at risk for neuropsychiatric decline may elucidate how heterogenous environmental exposures may lead to positive and negative health outcomes in specific populations.

1. INTRODUCTION

Due to the advent of combination antiretroviral therapy (ART), people living with HIV (PWH) in the United States are living longer. Over 50% of PWH are over the age of 50, a number projected to continue increasing (Centers for Disease Control [CDC], 2018). Despite reduced mortality (Heaton et al., 2011), neurocognitive impairment continues to be prevalent in HIV (Heaton et al., 2011; Marquine et al., 2018), occurring in 20-50% of PWH (Iudicello et al., 2019), with these rates increasing with older age (Y. Ding et al., 2017). HIV-associated neurocognitive impairment has been linked with difficulties in activities of daily living such as handling finances, multitasking, using the Internet (Heaton et al., 2004; Scott et al., 2011; Woods et al., 2017) and managing medications (Hinkin et al., 2002; Thames et al., 2011). Cross-sectional studies show elevated risk for neurocognitive impairment among some Latino/a/x/Hispanic (hereafter referred to as Latino) (Marquine et al., 2018; Rivera Mindt et al., 2008, 2014; Wojna et al., 2006) and non-Latino Black/African American (hereafter referred to as Black) PWH (Thompson et al., 2021; Vo et al., 2013; A. Winston et al., 2013) compared to non-Latino Whites (hereafter referred to as White) PWH, and two longitudinal studies among PWH have identified Latino ethnicity as a predictor of neurocognitive decline (Cross et al., 2013; Heaton et al., 2015; Watson et al., 2022).

PWH also have higher rates of psychiatric comorbidities (Bhatia & Munjal, 2014; Paolillo et al., 2020; Rooney et al., 2019) than those living without HIV. Reported rates of depression among PWH (37%) are estimated to be five times greater than that of the general population (7%; Rooney et al., 2019). The consequences of depression among PWH are multifaceted, including worsened quality of life, poor medication adherence, faster HIV disease progression, and mortality (Paolillo et al., 2020). These patterns are significantly more troubling among older PWH, who are more likely to live alone and are at risk of social isolation, which have bidirectional relationships with depressive symptoms (Coyle & Dugan, 2012; Kamalyan et al., 2020; Paolillo et al., 2018, 2020). Though the underlying reasons for poor neurocognitive and psychiatric outcomes among PWH, particularly in older age and among minoritized groups are yet to be determined, there is increasing recognition that neighborhood factors (defined broadly as economic, social, organizational, or physical aspects of the environment) play a key role in conferring risk of illness (Kahana et al., 2016).

Neighborhood vulnerabilities adversely impact neurocognitive (Besser et al., 2017; Diez Roux & Mair, 2010) and psychiatric outcomes (Alegría et al., 2014; Karriker-Jaffe et al., 2012; Kim, 2010; Ross, 2000) among older adults without HIV, and are linked to the development of Alzheimer's Disease and related disorders (Powell et al., 2020). Individuals living in more structurally disadvantaged neighborhoods, which have higher rates of poverty and unemployment, (Sallis et al., 2011) lower levels of education (Glymour & Manly, 2008), and increased air pollution (Kulick et al., 2020), are at higher risk of accelerated morbidity and mortality. Scant research exists on the impact of neighborhood vulnerabilities among PWH. Previous studies have focused on how these structural factors may be related to HIV risk behaviors, infection, incidence, and prevalence (Burke-Miller et al., 2016; Kahana et al., 2016; Latkin et al., 2013; Napravnik et al., 2006), rather than HIV-associated health outcomes. US neighborhoods were designed to be and largely remain racially segregated (Kovalchik et al., 2015; Rothstein, 2017; Yang et al., 2020), creating drastic differences in the structural and sociocultural quality of communities which in turn influence health disparities across the lifespan in the general population (Brondolo et al., 2009; Glymour & Manly, 2008; O'Brien et al., 2020; Yang et al., 2020). Less is known about how neighborhood determinants may impact the health of individuals at the intersection of aging, living with HIV, and dealing with historical oppression.

The COVID-19 pandemic disproportionately impacted minoritized groups (Chowkwanyun & Reed, 2020; Hooper et al., 2020; Lamb et al., 2020), and during containment efforts, confined them to neighborhoods (Ammar et al., 2020) with greater levels of structural vulnerabilities (Churchwell et al., 2020; Garcia et al., 2021; Krieger, 2020) while also reducing healthy coping strategies, such as outdoor leisure, physical exercise, and social connection, that may have helped outweigh the stressful consequences of the outbreak (Nicola et al., 2020; Sang et al., 2021). Higher rates of COVID-19 cases and deaths were documented among individuals from minoritized groups, lower socioeconomic status, crowded housing, and higher levels of segregation (Adhikari et al., 2020; Krieger, 2020; Lowe et al., 2021; Millett, Honermann, et al., 2020; Millett, Jones, et al., 2020; Ruprecht et al., 2021). Furthermore, in a national sample of US adults, the prevalence of depressive symptoms rose to be three times higher during COVID-19 as compared to before (Ettman et al., 2020). Aspects of the COVID-19 pandemic as well as its repercussions such as grief (Goveas & Shear, 2020), financial instability (Ettman et al., 2020a), and decreased access to psychological care (Purtle, 2020) may have disproportionately impacted the mental health of vulnerable communities.

Objective measures of neighborhood sociodemographic, economic, and physical characteristics are available through public data (*IPUMS USA*, 2021) and are standardized based on geographic region. These measures have been related to various health outcomes among people living without HIV (Karriker-Jaffe et al., 2012; Powell et al., 2020; Ross, 2000; Sallis et al., 2011; Soltero et al., 2015), though their associations with neuropsychiatric outcomes have not yet been investigated among PWH. The proposed study directly addresses a gap in the literature by relating objective metrics (i.e., geospatial indicators, public health data) of neighborhood vulnerabilities to comprehensive neurocognitive and psychiatric data among a diverse group of older PWH.

Examining the interplay of pre-existing and COVID-19 specific neighborhood characteristics on neurocognitive decline and worsened mood for diverse older PWH may help inform the public health burden of treating this population. It is particularly crucial to understand these relationships during a time of historic disruption to society to provide targeted care in future scenarios.

1.1 HIV and Older Age are Linked to Increased Risk for Neurocognitive Impairment and Depressed Mood

Approximately 40% of PWH show neurocognitive impairment (Goveas & Shear, 2020), with the prevalence and severity expected to rise as PWH age. This remains problematic as neurocognitive impairment contributes to difficulties in everyday functioning such as HIV medication adherence (Hinkin et al., 2002; Thames et al., 2011) and household and financial management (Heaton et al., 2004). Furthermore, psychiatric conditions, the most common of which is depression (Arseniou et al., 2014; Bhatia & Munjal, 2014; Ciesla & Roberts, 2001; Nanni et al., 2015; Paolillo et al., 2020; Rooney et al., 2019), are highly comorbid with HIV. Reported estimated rates of depression among PWH are as high as 37%, five times greater than that of the general population (Nanni et al., 2015; Pence et al., 2006; Rooney et al., 2019). For older adults, social isolation, loss of loved ones, medical difficulties and loneliness can increase risk of depression. Studies by our group have shown that older PWH may have a constricted life-space as they spend the majority of their time at home (79%) and alone (59%), which was associated with concurrent lower ratings of happiness (Kamalyan et al., 2020). The consequences of depression include worse quality of life, poorer medication adherence, worse viral suppression, and mortality (Rabkin, 2008). Given the high burden of depression among PWH, these disparities are particularly concerning, and may be the result of systemic factors.

1.2 Neighborhood Vulnerabilities are Related to Poor Neurocognitive and Psychiatric Outcomes

A number of studies suggest that the physical and social environments in which people live have an important influence on their health (Barnett et al., 2018; Rutter, 2005; Weich et al., 2002). As older adults are less mobile than their younger counterparts (Barnes et al., 2007; Coyle & Dugan, 2012; Kamalyan et al., 2020; Paolillo et al., 2018; Polku et al., 2015), environmental risk factors in their neighborhoods may be particularly detrimental to their cognitive and psychiatric health (Barnett et al., 2018; Ivey et al., 2015; Yen et al., 2009). The "weathering" hypothesis proposed by Geronimus and colleagues (2006) suggests that the cumulative impact of repeated social, economic, and political adversity leads to increased health deterioration for minoritized populations in the US (Geronimus et al., 2006). Major disparities in walkability, green space, socioeconomic status, crime, pollution, and disorder (Lovasi et al., 2009; Sallis et al., 2011; Zhu & Lee, 2008) have been documented among Black and Latino neighborhoods (Diez Roux & Mair, 2010; Glymour & Manly, 2008) as compared to White neighborhoods. More disadvantaged neighborhoods may also lack structures for social support (Schieman, 2005; Soltero et al., 2015), are likely to have higher levels of crime (Krivo & Peterson, 1996; A. Y. Oh et al., 2010; Ross & Mirowsky, 2001), and lack access to health resources (Kirby & Kaneda, 2005), all which may increase stress (Yen et al., 2009), depression (Joshi et al., 2017), and substance use (Karriker-Jaffe et al., 2012). Individuals in communities with poor physical/built neighborhood features and lower socioeconomic status have higher rates of neurocognitive impairment and psychiatric disorders (Besser et al., 2017; Diez Roux & Mair, 2010; Sheffield & Peek, 2009; Tallon, 2017). Crucially, there have been no studies assessing how these linkages operate in older diverse PWH. Older minoritized individuals with living with HIV have higher rates of HIV-associated neurocognitive impairment (Marquine et al., 2018) and decline (Heaton et al., 2015; Watson et al., 2022), as well as Alzheimer's Disease and related disorders (Chin et al., 2011; Clark et al., 2005; Demirovic et al., 2003; Mehta et al., 2008; Tang et al., 2001) and are more likely to live in disadvantaged neighborhoods due to systemic racism embedded within policies and institutions (Mugavero et al., 2013). Understanding how neighborhood vulnerabilities impact neuropsychiatric outcomes for aging PWH is crucially needed to identify those at increased risk for worsened outcomes during and after the COVID-19 pandemic, and to develop programs to help mitigate these health disparities.

1.3 COVID-19 Pandemic Impact on Neighborhoods

On March 11th, 2020, the World Health Organization (WHO) declared the outbreak of a novel coronavirus disease (COVID-19) to be a global pandemic (McNeil Jr, 2020). Between then and the spring of 2023, prevention efforts, such as stay-at-home-orders (Newsom, 2020), physical distancing (CDC, 2020b), travel restrictions (US Department of State, 2020), loss of or change in employment, inadequate resources for medical care (*Coronavirus Update*, 2020), and record-setting economic loss (Kochhar, 2020) were among many major stressors specific to this time that undoubtedly have lasting repercussions. Research in health outcomes after natural disasters (Hikichi et al., 2016, 2020) and recessions (Patel, 2019) has established that emotional distress is likely to be echoed during and after a major stressor (i.e., the COVID-19 pandemic (Pfefferbaum & North, 2020), along with increased rates of cognitive impairment (Hikichi et al., 2016, 2020). Furthermore, as older PWH may already experience heightened rates of loneliness and social isolation (Emlet, 2006), stay-at-home orders may have worsened their emotional well-being and health (Marziali et al., 2020). It is likely that PWH, particularly older diverse PWH, may have disproportionately suffered from the stress of living through the COVID-19 pandemic (Shiau et al., 2020).

Crucially, there was a unequal burden of COVID-illness and related stress among minoritized communities (Hooper et al., 2020). Neighborhoods largely composed of Latinos and Blacks had disproportionally greater negative economic and social repercussions of COVID-19 prevention efforts (CDC, 2020b), particularly in southern California (de Joseph, 2020; Lauter, 2020; D. L. Oh et al., 2022). Black and Latino individuals are more likely to live in crowded housing and neighborhoods (Hooper et al., 2020), have more medical comorbidities, and are more likely to be employed in service and transportation industries (e.g., grocery store workers, bus drivers, custodians, factory workers, home health aides). This type of work allows society to function and cannot be accomplished off-site (Krieger, 2020; Rosalsky, 2020), increasing risk of COVID-19 transmission in these communities. Higher rates of COVID-19 were reported among minoritized groups, as well as higher rates of hospitalizations and deaths due to COVID-19 (Adhikari et al., 2020; Andrasfay & Goldman, 2021; CDC, 2020a; Millett, Honermann, et al., 2020; Ruprecht et al., 2021). These communities were also shown to have delayed access to testing for COVID-19 (Bilal et al., 2020; Rubin-Miller et al., 2020) and vaccine administration (Painter, 2021). The ability to safely isolate, work remotely with full digital access, and sustain a monthly income are all highly correlated with socioeconomic status (Hooper et al., 2020; Yancy, 2020) and are products of generations of systemic racism within our healthcare, governmental and social systems (Feagin & Bennefield, 2014; Gal et al., 2020; Henricks, 2015; Rothstein, 2017) which marginalize minoritized and fuel racial/ethnic health disparities (Brondolo et al., 2009; Churchwell et al., 2020; O’Brien et al., 2020; Yearby, R., 2020). We hypothesize that the COVID-19 outbreak will have contributed to increased neurocognitive decline and worsened mood among older diverse

PWH, particularly those living in structurally disadvantaged communities which have been disproportionally impacted by this pandemic (Hooper et al., 2020).

1.4 Geospatial Analyses

Neighborhoods contain built (e.g., parks) and socio-economic (e.g., demographic) attributes that may reflect historic racist policies which underlie racial/ethnic inequities and disparities in health (Glymour & Manly, 2008). In a 2017 review (Besser et al., 2017), eight of 15 studies found that lower neighborhood socioeconomic status, using composite measures based on US Census data, was associated with worse cognition, both cross-sectionally and longitudinally. Geographic Information Systems (GIS) and spatial analysis techniques (Krieger et al., 2003; Moore & Carpenter, 1999; Rushton, 2003) have allowed for growing innovative research in aging and neurocognitive outcomes (Besser et al., 2017; Meersman, 2005). Most analyses with GIS have focused on how separate environmental (e.g. pollution) (Gatto et al., 2014; Kulick et al., 2020; Tallon, 2017) and built (e.g. walkability) (Diez Roux & Mair, 2010; Watts et al., 2015) neighborhood characteristics influence neurocognition and age-related health outcomes. Among PWH, GIS data have only been applied to understand predictors of HIV prevalence and risk of HIV infection (Gant et al., 2014; Wheeler, 2016) and only one study among Latino PWH used median income as a proxy for neighborhood socioeconomic status (Rivera Mindt et al., 2008). In contrast, composite measures of the neighborhood are more advantageous as they weight multiple features of the environment based on their contribution to the latent variable and can combine both socio-economic and physical attributes of an area, thus resulting in a more comprehensive reflection of a neighborhood. However, no study has yet investigated how composite measures of neighborhood vulnerabilities may relate to neuropsychiatric health outcomes for PWH.

1.5 Specific Aims and Hypotheses

This project aims to fill critical gaps in the literature by analyzing whether neighborhood vulnerabilities influence neurocognitive and psychiatric outcomes in a diverse cohort of older (50+) PWH before and during a global pandemic. The aims of this study are:

Aim 1. Determine the impact of neighborhood vulnerabilities (e.g., sociocultural/physical aspects of the neighborhood) and the pandemic's impact on neighborhoods (e.g., rates of COVID-19 infection, availability of testing locations, rate of vaccinations) on individual neurocognitive decline after the COVID-19 outbreak in diverse older PWH. ***Hypothesis 1a:*** Living in a neighborhood with worse levels of neighborhood vulnerabilities before the onset of the COVID-19 outbreak will be associated with greater neurocognitive decline approximately a year after the onset of the pandemic. ***Hypothesis 1b:*** The differential impact of the COVID-19 pandemic on neighborhoods will interact with neighborhood vulnerabilities to exacerbate neurocognitive decline approximately a year after the onset of the pandemic.

Aim 2: Determine whether neighborhood vulnerabilities and the pandemic's impact on neighborhoods relate to worse individual mood after the COVID-19 pandemic among diverse older PWH. ***Hypothesis 2a:*** Living in a neighborhood with worse levels of neighborhood vulnerabilities will be associated with increased symptoms of low mood approximately a year after the onset of the COVID-19 pandemic compared to before its onset. ***Hypothesis 2b:*** The disproportionate impact of the COVID-19 pandemic on neighborhoods will interact with neighborhood vulnerabilities to worsen symptoms of low mood approximately a year after the onset of the pandemic.

2. METHODS

The proposed study analyzed longitudinal data from individuals enrolled in ongoing prospective observational cohort studies at the UCSD HIV Neurobehavioral Research Program (HNRP). In accordance with HNRP policy, I received formal approval to use longitudinal data and de-identify participant addresses for the proposed study. All participants provided written informed consent and HNRP study procedures were approved by local Institutional Review Boards.

2.1 Participants

Participants were community-dwelling adults who participated in observational cohort studies at the UCSD HNRP. Inclusion/exclusion criteria for parent studies were similar across parent studies: participants living in southern California were excluded if they had a history of head injury with loss of consciousness greater than 30 minutes, or other neuromedical comorbidities that may affect cognitive functioning (i.e., stroke, prior head injury, opportunistic infection), or significant sensory or physical issues that would interfere with neurocognitive testing (Heaton et al., 1995; Marquine et al., in progress; Montoya et al., 2015; Watson et al., 2019). Inclusion criteria for present analyses were: 1) positive HIV serostatus; 2) age 50 and over; 3) fluent in English or Spanish; 4) completing a study visit between March 1st, 2019, and March 1st, 2020 (i.e., before COVID-19 onset and associated stay-at home orders in CA); 5) having data available on demographic factors (i.e., age, sex, years of education, race/ethnicity) and neuropsychological data for at least five cognitive tests; and 6) having a complete address, PO Box, or zip code on file. Exclusion criteria included being a part of an HNRP intervention protocol; and 7) not living within San Diego or Riverside Counties in California, as data for physical neighborhood characteristics are not equally available for all counties in the region. Individuals who did not have an address on file or who had neighborhood factor scores greater than three standard deviations above the sample mean were also excluded. We did not exclude participants who reported testing positive for COVID-19 during the study period as COVID-19 infection rates in the U.S. were higher in socioeconomically disadvantaged neighborhoods (Garcia et al., 2021; Millett, Honermann, et al., 2020; Millett, Jones, et al., 2020; S. B. Tan et al., 2021), and very few participants across all studies at the HNRP (n=91) reported testing positive with COVID-19 before June 30th, 2022 (end of study period).

A subset of participants completed a study visit between March 2021 through June 30th, 2022, and had neuropsychological test data on at least five cognitive tests during this visit. These data were used to analyze change in cognition and mental health, and to perform multiple imputation procedures on the overall sample at follow-up. Our final pool of participants was N=180 at baseline with N=79 having follow-up data. This 56.1% attrition rate was much greater than we had anticipated (see Handling Missing Data).

2.2 Neighborhood Characteristics

Table 1 depicts the US Census 2020 and American Community Survey (ACS) five-year estimates (2016-2020) (*Census Bureau Data*, n.d.) and publicly available data gathered for southern California via GIS methods at the census tract or zip code level. All geospatial analyses were conducted in ArcGIS Pro Version 2.4.1. These data were used in factor analyses to create composite measures capturing the sociocultural and physical neighborhood environment, as well as the impact of COVID-19 on neighborhoods.

For the proposed sociocultural composite, a total of ten variables were selected based on prior and ongoing work quantifying neighborhood characteristics in San Diego County (Carlson et al., 2022; Gallo et al., 2019, 2022; Savin et al., 2022) as well as additional aspects of the environment that were linked to worse health outcomes during the period of restrictions associated with the COVID-19 pandemic (e.g., having multiple people in the same dwelling, identifying as a racial/ethnic minority, being woman, impacts on job availability) and having limited access to internet). Variables included in the sociocultural composite were demographics (percent of the population Hispanic or Latino, percent of population not born in the US), crowded (percent of households with more than one person per room), impact of pandemic on women (percent female-headed households with dependent children), school-aged children (percent of population under the age of 18), employment stability (percent of employed males over the age of 16 in management, business, science, and arts occupations), poverty (percent of households with income in the last 12 months below the federal poverty line), transportation (percent of households without a car), and technology (percent of households without any type of computer, percent of households without internet subscriptions). These variables were used in exploratory factor analyses, as described below (see Composite Creation).

For the physical composite, a total of eight variables collected via satellite imagery and publicly available addresses were selected based on prior work (Carlson et al., 2022; Gallo et al., 2019), as well as additional variables selected a priori to reflect specific physical/built aspects of the environment that were particularly relevant during restrictions due to the COVID-19 pandemic (i.e., reduced access to open spaces, healthy food options, and medical care). Environmental aspects included a pollution burden index from the CalEnvironScreen Version 4.0 (Zeise & Blumenfeld, 2021), a walkability index (i.e., equally weighted index of intersection density, residential density, and land use mix) (Frank et al., 2009), living in a food desert (i.e., an index of healthy food compared to non-healthy food options) (*Census Tract Level State Maps of the Modified Retail Food Environment Index (MRFEI),* 2012) and the distance to the nearest park.

Physical/built aspects included distance to the nearest recreation center, distance to the nearest liquor store, distance to transit stops, and distance to nearest health center (*Health Sites*, 2023). These variables were used in exploratory factor analyses (EFA), as described below (see Composite Creation). Riverside County did not have available transit stop, recreation center, and walkability data, and thus these values were only used to calculate an EFA applicable for San Diego County.

For the impact of COVID-19 on neighborhoods composite, a total of four variables were available for both San Diego and Riverside County at the zip code level: percent of cumulative COVID-19 cases per zip code population, percent of zip code population fully vaccinated (i.e., at least two initial vaccinations), distance to nearest COVID-19 testing center, and a measure of vaccine hesitancy per zip code population (*Vaccine Hesitancy (Any) by ZIP Code*, n.d.). The addresses for COVID-19 testing centers for Riverside and San Diego were pulled by hand using Google Maps data. These variables were used in exploratory factor analyses, as described below (see Composite Creation).

Table 1. Neighborhood constructs proposed to measure vulnerabilities and the impact of COVID-19 on the neighborhood

Neighborhood Construct	**Variables Included**	**Sources of Data**	**Quantified**
Sociocultural vulnerabilities	% crowded households (>1 person per room) % of the population under 18 years old % female headed households with dependent children % of employed males over the age of 16 in management, business, science, and arts occupations % of households with income in the last 12 months below the federal poverty line % of households without a car % of households without any type of computer % of households without any type of internet access % of the population Hispanic % of the population not born in the US	American Community Survey 5-year estimates (2016-2020)	Average value for 2020 census tracts in San Diego and Riverside counties
Physical vulnerabilities	Walkability Index *an equally weighted index of intersection density, residential density, and land use mix* Distance to nearest recreation center, km *bike paths, recreation business, coast lines, schools, lakes, parks, streams, recreation centers*	SANDAG (years)	Average value for 2020 census tracts in San Diego County only

Table 1. Neighborhood constructs proposed to measure vulnerabilities and the impact of COVID-19 on the neighborhood, continued

Neighborhood Construct	**Variables Included**	**Sources of Data**	**Quantified**
Physical vulnerabilities	Pollution Burden Index *average of Exposure Indicators* *(i.e., Ozone and PM2.5 emissions, diesel particulate matter, drinking water contaminant, lead risk in housing, pesticide use, toxic releases from factories, traffic congestion) and Environmental Effects Indicators (i.e., cleanup sites, groundwater threats, hazardous waste, toxic water), half weighted*	CalEnvironscreen Version 4.0 (2021)	Average value for 2020 census tracts in San Diego and Riverside counties
	Living in a food desert *Modified Retail Food Environment Index: number of healthy food retailers / (number of healthy + number of less healthy food retailers) x 100*	Dun and Bradstreet retail database (2017)	Average value for 2020 census tracts in San Diego and Riverside counties
	Distance to nearest liquor store *active off-site non-bar or restaurant liquor licenses*	California Department of Alcoholic Beverage Control (2022)	Nearest liquor store to 2020 census tracts in San Diego and Riverside counties, kilometers
	Distance to nearest health center *Centers for Medicare and Medicaid Services and Health Center Service Delivery centers*	US Health Resources and Services Administration (HRSA) agency of the U.S. Department of Health and Human Services) (2022)	Nearest health center to 2020 census tracts in San Diego and Riverside counties, kilometers

Table 1. Neighborhood constructs proposed to measure vulnerabilities and the impact of COVID-19 on the neighborhood, continued

Neighborhood Construct	**Variables Included**	**Sources of Data**	**Quantified**
Physical vulnerabilities	Distance to nearest park *national forests and parks, county parks and preserves, city parks, and community parks*	San Diego County: SANDAG dataset representing a consolidation of parks datasets from the County of San Diego, incorporated cities, San Diego Port District, SanGIS and State Parks (2022) Riverside County: Stanford Digital Repository dataset representing a consolidation of city governments, park and recreation districts, county and state governments, and the US Forest Service data (2019)	Nearest park to 2020 census tracts in San Diego and Riverside counties, kilometers
Impact of COVID-19	Cumulative number of cases per population	San Diego County: SANDAG (through June 30th, 2022) Riverside County: Calculated by hand from weekly reports published on Riverside County of Public Health (through June 30th, 2022)	Count for 2020 zip codes in San Diego and Riverside counties
	% fully vaccinated *at least the initial two vaccinations*	California Health and Human Services Open Data Portal (through June 30th, 2022)	Percentage value for 2020 zip codes in San Diego and Riverside counties
	Distance to nearest COVID-19 testing center	San Diego County: San Diego County Data Portal, (pulled May 25, 2022) Riverside County: Calculated by hand from Google Maps data (pulled May 31st 2022)	Nearest testing center to zip codes in San Diego and Riverside counties, kilometers

Table 1. Neighborhood constructs proposed to measure vulnerabilities and the impact of COVID-19 on the neighborhood, continued

Neighborhood Construct	Variables Included	Sources of Data	Quantified
Impact of COVID-19	Vaccine hesitancy per population *CMU/Facebook survey respondents who answered "No, probably not," or "No, definitely not" when asked "If a vaccine to prevent COVID-19 were offered to you today, would you choose to get vaccinated?" per ZIP Code Tabulation Areas (ZCTAs)*	The Delphi Group at Carnegie Mellon University U.S. COVID-19 Trends and Impact Survey, in partnership with Facebook, institute for Health Metrics and Evaluation (2021)	Average value for 2020 zip codes in San Diego and Riverside counties

Shapefiles of county, census tract, and zip code boundaries for 2020 for both Riverside and San Diego County were downloaded from the respective county's GIS websites (i.e., (*SanGIS GIS Data Warehouse*, 2015) https://rdw.sandag.org/; (*Riverside County Mapping and Spatial Data Portal*, n.d.), https://gisopendata-countyofriverside.opendata.arcgis.com/). As populations are very rarely distributed equally within a given boundary (Hwang & Rollow, 2000), population-weighted centroids were downloaded for each of the census tracts (*Census Bureau Data*, n.d.) and zip codes (*HUD Open Data Site*, 2020), and connected to the respective boundaries' shapefiles. A 1km buffer (a bounded region around a person's home and limited to areas within 50m of any street), a generally accepted and used buffer size and type (Brownson et al., 2009; James et al., 2014) was created around each centroid in order to calculate more accurate distance measurements per centroid. A tract's population centroid may be distant from its geographic centroid particularly in large tracts (e.g., rural areas) where people may be concentrated in a particular area (Luo & Wang, 2003).

All Census variables from the ACS 2016-2020 five-year estimates were downloaded from data.census.gov, cleaned, and uploaded to ArcGIS to connect values to census tract shapefile boundaries. Individual variable values per census tract were used for sociocultural construct EFA. As for the physical/built data, the download of health center locations included the respective longitude and latitude information, which was used to join to the respective county's shapefile. The addresses of liquor stores were geocoded to join to the respective county's shapefiles. Data for parks, transit stops, and recreation centers were downloaded as individual shapefiles and were joined to the respective county's shapefile. Values for living in a food desert were created based on 2017 census tract boundaries and the CalEnvironScreen calculations are based on the US Census Bureau's 2010 census tract boundaries. Thus, these two variables were averaged for the 2020 population-weighted centroid's buffer. All distance values were averaged per population-weighted centroid and used for the physical construct EFA. For the impact of COVID-19 on the neighborhood construct, percent of cumulative COVID-19 cases per zip code population, vaccination rates, and vaccine hesitancy data were joined to the respective county's zip code shapefile. The addresses of COVID-19 testing centers were geocoded and joined to the respective zip code shapefiles. See Table 1 for additional details about each of the neighborhood variables, including data sources, collection methods, and timepoints.

Participant's mailing addresses were collected by the HNRP to contact participants for future visits and other center related communication. These addresses are only available for their most recent visit. Out of the entire sample, 11 participants had a PO Box, or the address of a business listed, thus the population-weighted center of the census tract associated with the zip code of the address was geocoded. The remaining 172 complete address on file were geocoded. A 1km street network buffer was established around each address. Each neighborhood variable and factor was averaged per participant's buffer region.

2.3 Neuropsychological Evaluation

At each study timepoint, participants completed a comprehensive battery of tests designed to assess neurocognitive domains most affected in HIV (i.e., verbal fluency, executive functioning, processing speed, learning, delayed recall, attention/working memory, and motor skills) (Cysique et al., 2011). See Table 2 for a list of neuropsychological tests that were used to examined global cognition in the current study.

Table 2. Administered neurocognitive tests at baseline by domain for the overall sample (N=180) and for the subset with complete neurocognitive follow-up data (N=79)

Domain	Test[a]	Overall sample	Subset with follow-up data
Verbal Fluency	Animal Fluency	173	77
	Letter Fluency[b]	158	72
Attention/Working Memory	Paced Auditory Serial Addition Test-50	164	75
	WAIS-III Letter Number Sequencing	107	44
Speed of Information Processing	WAIS-III Digit Symbol	177	79
	WAIS-III Symbol Search	176	79
	Trail Making Test A	172	76
Executive Functioning	Wisconsin Card Sorting Test-64	162	76
	Trail Making Test B	171	76
Learning	Hopkins Verbal Learning Test-Revised, Total Recall	177	77
	Brief Visuospatial Memory Test-Revised, Total Recall	175	78
Memory	Hopkins Verbal Learning Test-Revised, Delayed Recall	175	76
	Brief Visuospatial Memory Test-Revised, Delayed Recall	175	78
Motor Skills	Grooved Pegboard dominant hand	173	78
	Grooved Pegboard non-dominant hand	172	76
Global Mean Scaled Score[c]	--	180	79

Note: WAIS III = Wechsler Adult Intelligence Scale 3rd Edition
a: all test scaled scores adjusted for practice-effects
b: either FAS if primarily English-speaking or PMR if primarily Spanish-speaking (n=18)
c: calculated using all available individual test scores per individual

Baseline visits were conducted in-person. Due to the limitations to in-person testing during the pandemic, all follow-up visits were conducted as a hybrid of remote (i.e., via video conference or telephone) and in-person testing. For remote testing situation, examiner setups were standardized to the extent possible (Kohli et al., 2023). These standardizations included encouraging participants to complete assessments seated in a private and quiet location in their homes to ensure confidentiality and minimize interruptions, replicating a laboratory assessment. Participants were also encouraged to use computers with a camera and microphone and to wear headphones to improve audio quality. While all examiners operated from the same video-based platform, internet connection quality and computer hardware varied between examiners and between participants, and thus time was taken to check internet connections prior to the administration of any assessments. Participants who connected by landline telephone received audio-only measures and participants who connected by tablet, smartphone, or personal computer received both audio and visual measures. Additional accommodations and procedures for teleneuropsychological testing, as well as the reliability and validity of these teleneuropsychological assessments have been published elsewhere (Kohli et al., 2023).

To examine longitudinal neurocognitive change, raw test scores among the subset of participants with complete baseline and follow-up neuropsychological data were transformed into scaled scores and adjusted for practice effects (Carey et al., 2004). They were then averaged to create a practice adjusted global scaled score (GSS) for both timepoints. GSS at baseline was subtracted from GSS at follow-up to create a continuous value reflecting change in cognitive performance. A negative value was indicative of worse cognition at follow-up.

2.4 Psychiatric and Substance Use Characteristics

Participants completed questionnaires and semi-structured interviews assessing symptoms of depression, anxiety, general mental health or quality of life, and substance use patterns. The main psychiatric outcome for the proposed study was originally symptoms of depression. When proposing this study, depressive symptoms were to be assessed via the Beck-Depression Inventory, 2nd Edition (BDI-II; Beck, A.T. et al., 1996), as this measure was administered across studies at the HNRP prior to the onset of the COVID-19 pandemic. Unfortunately, remote visits eliminated the opportunity to have clinical coverage in the case of a participant endorsing suicidality on the BDI-II. This questionnaire was not administered throughout the follow-up window, and only was reintroduced in January of 2022. Thus, no single measure of depression was given consistently across prospective studies conducted at the HNRP between March 2021 and June 30th, 2022. We re-conceptualized as mental health broadly in order to utilize the health status and quality of life data from the Medical Outcomes Study HIV Health Survey (MOS-HIV) (A. W. Wu et al., 1997). This measure was the most commonly given questionnaire of mental health symptomology across the observational cohort studies from which data was collected at both timepoints.

The MOS-HIV is a 35-item questionnaire includes ten dimensions: health perceptions, pain, physical, role, social and cognitive functioning, mental health, energy, health distress and quality of life (A. W. Wu et al., 1997). Participants answered how much of the time they felt a certain way in the past 4 weeks on a Likert-type scale (1-All the time to 6-None of the time). Example items that conceptually measure mental health symptoms include “how much of the time, during the past 4 weeks, have you been a very nervous person…. have you felt calm and peaceful…. have you felt downhearted and blue…have you been a happy person…. have you felt so down in the dumps that nothing could cheer you up?” Prior studies have derived physical health and mental health factors based on exploratory and confirmatory factor analyses (Revicki et al., 1998). Revicki and colleagues showed that the mental health, health distress, QoL and cognitive function scales of the MOS-HIV loaded most strongly onto the mental health summary score (MSS), which additionally included the vitality, general health, and social function scales. MOS-HIV mental health summary scores (MSS) were transformed to T-scores (M=50, SD=10), with greater scores indicative of better mental health. Eighty-seven participants had a value for MSS at baseline (47.5%), 50 participants at follow-up (63.2%), and 34 participants had values at both visits (43%). A change in mental health symptoms was calculated by subtracting MSS scores at follow-up from MSS scores at baseline, creating a continuous value for analyses among the subset with data at both timepoints (n=34). A negative change score was indicative of worsened mental health at follow-up.

Participants completed the Composite International Diagnostic Interview (Version 2.1) (Kessler & Üstün, 2004; Wittchen et al., 1991) for current (within past 12 months) and lifetime diagnosis of mood and substance use disorders (i.e., alcohol, cannabis, opioids, methamphetamine, cocaine, sedatives and hallucinogens) which were assigned based on the Diagnostic and Statistical Manual-Fourth Edition (DSM-IV) criteria.

2.5 Self-reported Everyday Functioning

Participants completed questionnaires and semi-structured interviews assessing everyday functioning. Reports of cognitive difficulties in everyday life were measured by the Patient's Assessment of Own Functioning Inventory (PAOFI) (Chelune et al., 1986), with a greater total score indicating greater number of reported cognitive symptoms and functional impairment in daily life. Employment status was measured by either 1) the PAOFI question "Are you presently holding a job?" or 2) an employment history question "Are you currently employed" during each visit. Responses for both questions were recoded into one employment status variable (i.e., employed: PAOFI responses of ‘Yes, full-time’ ‘Yes, part-time,’ and employment history response ‘Yes’; unemployed: ‘No’ response on both questions). Participants also completed the modified Instrumental Activities of Daily Living scale (IADL), (Heaton et al., 2004) which asks participants to indicate how they are performing now and at their best for several aspects of everyday functioning. Needing and obtaining more help with two or more activities of daily living was recoded as “IADL dependent.”

2.6 Neuromedical Evaluation

Participants completed neuromedical evaluation at baseline and during the in-person portion of follow-up visits including: 1) self-reported current and nadir CD4 counts; 2) CDC HIV staging; 3) estimated duration of HIV infection; 4) current antiretroviral therapy (ART) regimen; 5) comorbid medical conditions (e.g., hepatitis C co-infection, diabetes); 6) HIV RNA measured in plasma; and 7) routine clinical chemistry panels (e.g., glucose, lipids). HIV serostatus at baseline was determined by enzyme-linked immunosorbent assay (ELISA) with a confirmatory Western Blot. Nadir CD4, estimated duration of infection, and current and past use of ART were ascertained by self-report and review of medical records when available. We computed the Veterans Aging Cohort Study (VACS) Index (Justice et al., 2013), which combines age, traditional HIV biomarkers (HIV-1 plasma RNA and current CD4 count), and non-HIV biomarkers (indicators of renal and liver function, anemia, and Hepatitis C co-infection). It is predictive of NCI and decline in HIV (Marquine et al., 2014, 2018). Medical comorbidities assessed included body mass index (BMI, weight/height, kg/m^2) as well as self-report of having diabetes, hepatitis C virus (HCV) co-infection and any cardiovascular risk factors (i.e., hypertension, hyperlipidemia, cerebrovascular accident (CVA)).

2.7 Statistical Analyses

Descriptive Statistics. We computed descriptive statistics for demographics, HIV disease characteristics, psychiatric/substance use and medical comorbidities at baseline for the overall sample and among the subset of participants with complete follow-up data. Descriptive statistics were also calculated for the components of neighborhood vulnerabilities, the impact of COVID-19 on the neighborhood, as well as for GSS and MSS at baseline and follow-up. Distributions of sample characteristics of continuous measurement scales were examined for normality.

Covariate selection. Demographic (i.e., age, sex, years of education), HIV disease characteristics (i.e. AIDS Status, nadir CD4, estimated duration of HIV infection, exposure to ART), comorbid medical conditions (i.e., BMI, HCV, diabetes, cardiovascular risk factors) and markers of every day functioning (i.e., employment status, IADLs) among PWH are known to be associated neurocognitive impairment/decline (Alley et al., 2007; Cherner et al., 2005; Deary et al., 2009; Ellis et al., 2011; Heaton et al., 2004; Kamalyan et al., 2021; Rourke et al., 1999; L. H. Rubin et al., 2019, 2020; Vance et al., 2014) and psychiatric outcomes (Clements-Nolle et al., 2001; Lopes et al., 2012). We investigated the relationship between these variables at baseline and our outcomes among the sample with complete follow-up data using two-sample t-tests, ANOVA, and Pearson r correlations tests. Variables that were significantly associated with change in GSS and/or MSS at $p<.05$ were included in models, as well as months between visits and the baseline value of GSS or MSS, as covariates. To preserve degrees of freedom and create a parsimonious model, non-significant covariates in the multivariable model were removed and the model re-run ($p>.05$).

Composite Creation. The variables described in Table 1 were proposed to reflect three separate constructs (i.e., sociocultural characteristics, physical characteristics, and the impact of COVID-19 on the neighborhood) using three distinct exploratory factor analyses (EFA; Ford et al., 1986; Watkins, 2018). Due to the nature of the theoretical constructs, it was assumed that factors would be correlated. Thus, principal axis factoring (PAF) using direct oblimin rotation (Jennrich & Sampson, 1966) was conducted to explore the dimensionality of the neighborhood vulnerabilities and the impact of COVID-19 on the neighborhood, with each analysis using both San Diego and Riverside County in conjunction. The following indicators were evaluated to determine the plausibility of the factor structure: initial correlation of individual variables (Watkins, 2018), eigenvalues greater than 1 (Aronson et al., 2007; McDonell & Waters, 2011); graphical depiction of eigenvalues (i.e., a scree plot) indicating the number of "true" factors by an "elbow" or distinct break in the slope of the scree plot (Cattell, 1966); model fit indices of Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy value, (KMO values $\geq$.70 are desired (Hoelzle & Meyer, 2013; Watkins, 2018), but values $\leq$ .50 are generally considered unacceptable (Child, 2006; Kaiser, 1974; Watkins, 2018), indicating that the correlation matrix is not factorable) and Bartlett's test of Sphericity (i.e., a statistically significant chi-square value (Bartlett, 1954); individual variable communalities $\geq$.3 (Fabrigar et al., 1999); at least three variables loading on each factor (Child, 2006; Watkins, 2018) with a loading $\geq$ .50 in the same direction; each variable loading saliently on only one factor (i.e., no complex or cross-loadings) (Watkins, 2018) and all factors should be theoretically meaningful (DiStefano et al., 2009; Ford et al., 1986; Watkins, 2018). To further confirm the factor structures, parallel analysis was used on each hypothesized construct (Hayton et al., 2004; Humphreys & Montanelli, 2010). Final factor scores were saved per census tract across both counties using the regression method given the direct oblimin rotation used in factor creation.

Findings will be considered statistically significant at $p<0.05$; however, due to a potentially having a lower sample size than needed to detect associations between neighborhood indicators and individual data (see Missing Data), we evaluated all beta estimates for their effect sizes and confidence intervals as well as *p*-values. Statistical assumptions were checked throughout the steps of the analytical design. JMP Pro 16.0, SPSS 28.0.1.1 and R 4.2.3-package statistical software were used for all aims.

Multivariable linear regression models were the primary approach used to examine all hypotheses. Factors reflecting the sociocultural and physical characteristics of the neighborhood derived from factor analyses were the primary exposures and the indicator of the impact of COVID-19 on neighborhoods was analyzed as a potential effect modifier (interaction) (see Factor Analyses in Results section). Neurocognitive decline was operationalized as a continuous variable, i.e., change in GSS from baseline to follow-up. Worsened mental health symptoms were also operationalized as a continuous variable, change in MSS from baseline to follow-up. Pearson product-moment correlation coefficients between neighborhood factors and GSS and MSS change respectively were run to establish preliminary unadjusted relationships between independent and dependent variables.

For hypothesis 1a, factors reflecting both the sociocultural and physical characteristics of the neighborhood were included as continuous independent predictors of neurocognitive decline (i.e., change in GSS). Given possible multicollinearity between the neighborhood factors, we investigated potential suppression effects (i.e., evidence of a stronger, weaker, no longer significant, or reverse directionality of relationships between variables and the outcome) (Kraha et al., 2012). Standardized regression estimates (β) for model results were compared against simple Pearson correlations (r) between neighborhood factors and each outcome. Standardized regression values between zero and the Pearson correlation were considered to not show evidence of suppression and thus adequate model results. In addition, all possible subset regressions were conducted in the case of persistent suppression effects to find the best combination of predictors per model (Pedhazur, 1982). Non-significant factors (p>.05) were removed and models re-run. For hypothesis 1b, we included the mean centered percent of cumulative COVID-19 cases per zip code population as an additional independent predictor of change in GSS and as part of three interaction terms: Sociodemographic by COVID-19 case rates, Economic by COVID-19 case rates, and Undeveloped by COVID-19 case rates. Non-significant interaction terms (p >.10) were removed and the model re-run. For hypothesis 2a and 2b, models and model selection for these hypotheses were similar to aim 1, with the outcome being change in MSS.

2.8 Handling Missing Data

Initial analyses were proposed for a follow-up window through March 30th, 2022, and by applying the HNRPs ~10% low attrition rate. Additionally, a study by Sheffield and Peek (2009) that reported a beta coefficient of -0.28 (SE: 0.13) for the role of neighborhood economic disadvantage on cognitive decline in older Mexican Americans, comparing the effect of lowest and highest economic disadvantage quartiles (Sheffield & Peek, 2009). Using this prior study, we had conducted power analyses to estimate the potential to detect an effect with our sample size. We anticipated that aim 1 would be powered (1-β= 0.96) to detect small-to-medium effect sizes (f2 = 0.09), with a two-tailed a = 0.05, and up to 10 covariates, and aim 2 would be powered (1-β= 0.94) to detect small-to-medium effect sizes (f2 = 0.09), with a two-tailed a = 0.05, and up to 10 covariates. Power analysis was conducted using GPower (Erdfelder et al., 1996).

However, the many difficulties associated with retaining participants and collecting data during the COVID-19 pandemic (Padala et al., 2020) led to an increased attrition rate, even after extending the initial timeframe for follow-up data collection through June 30th, 2022. Our final 56.1% attrition rate was much greater than we had anticipated (i.e., 10%). After investigating potential causes for this, we concluded that the potential follow-up visits for 101 participants were due to individuals documented as either having moved out of state (n=2), withdrawn from their study after the baseline visit (n=4), were lost to follow-up (n=7), had passed away (n=9), had finished their parent study's protocol between March 2020 and March 2021 and, although had been eligible for other ongoing studies at the center, were currently inactive at the HNRP (n=22), were difficult to schedule for their next center visit (n=25), or were scheduled to be seen next outside of this study's follow-up window (n=32). These categories were combined to create a variable called "reasons for no-follow-up", with three levels: 1) 'permanently gone' (i.e., moved, died, n=11); 2) 'lost' (i.e., lost to follow up, withdrawn from parent study after baseline, and inactive in eligible ongoing studies, n=33); and 3) 'not available' (i.e., difficult to schedule for next visit, and passed the current study's follow-up window, n=57).

As we did not have follow-up data for over half of participants, missing data patterns for independent and dependent variables and as well as covariates were analyzed for either missing completely at random (MCAR), missing at random (MAR) or not missing at random (NMAR) types of systematic nonresponse (Kenward & Carpenter, 2007). Whether missing data are MAR or MNAR cannot be fully determined from the data but by speculating on missing data patterns (Grittner et al., 2011). Our assessment of the missing data suggested that the data are at least partially MAR and that at least some variables included in our dataset could be used to make these corrections. Once a MAR missing data pattern assumption was made, a multiple imputation (Kenward & Carpenter, 2007; Schafer, 1999; Sterne et al., 2009) was conducted to yield accurate estimates of missing data. Of note, if the assumption that the missing data patterns are in fact NMAR, then the results of the imputation will retain a degree of bias, particularly as we aim to impute data for over half of the study sample.

Following Rubin (1988), we conducted multiple imputation by chained equations (MICE) using the *mice* package in R Version 4.2.3. The MICE procedure has several advantages: it can manage uncertainty and different types of variables in the imputation procedure, resulting in more accurate predictions (Grittner et al., 2011). We constructed 100 imputed data sets, with independent draws for every 1000 iterations (Enders, 2017; D. B. Rubin, 1988), to impute GSS and MSS scores at follow-up. We included potential predictors of missingness (i.e., age, education, GSS and MSS scores at baseline, AIDS status at baseline, employment status, reasons for no follow-up), as well as significant covariates to include in the multivariable model on imputed datasets (i.e., years exposure to ARTs, see Results Section 3.4). Data for MSS at baseline and months between visits were not available for the entire sample. As such, these missing values were filled in with randomly chosen values by the *mice* package prior to using these variables in the imputation of change GSS and MSS at follow-up, as well as in the iterative regression models. The method of imputation for numeric values (i.e., age, education, GSS and MSS scores, years exposure to ARTs and months between visits) was predictive mean matching ('pmm'), the method for two-level categorical variables (i.e., AIDS, employment status) was logistic regression ('logreg') and the method for more than two-level categorical variables (i.e., reasons for no follow-up) was polytomous logistic regression ('polyreg').

Each of the 100 imputed data files were then examined to ascertain the quality of the imputed data by first evaluating the convergence of the imputation process. This is accomplished using the rhat value, which compares the mean, standard deviation and ranges of the imputed scores to the initial dataset's scores (i.e., values < 1.01 are desirable) (Grund et al., 2016). Once the imputed data passed diagnostics, new GSS and MSS change scores were calculated for each imputed dataset based on the imputed values for GSS 2, MSS1, and MSS2, as well as interaction terms for each neighborhood factor and COVID-19 Case Rates. Model structure followed the same methods as listed in primary aims, thus, multivariable linear regressions on the calculated GSS and MSS change scores were run for each individual imputed file. Parameter estimates from each analysis were then averaged, with parameter standard errors combined using “Rubin’s rules” (D. B. Rubin, 1988), which incorporates both the within-imputation variance and the between-imputation variance. The estimates from the imputed regression analyses were compared to unimputed model results.

3. RESULTS

3.1 Overall Sample Characteristics

Table 3 lists demographic, HIV disease characteristics, medical, psychiatric/substance use and everyday functioning characteristics of the study sample at baseline. Participants ranged from 50 to 90 years old, about 80% were male, and had between 2 to 20 years of education. Over half of the sample identified as Non-Hispanic White, and only 18 participants were tested in Spanish. The majority of the sample had primary addresses located in San Diego County, with 10% in Riverside County. More than half of the sample met criteria for AIDS and the average estimated duration of HIV infection was about 22 years. The median nadir CD4 cell count was 168/μL, while current CD4 count was 591/μL. Most of the sample was on ART, with an average around 16 years of ART exposure. Among those on ART, almost all had undetectable plasma viral load (<50 copies/mL). VACS Index scores of the sample ranged from 12-85, with higher scores indicative of worse functioning.

In terms of comorbidities, average BMI was around 27 kg/m^2, 22% of participants were co-infected with HCV, rates of cardiovascular risk factors ranged from 13% with a history of a CVA to 67% with hyperlipidemia. About two-thirds of the sample reported meeting criteria for lifetime major depressive disorder, and only 10 participants met criteria for current major depressive disorder. Over two-thirds of the sample also reported meeting lifetime criteria for any substance use disorder diagnosis, driven largely by over half the sample having a lifetime alcohol use disorder diagnosis. About a quarter to a third of the sample met criteria for lifetime cannabis, cocaine, methamphetamine use, or any other drug use disorder. On metrics of everyday functioning, the overall sample reported around 5 cognitive symptoms on the PAOFI, 23% of the overall sample reported being IADL dependent, and 75% reported being unemployed at baseline.

Baseline characteristics among the subset of participants who had complete neuropsychological data during the follow-up window (N=79) are also shown in Table 3. Differences in sample characteristics between the overall sample and the subset were calculated using dependent sample t-tests for continuous variables and McNemar's tests for categorical variables. The only significant differences in characteristics between the overall sample and subset were in education (p=.01) and employment status (p=.04). Among this subset, participants ages ranged from 50 to 76 years old, 78% were male, and had between 8 to 20 years of education. Over half of the sample identified as Non-Hispanic White, and only 9 participants were tested in Spanish. The majority of the sample had primary addresses located in San Diego County, with 9% in Riverside County. More than half of the sample met criteria for AIDS and the average estimated duration of HIV infection was about 23 years. The median nadir CD4 cell count was 180/μL, while current CD4 count was 653/μL. Most of the sample was on ART, with an average around 18 years of ART exposure. Among those on ART, almost all had undetectable plasma viral load (<50 copies/mL). VACS Index scores of the sample ranged from 12-85, with higher scores indicative of worse functioning.

Prevalence of comorbidities at baseline among this subset were similar to the overall sample, as average BMI was around 27 kg/m^2, 22% were co-infected with HCV, rates of cardiovascular risk ranged from 11% with history of CVA to 72% with hyperlipidemia. About two-thirds of the subset reported meeting criteria for lifetime major depressive disorder, with only three participants meeting criteria for current major depressive disorder. Seventy percent of the subset also reported meeting criteria for lifetime any substance use diagnosis, once again driven by 59% of the subset having a lifetime alcohol use disorder diagnosis. About a quarter to a third of the sample met criteria for lifetime cannabis, cocaine, or methamphetamine use, or any other drug use disorder. On metrics of everyday functioning, the subset also reported around 5 cognitive symptoms on the PAOFI, 23% of the overall sample reported being IADL dependent, and 64% reported being unemployed at baseline.

Among this subset of participants who had complete follow-up data, the average global scaled score at baseline was 8.94 (*SD*=1.88) and 8.99 (*SD*=2.13) at follow-up, with the average change over time 0.05 (*SD*=0.99) scaled scores. Average MSS T-Scores at baseline for this subset were 51.2 (*SD*=9.62) and 50.1 (*SD*=9.48) at follow-up, and the average MSS change over time was -1.76 (*SD*=6.91) T-scores.

Table 3. Demographic, HIV, medical, psychiatric/substance use, and everyday functioning characteristics of the study sample at baseline

	Overall sample (N=180)	Subset of sample with follow-up data (N=79)
Demographics		
Age (years), *Mean (SD)*	61.1 (7.6)	62.2 (6.9)
% Male, *(n)*	83 (150)	78 (62)
Years of Education, *Mean (SD)*[†]	14.0 (2.9)	14.7 (2.7)
Race and Ethnicity, % *(n)*		
Non-Hispanic White	60 (108)	61 (48)
Hispanic/Latino	24 (44)	28 (22)
Black	16 (28)	12 (9)
Language of Testing, % *(n)*		
English	90 (162)	91 (72)
Spanish	10 (18)	9 (7)
County, % *(n)*		
San Diego	91 (163)	92 (73)
Riverside	9 (17)	8 (6)
Months between baseline and follow-up, *Mean (SD)*	--	23.9 (5.5)
HIV Disease Characteristics		
AIDS, % *(n)*	64 (116)	62 (49)
Estimated years of infection, *Mean (SD)*	22.3 (9.4)	22.5 (9.4)
Nadir CD4, *Median [IQR]*	168 [35, 309]	180 [50, 338]
CD4 absolute, *Median [IQR]*[a]	591 [444, 840]	653 [478. 997]
On ART, % *(n)*	89 (154)	89 (70)
undetectable plasma viral load, % *(n)*[b]	95 (117)	97 (58)
Years exposure to ART, *Mean (SD)*	15.8 (8.6)	18.0 (8.5)
VACS Index, *Mean (SD)*[c]	31.8 (15.9)	30.7 (14.4)
Medical Comorbidities		
Body mass index (kg/m^2), *Mean (SD)*[d]	27.2 (5.7)	27.3 (6.3)
HCV Co-infection, % *(n)*	22 (39)	22 (17)
Diabetes, % *(n)*	28 (48)	29 (23)
CVA, % *(n)*	13 (22)	11 (9)
Hypertension, % *(n)*	64 (113)	66 (52)
Hyperlipidemia, % *(n)*	67 (117)	72 (57)

Table 3. Demographic, HIV, medical, psychiatric/substance use, and everyday functioning characteristics of the study sample at baseline, continued

	Overall sample (N=180)	**Subset of sample with follow-up data (N=79)**
Psychiatric/Substance Use		
LT MDD, % *(n)*	65 (108)	68 (51)
Current MDD, % *(n)*[e]	7 (10)	4 (3)
LT Any Substance Dx, % *(n)*	68 (115)	70 (53)
LT Alcohol Use Dx, % *(n)*	55 (93)	59 (45)
LT Cannabis Use Dx, % *(n)*	37 (62)	32 (24)
LT Cocaine, % *(n)*	26 (42)	25 (19)
LT Methamphetamine Use Dx, % *(n)*	30 (50)	28 (21)
LT Other Drug Dx, % *(n)*	22 (40)	24 (19)
Current Any Substance Use Dx, % *(n)*[e]	4 (7)	4 (3)
Positive Utox, % *(n)*[d]	13 (21)	11 (8)
Everyday Functioning		
PAOFI Total, *Mean (SD)*	5.2 (6.5)	4.8 (5.6)
Dependent IADLs, % *(n)*[f]	23 (35)	23 (16)
Unemployed, % *(n)*[†]	75 (135)	64 (47)

Note: SD = Standard Deviation; IQR: Interquartile Range; ART=antiretroviral therapy; VACS=Veterans Aging Cohort Study; HCV = Hepatitis C virus; CVA = Cardiovascular Accident; LT =Lifetime; MDD=Major Depressive Disorder; Dx=Disorder; Utox=urine toxicology screening; PAOFI=Patient's Assessment of Own Functioning Inventory.

†: significantly different between the overall sample and the subset (p<.05), calculated using dependent sample t-test or McNemar's test

a: available for n=143 at baseline, n=66 for subset with follow-up data; b: only among a subset of those on ART (n=154 for overall sample; n=70 for subset with follow-up data), <50 copies/mL; c: available for n=131 at baseline, n=64 for subset with follow-up data; d: available for n=156 at baseline, n=67 for subset with follow-up data; e: available for n=157 at baseline, n=75 for subset with follow-up data; f: available for n=153 at baseline, n=71 for subset with follow-up data; g: positive for any substance

3.2 Factor Analyses

Sociocultural Factor Analysis. For the first EFA, all indicators of the sociocultural neighborhood vulnerabilities across San Diego and Riverside County were included in the model. Pearson correlations between the variables ranged from weak (r=-.10) to strong (r=.76) relationships (Table 4). Moderate to strong relationships were seen between % without internet and % without a computer (r=.76); % crowded and % Hispanic (r=.68); and % below the federal poverty line and % without internet (r=.62).

Table 4. Pearson r correlations between individual sociocultural variables across San Diego and Riverside County census tracts (N=1,255)

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1. % under 18 years old	1	--	--	--	--	--	--	--	--	--
2. % female households	.53*	1	--	--	--	--	--	--	--	--
3. % Hispanic	.45*	.48	1	--	--	--	--	--	--	--
4. % with no computer	-.05*	.14*	.36*	1	--	--	--	--	--	--
5. % without internet	-.01	.21*	.46*	.76*	1	--	--	--	--	--
6. % employed males	-.24	-.24*	-.33*	-.17*	-.20*	1	--	--	--	--
7. % foreign born	.24*	.29*	.54*	.24*	.25*	-.12*	1	--	--	--
8. % without a car	-.16*	.11*	.11*	.44*	.57*	-.02	.16*	1	--	--
9. % crowded	.41*	.52*	.68*	.23*	.36*	-.24*	.54*	.20*	1	--
10. % below poverty line	.10*	.38*	.46*	.48*	.62*	-.17*	.41*	.52*	.45*	1

Note: *: *p*-value<.001
1: % of the population under 18 years old;
2: % female headed households with dependent children;
3: % of the population Hispanic;
4: % of households without any type of computer;
5: % of households without any type of internet access;
6: of employed males over the age of 16 in management, business, science, and arts occupations;
7: % of the population not born in the US;
8: % of households without a car;
9: % crowded households (>1 person per room);
10: % of households with income in the last 12 months below the federal poverty line

The final PAF for the sociocultural vulnerabilities construct suggested that a 2-Factor solution best explained the data (Table 5). All variables were included in the final solution except for % of employed males over the age of 16 in management, business, science, and arts occupations. Upon inspection, the solution passed a priori metrics of model adequacy (i.e., eigenvalue for Factor 1 = 3.91, Factor 2 = 1.93; appropriate scree plot with an 'elbow'; KMO = .796, (KMO values ≥.70 are desired, (Hoelzle & Meyer, 2013; Kaiser, 1974)); Bartlett's test of Sphericity p <.001 (Bartlett, 1954)). Communalities ranged from .44 to .84 (communalities >.3 are desired (Fabrigar et al., 1999)). In addition, the parallel analysis comparing eigenvalues from the target data set with eigenvalues from randomly generated data indicated that a 2-Factor solution best represented the data: (a) Factor 1: 3.57 vs 0.15 and (b) Factor 2: 1.47 vs. 0.11.

The cumulative variance explained by the final 2-Factor solution was 55.56%, and the two factors respectively accounted for 39.05% and 16.51% of the variance. Using the rotated factor matrix for interpretation, five observed variables loaded on the first Factor (values ranged from .50 to .76) and four observed variables loaded on the second Factor (absolute values ranged from -.62 to -.90), comprising an acceptable factor structure (i.e., at least three variables loaded on each factor, with loadings > .50 in the same direction, without complex or cross-loadings (Child, 2006; Watkins, 2018)).

Factor 1 consisted of % Hispanic, % crowded, % of the population under 18 years old, % of female headed households with children under the age of 18, and % foreign born, meaningfully reflecting demographic and cultural aspects of the neighborhood (DiStefano et al., 2009; Ford et al., 1986). This factor was named 'Sociodemographic', with a higher z-score reflecting greater presence of demographic and housing features of the neighborhood more likely impacted by COVID-19. Factor 2 consisted of % of households without internet, % of households without a computer, % of households without a car, and % of households below the poverty threshold, which all loaded negatively onto the factor. This factor meaningfully reflected the economic aspects of a neighborhood and was named ‘Economic’ with a higher z-score reflecting greater presence of economic features of the neighborhood that would have heightened the impact of COVID-19 (Table 5). The correlation between the Sociodemographic and Economic factors were small (e.g., r=-.27).

Table 5. Loadings of individual neighborhood variables on the Sociodemographic and Economic Factors across San Diego and Riverside County (N=1,255)

	Sociodemographic	**Economic**
% Hispanic	**.76**	-.20
% crowded	**.75**	-.15
% under 18 years old	**.70**	.30
% female households	**.66**	-.01
% foreign born	**.50**	-.18
% without internet	.08	**-.89**
% without a computer	.02	**-.74**
% without a car	-.09	**-.68**
% below poverty line	.31	**-.61**

Note: Extraction Method: Principal Axis Factoring, rotation method: direct oblimin with Kaiser Normalization, rotation converged in 8 iterations. Bolded values indicate loadings of variables used in each factor

Physical Factor Analysis. For the second EFA, indicators of the physical neighborhood vulnerabilities across San Diego and Riverside County were included in the initial model, however, the model did not converge. Upon inspection, as Riverside County did not have walkability data, nor distance to nearest recreation center or nearest transit stop, this was the most likely explanation for poor model construction. Thus, the dataset was split by county and separate EFAs for the physical vulnerabilities were conducted for San Diego and Riverside County respectively.

For the EFA for San Diego County physical vulnerabilities, indicators of the physical neighborhood vulnerabilities for this county were included in the model (Table 6). Correlations were mostly weak (rs=.20-.30s), however, the highest correlations were between distance to nearest recreation center and distance to nearest park (r=.70) and distance to nearest transit stop and distance to nearest liquor store (r=.62).

All variables were included in the final solution except for walkability, Pollution Burden Index, and living in a food desert. The final PAF for the physical vulnerabilities construct for San Diego County only suggested that a 1-Factor solution best explained the data (Table 7). The solution passed a priori metrics of model adequacy (i.e., eigenvalue for Factor 1 = 2.80, an appropriate scree plot with an 'elbow'; KMO = .667 (KMO values $\leq$ .50 are generally considered unacceptable (Child, 2006; Kaiser, 1974; Watkins, 2018)); Bartlett's test of Sphericity *p* <.001 (Bartlett, 1954)). Communalities ranged from .35 to .51 (communalities >.3 are desired (Fabrigar et al., 1999)). In addition, the parallel analysis indicated that a 1-Factor solution best represented the data (i.e., target dataset eigenvalue 2.12 vs randomly generated data eigenvalue 0.19).

The variance explained by the factor was 45.09%. Using the unrotated factor matrix for interpretation, five observed variables loaded on the Factor (values ranged from .59 to .71), consisting of distance to liquor stores, health centers, recreation centers, transit stops and parks, reflecting an acceptable factor structure (i.e., at least three variables loaded on each factor, with loadings > .50 in the same direction, without complex or cross-loadings (Child, 2006; Watkins, 2018)). This factor meaningfully reflected the accessibility of and resources within a neighborhood and was named 'Undeveloped San Diego', with a greater z-score reflecting fewer physical resources in the neighborhood (Table 7).

An EFA was conducted for the physical vulnerabilities construct for Riverside County using indicators of the physical environment for this county using similar methods as listed above. Correlations were mostly negligible (r<.10) to weak (r-.11) (Table 6). Three strong relationships emerged between distance to nearest liquor store and health center (r=.83), and to the nearest park (r=.78) and between distance to nearest park and health center (r=.71).

The final PAF for the physical vulnerabilities construct for Riverside County suggested that a 1-Factor solution best explained the data. Similar to the EFA for San Diego County only, all variables were included in the final solution except for Pollution Burden Index and living in a food desert (Table 7). The solution passed a priori metrics of model adequacy (i.e., eigenvalue for Factor 1 = 2.55, an appropriate scree plot with an 'elbow'; KMO = .734 (KMO values ≥.70 are desired, (Hoelzle & Meyer, 2013; Kaiser, 1974)), Bartlett's test of Sphericity p <.001 (Bartlett, 1954)). Communalities ranged from .70 to .90 (communalities >.3 are desired (Fabrigar et al., 1999)). The parallel analysis also indicated that a 1-Factor solution best represented the data (i.e., target data eigenvalue: 2.27 vs randomly generated data eigenvalue: 0.16).

The variance explained by the factor was 77.71%. Using the unrotated factor matrix for interpretation, three observed variables loaded on the Factor (values ranged from .82 to .95), consisting of distance to liquor stores, health centers and parks, suggesting appropriate factor structure (i.e., at least three variables loaded on each factor, with loadings > .50 in the same direction, without complex or cross-loadings (Child, 2006; Watkins, 2018)). This structure once again meaningfully reflected aspects of resources within a neighborhood and was named 'Undeveloped Riverside', with similar directionality as 'Undeveloped San Diego'. 'Undeveloped San Diego' and 'Undeveloped Riverside' were combined into one variable called 'Undeveloped' reflecting the appropriate value per census tract, with higher z-scores indicative of less resources and development in the neighborhood (Table 7).

Table 6. Pearson r correlations between individual physical variables for San Diego and Riverside County census tracts respectively

San Diego County *(n=738)*								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1. Pollution Burden Index	1	--	--	--	--	--	--	--
2. Living in a food desert	.10	1	--	--	--	--	--	--
3. Kilometers to nearest liquor store	-.23	-.01	1	--	--	--	--	--
4. Kilometers to nearest health center	-.24	.04	.52	1	--	--	--	--
5. Kilometers to nearest park	-.18	.01	.31	.29	1	--	--	--
6. Kilometers to nearest recreation center	-.10	-.04	.42	.46	.70	1	--	--
7. Kilometers to nearest transit stop	-.30	.05	.62	.54	.33	.29	1	--
8. Walkability Index	.20	.02	-.26	-.24	-.23	-.25	-.27	1
Riverside County *(n=517)*								
	1	**2**	**3**	**4**	**5**	--	--	--
1. Pollution Burden Index	1	--	--	--	--	--	--	--
2. Living in a food desert	-.09	1	--	--	--	--	--	--
3. Kilometers to nearest liquor store	-.11	-.07	1	--	--	--	--	--
4. Kilometers to nearest health center	-.11	.07	.83	1	--	--	--	--
5. Kilometers to nearest park	-.05	.01	.78	.71	1	--	--	--

Note: Distance variables (3-7) are measured in kilometers

Table 7. Loadings of individual variables on the Undeveloped Factor for San Diego County (N=738) and Riverside County (N=517) separately

	Undeveloped San Diego	**Undeveloped Riverside**
Kilometers to nearest liquor store	**.71**	**.95**
Kilometers to nearest health center	**.69**	**.87**
Kilometers to nearest park	**.69**	--
Kilometers to nearest recreation center	**.67**	--
Kilometers to nearest transit stop	**.59**	**.82**

Note: = Principal Axis Factoring, only one factor was extracted thus the solution could not be rotated. 7 iterations required for San Diego; 10 iterations required for Riverside County. Bolded values indicate loadings of variables used in each factor.

Impact of COVID-19 Factor Analysis. The EFA for the COVID-19 impact on the neighborhood followed similar methods. The initial model included the percent of cumulative COVID-19 cases per zip code population, percent of zip code population fully vaccinated, distance to nearest COVID-19 testing center, and a measure of vaccine hesitancy per zip code population. Correlations were mostly weak, with vaccine hesitancy and percent of the zip code population fully vaccinated only moderately correlated (r=-.40) (Table 8).

Table 8. Pearson r correlations between metrics of the impact of COVID-19 on the neighborhood across zip codes in San Diego and Riverside County (N=171)

	1	**2**	**3**	**4**
1. Case Rate	1	--	--	--
2. Fully Vaccinated	.23	1	--	--
3. Kilometers to Testing Center	-.26	-.33	1	--
4. Vaccine Hesitancy	.38	-.40	.06	1

Note:
1: % positive cases per zip code population;
2: % fully vaccinated per zip code population;
3: Distance to nearest COVID-19 testing location;
4: Level of vaccine hesitancy based on survey results

The first PAF for the impact of COVID-19 on the neighborhood suggested a 2-Factor solution, but did not pass all a priori metrics of model adequacy (i.e., eigenvalue for Factor 1 = 1.57; Factor 2 = 1.43, no elbow depicted in the scree plot; KMO =.409, (KMO values $\leq$ .50 are generally considered unacceptable (Child, 2006; Kaiser, 1974; Watkins, 2018)); Bartlett's test of Sphericity p <.001 (Bartlett, 1954)), communalities ranging from .21 to .73 (communalities >.3 are desired (Fabrigar et al., 1999)). The cumulative variance explained by the suggested solution was 55.33%, and the two factors individually accounted for 29.33% and 26.01% of the variance, respectively, with vaccine hesitancy loading positively (.76) and percent of zip code fully vaccinated loading negatively (-.72) on the first factor, and only case rate loading on the second factor (.78) as distance to testing location did not have a sufficient loading (-.37). This indicated single variables per factors, which is not desired (i.e., at least three per factor). Furthermore, a parallel analysis indicated that a 1-Factor solution best represented the data when eigenvalues from the target data set were compared to eigenvalues from randomly generated data: 1.03 vs 0.26. However, when the EFA was rerun to extract one factor, the model did not converge.

Taking these results in conjunction with the weakly correlated Pearson correlations that indicated that the largest shared variability across the impact of COVID-19 variables was around 16% (i.e., r=-.40 squared), there was no indication of a shared common factor between these variables. Thus, the impact of COVID-19 on the neighborhood was operationalized as the percent of cumulative COVID-19 cases per zip code population for these analyses and averaged for each participant's 1km buffer region around their address (i.e., 'Case Rates'), with higher values indicating greater case rates in the neighborhood (i.e., higher impact of COVID-19).

The 'Sociodemographic, 'Economic', and 'Undeveloped' factors were all saved per census tract as regression factor scores. As such, the mean for the 'Sociodemographic factor was 1.26e-16 (*SD*=0.92), the mean for the 'Economic' factor was -3.89e-17 (*SD*=0.95), and the mean for the 'Developed' factor was -7.94e-17 (*SD*=0.96) (Appendix Table 1). All regression factor scores per census tract were then linked to each participant by calculating the average factor score per 1km buffer region around their address.

3.3 Descriptive Statistics of Neighborhood Factors

Table 9 displays the mean, standard deviation, range, median and interquartile range of the neighborhood factors for the subset of the sample with complete follow-up data, as well as for the cumulative COVID-19 case rate per zip code population. Values are all in comparison to other census tracts or zip codes in San Diego and Riverside County. The average levels of sociodemographic, economic, and undeveloped characteristics in this subset were between 0 and -0.5, with the minimum values between -0.5 and -2, and the maximum values between 0 and 2.1 (Table 9). The average percent of cumulative COVID-19 case rates for the neighborhoods where our subset of participants lived was 23%, with a range of 13 to 51%. We centered the average cumulative case rate per zip code population at the sample mean to include in regression analysis for ease of interpretation (i.e., 'Centered Case Rates'). Appendix Table 2 depicts the descriptive statistics for each of the individual neighborhood vulnerabilities for this subset.

Table 9. Descriptive statistics of neighborhood factors for the subset of the sample with complete follow-up data in relation to census tracts in San Diego and Riverside County, CA (N=79)

	Mean (SD)	Minimum	Median [IQR]	Maximum
Sociodemographic	-0.28 (0.80)	-1.54	-0.55 [-0.88, 0.19]	2.05
Economic	-0.22 (0.57)	-1.92	-0.08 [-0.52, 0.18]	0.86
Undeveloped	-0.46 (0.30)	-0.77	-0.59 [-0.67, -0.34]	0.77
Case Rates[a]	22.7 (6.6)	13	21 [18, 27]	51

Note: a = % cumulative cases per zip code population; SD = Standard Deviation; IQR: Interquartile Range

3.4 Correlations Between Neighborhood Factors and Changes in Cognition and Mood

Table 10 depicts Pearson r correlations across Sociodemographic, Economic, Undeveloped factors and Case Rates, as well as between these neighborhood vulnerabilities, Case Rates, and the independent outcomes of change in global scaled score and MOS-HIV Mental Health Summary T-score for the subset of the sample with complete follow-up data. Many of the relationships were negligible to weak (rs = |.01| to |.19|), however, the relationship between average COVID-19 case rates and the Sociodemographic factor was strongly positive (r=.83, p<.001). There were additional moderate negative correlations between the Sociodemographic and Economic factors (r=-.59, p<.001) and the average COVID-19 case rates and the Economic factor (r=-.52, p<.001). There was a weak negative correlation between the Undeveloped factor and the Economic factor (r=-.17, p=.02) (Table 10).

Table 10. Pearson r correlations across neighborhood factors, and between neighborhood factors and change in cognition and mental health in the sample with follow-up data (N=79)

	1	**2**	**3**	**4**
1. Sociodemographic Factor	1	--	--	--
2. Economic Factor	-.59**	1	--	--
3. Undeveloped Factor	.04	.17*	1	--
4. Case Rates	.83**	-.52**	.01	1
Change in GSS	.04	.10	-.17	.03
Change in MSS	-.17	.19	-.08	-.08

Note: ** indicates *p*-value<.001, * indicates *p*-value<.05; GSS = global mean scaled score; MSS = MOS-HIV Mental Health Summary T-score

3.5 Univariable Associations Between Sample Characteristics and Outcomes of Interest

To identify significant variables to be included in the multivariable models as potential covariates, we first examined univariable associations of change in GSS and MSS respectively with sample characteristics (i.e., demographic, HIV disease characteristics, medical comorbidities, and psychiatric/substance use variables) among the subset of the sample with complete follow-up data (Table 11). Only more years of exposure to ARTs (r=.26, *p*=.02) was significantly associated with less decline in GSS over time. Only MSS at baseline (r=-.36, *p*=.04) was significantly associated with more decline in MSS. Though months between visit did not show a significant association with either outcome and GSS at baseline was not associated with change in GSS, we included both variables in the initial multivariable regression models for theoretical reasons, following the statistical plan for removing terms not significant at *p*<.05 and re-running the model.

Table 11. Univariable association of change in GSS and MSS, respectively, with sample characteristics (n=79)

	Change in GSS		Change in MSS	
	r/d/η^2	*p*	r/d/η^2	*p*
Demographic				
Age[a]	-.00	.99	-.28	.11
Male[b]	0.14	.59	0.44	.26
Years of Education[a]	.01	.93	.20	.27
Race/Ethnicity[c]	0.04	.22	0.04	.57
Months between baseline and follow-up[a]	-.02	.87	.22	.20
HIV Disease Characteristics				
AIDS[b]	0.10	.69	0.11	.76
Estimated years of infection[a]	.11	.32	.03	.86
Nadir CD4[a]	.04	.77	-.14	.41
CD4 absolute[a]	.19	.12	-.04	.82
Years of exposure to ART[a]	.26	.02*	.22	.21
VACS Index[a]	-.03	.80	-.24	.20
Medical Comorbidities				
Body mass index[a]	.00	.97	-0.4	.80
HCV Co-infection[b]	-0.08	.77	0.05	.94
Diabetes[b]	-0.17	.52	-0.22	.65
CVA[b]	0.14	.78	0.14	.85
Hypertension[b]	0.03	.91	0.25	.41
Hyperlipidemia[b]	-0.22	.40	-0.01	.97
Psychiatric/Substance Use				
LT MDD[b]	0.04	.87	-0.21	.47
Current MDD[b]	0.34	.40	--	0
LT Any Substance Dx[b]	-0.17	.45	-0.56	.12
LT Alcohol Use Dx[b]	-0.13	.57	-0.37	.29
LT Cannabis Use Dx[b]	-0.28	.33	-0.64	.22
LT Cocaine[b]	-0.09	.76	-0.17	.66
LT Methamphetamine Use Dx[b]	0.14	.62	-0.36	.29
LT Other Drug Dx[b]	0.19	.48	-0.60	.31
Current Any Substance Use Dx[b]	-0.17	.87	--	0
Everyday Functioning				
PAOFI Total[a]	-.10	.41	-.08	.66
IADL Dependent[b]	-0.46	.22	0.07	.91
Unemployed[b]	0.06	.77	-0.06	.86
GSS at baseline[a]	-.002	.98	--	--
MSS at baseline[a]	--	--	-.36	.03*

Note: Among the subset of the sample with change in global scaled score (GSS, N=79) and MOS-HIV Mental Health Summary Score (MSS, N=34); ART=antiretroviral therapy; IQR: Interquartile Range; VACS=Veterans Aging Cohort Study; HCV = Hepatitis C virus; CVA = Cardiovascular Accident; LT =Lifetime; MDD=Major Depressive Disorder; Dx=Disorder; Utox=urine toxicology screening; PAOFI=Patient's Assessment of Own Functioning Inventory; *: *p*-value<.05, determined by [a]Pearson r correlations tests, [b]two-sample *t*-tests, and [c]ANOVA

3.6 Association Between Neighborhood Factors, COVID-19, and Neurocognitive Decline

Aim 1a. To investigate association between neighborhood factors and neurocognitive decline (i.e., negative change in GSS), we first ran a multivariable regression model on change in GSS including Sociodemographic, Economic, and Undeveloped factors as predictors, covarying for months between visits, GSS at baseline, and years of ART exposure, in the subset with complete follow-up neuropsychological data. After removing non-significant terms (i.e., months between visit p=.71; GSS at baseline p=.62), the final overall model on change in GSS (Table 12, Model 1) was not significant (p=.05). We compared the standardized coefficients (β) of all variables with their respective Pearson correlations (r) for suppression effects. Standardized coefficients were greater in comparison to the correlations for Sociodemographic (i.e., β.16 vs r=.04), Economic (i.e., β=.26 vs r=.10), and Undeveloped (i.e., β=-.17 vs r=-.16) factors, indicating a stronger relationship between each factor and change in GSS than the simple correlation, suggesting presence of a suppression effect.

Thus, we ran all possible subset regressions to find the best combination of predictors without evidence of suppression, removing non-significant terms (p>.05) per model. The final model on GSS change (Table 12, Model 2) included years of exposure to ARTs and the Undeveloped factor, with no evidence of suppression (i.e., βs were between 0 and r value). The overall model was significant (p=.04). There was a significant association between years of exposure to ARTs and positive change in GSS (b=0.03, p=.03), such that more years of ART exposure up to their baseline visit was associated with less decline in GSS. The Undeveloped factor was not significantly associated with GSS change (b=-0.47, p=.25), with the regression estimate equivalent to about half the SD of GSS change for the sample.

Aim 1b. We next investigated whether COVID-19 case rates may moderate the association of neighborhood factors on change in GSS among the subset sample. The first model on GSS change included Sociodemographic, Economic, Undeveloped factors, and Case Rates as independent predictors, and the interaction terms between Case Rates and each neighborhood factor (i.e., Sociodemographic x Case Rates, Economic x Case Rates, Undeveloped x Case Rates). Covariates were months between visits, GSS at baseline, and years of ART exposure. After removing non-significant terms (i.e., months between visit p=.57; GSS at baseline p=.47), the overall model (Table 12, Model 3) was not significant (p=.87), and none of the interaction terms were significantly associated with change in GSS (ps>.05). Thus, we removed the interactions between Case Rates and neighborhood factors and re-ran the model investigating main effects. This resulted in a non-significant overall model (p=.24) and comparing standardized coefficients with simple correlations indicated a stronger relationship between Sociodemographic (β=.15 vs r=.04) and Economic factors (β=.25 vs r=.10) and GSS change, suggesting evidence of suppression effects.

Thus, we again ran all possible subset regressions, removing non-significant terms (p>.05) per model. The final model on GSS change (Table 12, Model 4) included years of exposure to ARTs, and the main effects of the Undeveloped factor and Case Rates, with no evidence of suppression (i.e., βs were between 0 and r value). The overall model was not significant (p=.10), and there remained a significant association between years of ART exposure and change in GSS (b=0.03, p=.04), such that more years of ART exposure up to the baseline visit was associated with less decline in GSS at follow-up. However, there was no significant association between change in GSS and either the Undeveloped factor (b=-0.47, p=.25) or Case Rates (b=0.14, p=.94), with the regression estimates ranging from about a quarter to half a SD of GSS change for the sample.

Table 12. Results of multivariable regressions on change in global mean scaled score (GSS) by neighborhood vulnerabilities (aim 1a), moderated by COVID-19 case rates (aim 1b) in the subset with follow-up data (N=79)

	R_{adj}^2, F Ratio, *df*	Estimate (95% CI)	*t*-ratio	*p*-value	β	r	S
Aim 1a - GSS Change							
Model 1	0.08,			.05			
Years of ART exposure	2.48, 68	0.02 (-0.03 to 0.21)	1.79	.07	.21	.25	N
Sociodemographic		0.21 (-0.17 to 0.58)	1.11	.27	.16	.04	Y
Economic		0.43 (-0.05 to 0.91)	1.78	.08	.26	.10	Y
Undeveloped		-0.64 (-1.46 to 0.19)	-1.58	.13	-.17	-.16	Y
Model 2				.04*			
Years of ART exposure	.06, 3.31,	0.03 (-1.32 to -0.07)	2.15	.03*	.25	.25	N
Undeveloped	70	-0.47 (-1.28 to 0.34)	-1.16	.25	-.13	-.16	N
Aim 1b - GSS Change							
Model 3	-0.06,			.87	--		-
Years of ART exposure	0.48, 64	0.01 (-0.05 to 0.07)	0.32	.75			-
Sociodemographic		-0.99 (-2.32 to 0.34)	-1.49	.14			
Economic		-0.11 (-1.14 to 0.93)	-0.21	.84			
Undeveloped		0.75 (-1.08 to 2.57)	0.82	.42			
Case Rates		8.61 (-7.88 to 25.1)	1.04	.30			
Sociodemographic x Case Rates		-1.71 (-15.1 to 11.7)	-0.25	.80			
Economic x Case Rates		-6.41 (-27.9 to 15.0)	-0.60	.55			
Undeveloped x Case Rates		17.84 (-20.7 to 56.4)	0.92	.36			
Model 4				.10			
Years of ART exposure	0.05,	0.03 (0.00 to 0.06)	2.14	.04*	.25	.25	N
Undeveloped	2.18, 69	-0.47 (-1.29 to 0.34)	-1.15	.25	-.13	-.16	N
Case Rates		0.14 (-3.56 to 3.85)	0.08	.94	.01	.03	N

Note: *: *p*-value<.05; Standardized regression values between zero and the Pearson correlation were considered to not show evidence of suppression (S); GSS = global mean scaled score; CI = Confidence Interval; ART = antiretroviral therapy

3.7 Association Between Neighborhood Factors, COVID-19, and Worsened Mood

Aim 2a. To investigate associations between neighborhood factors and worsened mental health (i.e., negative change in MOS-HIV Mental Health Summary scores; MSS), we first ran a multivariable regression model on change in MSS including Sociodemographic, Economic, and Undeveloped factors as predictors, covarying for months between visits and MSS at baseline, in the subset with follow-up data (n=34). After removing non-significant terms (i.e., months between visit p=.42), the final overall model on change in MSS (Table 13, Model 1) was not significant (p=.12). We compared the standardized coefficients (β) of all variables with their respective Pearson correlations (r) for suppression effects. Standardized coefficients were greater in comparison to the correlations for the Sociodemographic (i.e., β.-.27 vs r=-.21) and Undeveloped (i.e., β=-.08 vs r=-.09) factors, as well as for MSS at baseline (i.e., β=-.42 vs r=-.37). Standardized coefficients were lower in comparison to the correlations for the Economic (i.e., β=-.00 vs r=.21) factor. As this pattern reflected suppression effects, we again ran all possible subset regressions, removing non-significant terms (p>.05) per model.

The final model on MSS change (Table 13, Model 2) included MSS at baseline and the Economic factor, with no evidence of suppression (i.e., βs were between 0 and r value). The overall model was not significant (p=.08), and there was no significant association between either MSS at baseline (b=-0.25, p=.06), nor the Economic factor (b=1.88, p=.36) and change in MSS, with the regression estimate equivalent to about a third the SD of MSS change for the sample.

Aim 2b. We next investigated whether COVID-19 case rates may moderate the association of neighborhood factors on change in MSS at follow-up. The first model included Sociodemographic, Economic, Undeveloped factors, and Case Rates as independent predictors, as well as the interaction terms between Case Rates and each neighborhood factor (i.e., Sociodemographic x Case Rates, Economic x Case Rates, Undeveloped x Case Rates). Covariates were months between visits and MSS at baseline. After removing non-significant terms (i.e., months between visit p=.54), the overall model (Table 13, Model 3) was not significant (p=.09), and none of the interaction terms were significantly associated with change in MSS (ps>.05). Thus, we removed the interactions between Case Rates and neighborhood factors and re-ran the model. This resulted in a non-significant overall model (p=.16) and suppression effects for MSS at baseline (β=-.46 vs r=-.37), Sociodemographic (β=-.45 vs r=-.21), Undeveloped (β=-.14 vs r=-.09), and Case Rates (β=.24 vs r=-.10).

Next, although we ran all possible subset regressions, removing non-significant terms (p>.05), all models showed continued evidence of suppression for Case Rates (i.e., βs for this variable were not between 0 and Pearson r correlation with MSS change). The best model on MSS change considering the impact of COVID-19 on the neighborhood (Table 13, Model 4) included MSS at baseline, the Economic factor, and Case Rates, as it did not show presence of suppression effects for MSS at baseline or the Economic factor. Bearing that in mind, this overall model was not significant (p=.17), and there were no significant associations between either MSS at baseline (b=-0.26, p=.06), the Economic factor (b=1.52, p=.53) or Case Rates (b=-6.25, p=.79) and change in MSS. The regression estimate for the Economic factor was equivalent to about a third the SD of MSS change for the sample, while the estimate for Case Rates was equivalent to about 1 SD.

Table 13. Results of multivariable regressions on change in MOS-HIV mental health summary score (MSS) by neighborhood vulnerabilities (aim 2a), moderated by COVID-19 case rates (aim 2b) in the subset with follow up data (N=34)

	R_{adj}^2, F Ratio, *df*	**Estimate (95% CI)**	***t*-ratio**	***p*-value**	**β**	**r**	**S**
Aim 2a – MSS Change							
Model 1	0.11, 2.02,			.12			
MSS at baseline	29	-0.31 (-0.59 to -0.05)	-2.39	.02*	-.42	-.37	Y
Sociodemographic		-2.47 (-6.31 to 1.38)	-1.31	.20	-.27	-.21	Y
Economic		-0.05 (-5.07 to 4.97)	-0.02	.98	-.00	.21	Y
Undeveloped		-3.25 (-10.5 to 4.00)	-0.92	.37	-.15	-.09	Y
Model 2				.08			
MSS at baseline	0.10, 2.74,	-0.25 (-0.51 to 0.01)	2.15	.06	-.33	-.37	N
Economic	31	1.88 (-2.23 to 5.98)	-1.16	.36	.16	.18	N
Aim 2b - MSS Change							
Model 1	0.19, 1.98,			.09	--		-
MSS at baseline	25	-0.38 (-0.67 to -0.09)	-2.67	.01*			-
Sociodemographic		-5.01 (-11.1 to 1.11)	-1.69	.10			
Economic		1.91 (-3.38 to 7.21)	0.74	.46			
Undeveloped		0.17 (-10.3 to 10.6)	0.03	.97			
Case Rates		67.8 (-8.15 to 143.8)	1.84	.08			
Sociodemographic x Case Rates		-40.8 (-104.9 to 23.4)	-1.31	.20			
Economic x Case Rates		-66.7 (-170.0 to 36.6)	-1.33	.20			
Undeveloped x Case Rates		173.6 (-114.3 to 461.4)	1.24	.23			
Model 2				.17			
MSS at baseline	0.07, 1.79,	-0.26 (-0.52 to 0.01)	-1.97	.06	-.34	-.37	N
Economic	30	1.52 (-3.45 to 6.51)	0.62	.53	.13	.21	N
Case Rates		-6.25 (-54.5 to 42.0)	-0.26	.79	-.05	-.10	Y

Note: *: *p*-value<.05; Standardized regression values between zero and the Pearson correlation were considered to not show evidence of suppression (S); MSS = MOS-HIV Mental Health Summary Score; CI = Confidence Interval

3.8 Multiple Imputation

Nature and structure of missing data. Out of our overall sample seen at baseline, 56.1% (n=101) of individuals were not seen for a follow-up visit. GSS at follow-up was imputed for these individuals to then create a new change in GSS score for the overall sample. The MOS-HIV was administered at baseline for only 85 participants (47.2%), and at follow-up for only 50 participants (63.3%). However, only 34 participants were administered the MOS-HIV questionnaire at both visits (43.0%). Therefore, MSS values at baseline were imputed for 95 individuals and MSS values at follow-up were imputed for 29 individuals. The respective scores were subtracted then create a new change in MSS score based on imputed results for 45 individuals. Months between visits was imputed for individuals not seen for a follow-up visit (n=101) to include as a variable in all regression analyses on imputed datasets. Years of ART exposure was imputed for 17 individuals at baseline (9%) and 14 participants at follow-up (17.7%) to include as a covariate in regression analysis on change in GSS using the imputed datasets.

Upon inspection of patterns of missing data, older age, higher years of education, being unemployed and having AIDS at baseline were each associated with having missing data at follow-up (*p*s<.05). As we had these variables in our dataset to account for missingness, missing at random (MAR) could be assumed and these variables were included in the imputation analyses. Once 100 imputed datasets were created, convergence was checked, and all imputed values had acceptable rhat values (< 1.01). Multivariable regression models were run on change in GSS and MSS respectively across the 100 imputed datasets, and the estimates pooled.

Pooled estimates of associations between neighborhood factors and change in global scaled scores. Table 14 depicts the results of iterative multivariable regression models on change in GSS (Models 1-2). The first iterative regression model included Sociodemographic, Economic, and Undeveloped factors as predictors, covarying for months between visits, GSS at baseline, and years of ART exposure. We removed non-significant terms (i.e., months between visit *p*=.97), however, unlike the non-imputed results, GSS at baseline was retained as a covariate (*p*=.04), and years of ART exposure was only associated with change in GSS at a trend level (*p*=.08). Nevertheless, years of ART was kept in the model to compare its parameter estimates against the non-imputed model results. The final overall model (Table 14, Model 1) indicated non-significant associations between neighborhood factors and change in GSS (*p*s>.10), with similar parameter estimates to the non-imputed results across variables, now with smaller ranges in 95% confidence intervals. Table 14, Model 2 replicates the subset regression which included only the Undeveloped neighborhood factor as a predictor, covarying for GSS at baseline and years of ART exposure. This model also showed a similar, non-significant association between the Undeveloped factor and change in GSS (*p*=.34), with a similar range in the 95% confidence interval as the non-imputed results.

Pooled estimates of relationships between neighborhood factors and change in global scaled scores, moderated by COVID-19. Table 14 also shows results of iterative multivariable regression models on change in GSS, moderated by COVID-19 case rates (Models 3-4). After removing non-significant terms (i.e., months between visit *p*=.97), the final overall model (Table 14, Model 3) indicated non-significant interaction effects between neighborhood factors and Case Rates on change in GSS (*p*s>.10), with similar parameter estimates to the non-imputed results across variables, now with smaller ranges in 95% confidence intervals. Table 14, Model 4 replicates the subset regression which included only the main effects of the Undeveloped neighborhood factor and Case Rates, covarying for GSS at baseline and years of ART exposure. This model also showed similar, non-significant associations between change in GSS and both the

Undeveloped factor (*p*=.34) and Case Rates (*p*=.61), with a smaller range in 95% confidence intervals.

Table 14. Pooled estimates of iterative multivariable regressions on change in global mean scaled score (GSS) by neighborhood vulnerabilities, and moderated by COVID-19 case rates (N=180 per dataset)

	Estimate (95% CI)	***t*-ratio**	***df***	***p*-value**
GSS Change				
Model 1				
GSS at baseline	-0.10 (-0.20 to -0.00)	-2.02	82.2	.04*
Years of ART exposure	0.02 (-0.00 to 0.05)	1.73	65.0	.08
Sociodemographic	0.20 (-0.17 to 0.56)	1.07	64.5	.27
Economic	0.39 (-0.08 to 0.88)	1.67	80.7	.11
Undeveloped	-0.54 (-1.39 to 0.30)	-1.29	56.6	.20
Model 2				
GSS at baseline	-0.10 (-0.20 to -0.00)	-2.06	86.2	.04*
Years of ART exposure	0.03 (-0.00 to 0.05)	1.94	67.1	.06
Undeveloped	-0.39 (-1.20 to 0.42)	-0.96	59.3	.34
GSS Change				
Model 3				
GSS at baseline	-0.10 (-0.20 to -0.00)	-2.03	80.5	.05
Years of ART exposure	0.03 (-0.00 to 0.05)	1.89	63.2	.06
Sociodemographic	0.10 (-0.47 to 0.67)	0.36	71.8	.72
Economic	0.38 (-0.10 to 0.86)	1.56	79.4	.12
Undeveloped	-0.58 (-1.44 to 0.28)	-1.34	66.6	.19
Case Rates	1.51 (-7.37 to 10.4)	0.34	80.2	.74
Sociodemographic x Case Rates	1.64 (-3.15 to 6.44)	0.68	99.9	.50
Economic x Case Rates	3.78 (-4.89 to 15.4)	0.87	90.7	.39
Undeveloped x Case Rates	-2.04 (-17.5 to 13.4)	-0.26	102.2	.79
Model 4				
GSS at baseline	-0.10 (-0.20 to -0.00)	-2.04	85.8	.04*
Years of ART exposure	0.03 (-0.00 to 0.05)	1.96	66.8	.05
Undeveloped	-0.39 (-1.20 to 0.42)	-0.96	58.8	.34
Case Rates	0.93 (-2.68 to 4.54)	0.51	60.1	.61

Note: Computed across 100 datasets; *: *p*-value<.05; GSS = global mean scaled score; CI = Confidence Interval; ART = antiretroviral therapy

Pooled estimates of relationships between neighborhood factors and change in MOS-HIV mental health summary scores. Table 15 depicts the results of iterative multivariable regression models on change in MSS (Models 1-2). The first iterative regression model included Sociodemographic, Economic, and Undeveloped factors as predictors, covarying for months between visits and MSS at baseline. We removed non-significant terms (i.e., months between visit p=.33), and the final overall model (Table 15, Model 1) indicated non-significant associations between neighborhood factors and change in MSS (ps>.10), with similar parameter estimates and 95% confidence intervals to the non-imputed results across variables. Greater MSS at baseline was significantly associated with a greater decline in MSS at follow-up (b=-0.39, p=.001). This value is comparable to the estimate produced using non-imputed data (b=-0.26), though was not statistically significant (p=.06). Table 15, Model 2 replicates the subset regression which included only the Economic neighborhood factor as a predictor, covarying for MSS at baseline. This model also showed a similar, non-significant association between the Economic factor and change in MSS (p=.91), with a smaller range in 95% confidence intervals than the non-imputed results.

Pooled estimates of the association between neighborhood factors and change in MOS-HIV mental health summary scores moderated by COVID-19 case rates. Table 15 also depicts results of iterative multivariable regression models on change in MSS, moderated by COVID-19 case rates (Models 3-4). After removing non-significant terms (i.e., months between visit p=.31), the final overall model (Table 15, Model 3) indicated non-significant interaction effects between neighborhood factors and Case Rates on change in MSS (ps>.10), with similar parameter estimates to the non-imputed results across variables, now with smaller ranges in 95% confidence intervals. Table 15, Model 4 replicates the subset regression which included only the main effects of the Economic neighborhood factor and Case Rates, covarying for MSS at baseline.

This model also showed similar, non-significant associations between change in MSS and both the Economic factor (*p*=.90) and Case Rates (*p*=.94), though the pooled estimate for the Economic factor (b=0.29) decreased compared to non-imputed results (b=1.52) and the pooled estimate for Case Rates increased (b=1.49 vs b=-6.24). Confidence intervals were similar in ranges between the imputed and non-imputed results.

Table 15. Pooled estimates of multivariable regressions on change in MOS-HIV mental health summary score (MSS) by neighborhood vulnerabilities, moderated by COVID-19 case rates (N=180 per dataset)

	Estimate (95% CI)	***t*-ratio**	***df***	***p*-value**
Aim 2a – MSS Change				
Model 1				
MSS at baseline	-0.39 (-0.62 to -0.17)	-3.57	30.5	.001*
Sociodemographic	-0.62 (-3.96 to 2.71)	-0.38	39.1	.71
Economic	-0.15 (-4.53 to 4.24)	-0.07	45.9	.95
Undeveloped	-2.11 (-9.33 to 5.10)	-0.59	39.4	.56
Model 2				
MSS at baseline	-0.39 (-0.61 to 0.16)	-3.52	30.8	.001*
Economic	0.19 (-3.42 to 3.81)	0.11	0.91	.91
Aim 2b – MSS Change				
Model 3				
MSS at baseline	-0.39 (-0.62 to -0.17)	3.58	30.2	.001*
Sociodemographic	-1.95 (-6.23 to 2.32)	-0.91	60.8	.37
Economic	-0.12 (-4.44 to 4.20)	-0.06	47.8	.96
Undeveloped	-1.88 (-9.32 to 5.57)	-0.51	44.0	.61
Case Rates	30.8 (-38.4 to 100.1)	0.89	63.7	.38
Sociodemographic x Case Rates	-9.98 (-43.6 to 23.6)	-0.59	102.6	.56
Economic x Case Rates	-7.51 (-64.8 to 49.8)	-0.26	108.0	.80
Undeveloped x Case Rates	19.8 (-98.5 to 138.1)	0.33	83.8	.74
Model 4				
MSS at baseline	-0.39 (-0.61 to -0.16)	-3.51	30.8	.001*
Economic	0.29 (-4.11 to 4.68)	0.13	39.1	.90
Case Rates	1.49 (-39.7 to 42.7)	0.07	33.0	.94

Note: Computed across 100 datasets; *: *p*-value<.05; MSS = MOS-HIV Mental Health Summary Score; CI = Confidence Interval

3.9 Exploratory Analyses

Additive composite of functional decline. As the average change in global scaled score over time was 0.05 (*SD*=0.99) scaled scores and the average change in MSS was -1.76 (*SD*=6.91) T-scores, this suggested that perhaps most of our sample may have had relatively stable cognition and mood over the two years of follow-up. In the efforts to capture a way of showing how our sample may have declined over time, we created an additive measure of functioning. This composite measure summed the difficulties in everyday functioning based on decline in 1) objective cognitive testing (global scale scores $\leq$ 1.5 scaled scores at follow-up); 2) self-reported cognitive impairment (PAOFI Total score increase at follow-up); 3) mental health (MOS-HIV Mental Health Summary T-score increase $\geq$ 5 at follow-up); as well as being 4) IADL dependent; and 5) unemployed. Individuals with one or more categories of decline were coded as "declined" (n=29) for a binary measure of functional decline. We then used this categorical measure as our outcome of interest and followed previously stated procedures (See Statistical Analyses) to investigate the association between neighborhood factors and change in functioning.

We first ran univariable associations between change in functioning and sample characteristics using two-sample *t*-tests, ANOVA, and Chi^2 tests to identify potential covariates with the additive composite. Older age (p=.02), higher nadir CD4 count (p=.04), having hypertension (p=.01), and not having a diagnosis of lifetime methamphetamine use disorder (p=.03) at baseline were related to functional decline at follow-up and thus were included in multivariable models as a covariate, along with months between visits.

Table 16 shows the results of multivariable logistic regression models on decline in functioning. The first model we ran included Sociodemographic, Economic, and Undeveloped factors as predictors, covarying for months between visits, age, nadir CD4 count, hypertension and lifetime methamphetamine use disorder. After removing non-significant terms (i.e., months between visit p=.24; lifetime methamphetamine use disorder p=.25), the final overall model on change in functioning (Table 16, Model 1) was significant (p<.001), as higher age (p=.03), higher nadir CD4 count (p=.01), and having hypertension (p=.01) were associated with greater odds of functional decline. None of the neighborhood factors were related to higher odds of functional decline (ps >.05).

We next investigated whether COVID-19 case rates may moderate the association of neighborhood factors on decline in functioning (Table 16, Model 2). The first model included Sociodemographic, Economic, Undeveloped factors, and Case Rates as independent predictors, as well as the interaction terms between Case Rates and each neighborhood factor (i.e., Sociodemographic x Case Rates, Economic x Case Rates, Undeveloped x Case Rates). Covariates were months between visits, age, nadir CD4 count, hypertension and lifetime methamphetamine use disorder. After removing non-significant terms (i.e., months between visit p=.39; lifetime methamphetamine use disorder p=.14), the overall model was significant (p=.002), though none of the interaction terms were significantly associated with change in functioning (ps>.05). We then removed the interaction terms between Case Rates and neighborhood factors and re-ran the model. This resulted in a significant overall model (p=.001; Table 16, Model 2), with higher age (p=.03), higher nadir CD4 count (p=.01), and having hypertension (p=.02) related to greater odds of functional decline. There were no significant relationships between decline in functioning and any of the neighborhood factors, nor a significant main effect of Case Rates (ps>.05). In fact, the estimates for Case Rates had a very wide confidence interval.

Table 16. Results of multivariable regressions on change in an additive measure of functional decline by neighborhood vulnerabilities and moderated by COVID-19 case rates in the subset with follow up data (N=79)

	χ^2, df	**Odds Ratio (95% CI)**	***p*-value**
Functional Change			
Model 1	23.8, 6		<.001*
Age		1.11 (1.01 to 1.22)	.03*
Nadir CD4		1.00 (1.00 to 1.01)	.01*
Hypertension		5.33 (1.38 to 26.8)	.02*
Sociodemographic		0.44 (0.16 to 1.10)	.09
Economic		0.31 (0.08 to 1.19)	.09
Undeveloped		2.93 (0.41 to 23.8)	.30
Functional Change			
Model 2	23.8, 7		.001*
Age		1.11 (1.01 to 1.23)	.03*
Nadir CD4		1.00 (1.00 to 1.01)	.01*
Hypertension		5.27 (1.24 to 22.4)	.02*
Sociodemographic		0.50 (0.12 to 2.00)	.33
Economic		0.30 (0.07 to 1.18)	.09
Undeveloped		2.98 (0.41 to 24.1)	.28
Case Rates		0.08 (0.00 to 1,609,576)	.78

Note: *: *p*-value<.05; CI = Confidence Interval

Categorical change in cognition and mental health. In an effort to increase sample size at follow-up, we created binary categorical variables called “poor cognition” and “poor mental health” for both timepoints. For cognition, individuals with a global scaled score <7 were categorized as "poor," at baseline and follow-up. We compared follow-up “poor cognition” values to baseline. Of the 79 individuals with data at both timepoints, 73 individuals (92.4%) remained stable over two years, one participant improved to “normal” (i.e., global scaled score $\geq$7), and only five individuals declined over time. We did not pursue examining whether neighborhood factors would be associated with worsened “poor cognition” over time due to a very small sample declining.

For categorical mental health at baseline, we primarily used the BDI-II, as most individuals (n=161) were administered this measure of depression. A BDI-II total score of ≥ 14 was categorized as 'poor,' and < 14 as 'normal.' Six individuals at baseline did not have a BDI-II and were given the Profile of Mood States (POMS) (Nyenhuis et al., 1999). The POMS Depression and Dejection Scale has been shown to have adequate sensitivity (92%) and specificity (67%) when used a screener for depression among PWH with major depressive disorder (Wilkins et al., 1995). Thus, for the remaining six individuals without BDI-II at baseline, a raw score of ≥ 7 on the POMS Depression-Dejection subscale was categorized as "poor," <7 as "normal," (Patterson et al., 2006) and combined with the categorization using BDI-II. For the categorical variable at follow-up, the BDI-II was only administered to five individuals and was used for these participants based on the ≥ 14 cutoff categorization. The majority of individuals at follow-up were administered the MOS-HIV 34-item scale (n=50). A MOS-HIV Mental Health Summary Scale T-score at follow-up that was 1.5 standard deviations lower than the sample mean was categorized as "poor," (i.e., T-score < 35.92; "normal": T-score ≥ 35.92). Eleven individuals were not administered a MOS-HIV or BDI-II at follow-up. For these individuals the POMS Depression-Dejection subscale was used to categorized mental health at follow-up as "poor" (raw score of ≥ 7) or "normal" (raw score <7) and combined with others for a measure of "poor mental health" at follow-up (n=62). Sixty-one out of 79 people at follow-up had "poor mental health" values for both visits.

Change in categorical mental health was assessed by comparing follow-up "poor mental health" values to baseline. Of the sixty-one with data at both timepoints, 47 individuals (77.1%) remained stable over two years, 41 (67.2%) not having "poor mental health" at either visit. Six individuals improved at follow-up and eight declined. Given this lack of variability over time even when combining metrics across measures of mood to increase our sample size at follow-up, we did not pursue investigating whether neighborhood factors would be associated with worsened "poor mental health" over time.

Individual neighborhood markers of interest. Although the neighborhood factors 'Sociodemographic', 'Economic', and 'Undeveloped' were not significantly associated with change in cognition or mental health in our sample, these factors did not include all proposed neighborhood vulnerabilities. Thus, we were interested in investigating potential associations between both change in cognition and mood with individual neighborhood variables.

We first examined the univariable associations between change in GSS with individual neighborhood vulnerabilities among the subset with complete follow-up data using Pearson r correlations (Table 17). These relationships ran from negligible (i.e., |.01|) to weak (i.e., |.15|), and were not statistically significant (*p*s>.10). Associations between these individual variables and change in MSS were also negligible (i.e., |.01|) to weak (i.e., |.31|) and not statistically significant (*p*s>.05), except for % crowded households (r=-.36, *p*=.03). Thus, this individual variable was regressed onto change in MSS, covarying for months between visits and MSS at baseline on the sample with complete MSS data at follow-up (n=34).

Table 17. Univariable association of change in GSS and MSS respectively with individual neighborhood vulnerabilities among the subset with complete follow-up data (N=79)

Neighborhood Vulnerability	Change in GSS		Change in MSS	
	r	*p*-value	r	*p*-value
Pollution Burden Index	.04	.70	.08	.65
Living in a food desert	.11	.32	-.02	.90
Walkability index	.02	.86	-.01	.98
Kilometers to nearest liquor store	-.08	.47	-.03	.88
Kilometers to nearest health center	-.06	.59	-.03	.86
Kilometers to nearest park	-.06	.57	-.16	.36
Kilometers to nearest recreation center	-.09	.46	-.11	.59
Kilometers to nearest transit stop	-.05	.68	-.15	.42
% of the population under 18 years old	-.05	.67	-.16	.36
% female headed households[a]	.07	.53	-.17	.34
% of the population Hispanic	.02	.87	-.10	.56
% of households without a computer	-.15	.17	-.19	.27
% of households without internet	-.13	.24	-.19	.27
% employed males in professional occupations[b]	.04	.74	-.04	.83
% of the population not born in the US	.08	.50	-.09	.60
% of households without a car	-.12	.28	-.21	.23
% crowded households	.08	.50	-.36	.03*
% poverty	-.01	.91	-.15	.39

Note: *: *p*-value<.05; r = Pearson correlations; a=with dependent children; b= over the age of 16 in management, business, science, and arts occupations; GSS = global mean scaled score; MSS = MOS-HIV Mental Health Summary T-score

After removing non-significant terms (i.e., months between visits, *p*=.43), the overall model was significant (R^2_{adj}=.19; $F_{2,31}$=4.83; *p*=.01). Controlling for the significant negative relationship between MSS at baseline and change in MSS (b=-0.29, 95% CI (-0.53, -0.04), *p*=.02, β=-.38), Figure 1 depicts the statistically significant relationship between % crowded households and change in MSS (*p*=.04). This model indicated that for every 10% increase in crowded households in the participants' neighborhoods, MSS scores declined an additional 4.5 T-scores, indicating worsened mood at follow-up (b=-0.45, 95% CI (-0.88, -0.03), β=-.33), with the regression estimate for crowded housing equivalent to less than a tenth of the SD of MSS change for the sample. However, upon further investigation, this relationship was no longer significant (b=-0.38, 95% CI (-0.79, 0.02), p=.06, β=-.32) when one individual was excluded due to having a MSS change score greater than three standard deviations above the sample mean, though the effect was only attenuated by 16%.

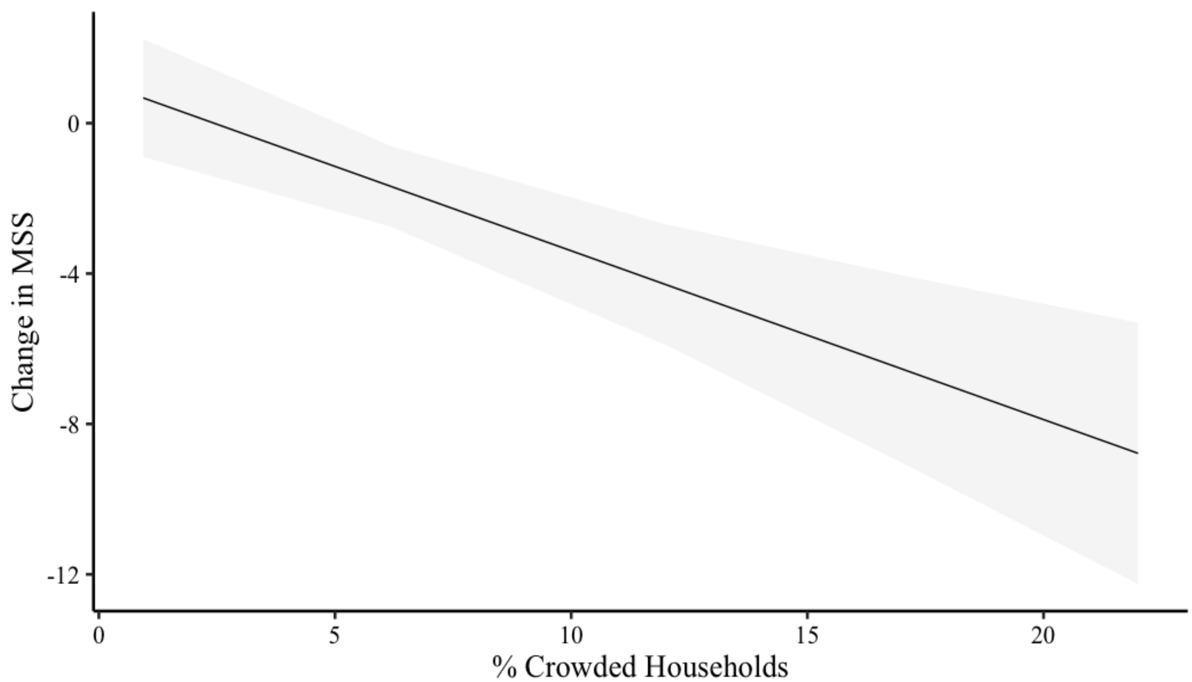

Figure 1. Association between % crowded households and change in MOS-HIV mental health summary score (MSS) in the subset with follow up data (n=34)

Note: R^2_{adj} = .19; $F_{2,31}$ = 4.83; p = .01, controlling for main effect of MSS at baseline (b=-0.29, 95% CI (-0.53, -0.04), p=.02, β=-.38)

Following our proposed aims, we next investigated whether COVID-19 case rates would modify the relationship between % crowded housing and change in MSS. The first model included % crowded housing and Case Rates as independent predictors, as well as their interaction term, covarying for months between visits and MSS at baseline. After removing non-significant terms (i.e., months between visit p=.66), the overall model was significant (R^2_{adj} = .18; $F_{4,29}$ = 2.84; p=.04), however, Case Rates did not significantly modify the association of % crowded housing with change in MSS (b=32.2, 95% CI (-624.2, 688.7), p=.92). Thus, we removed the interaction term and re-ran the model. This resulted in a significant overall model (p=.02) with statistically significant negative relationships between change in MSS and % crowded housing (b=-.79, 95% CI (-1.45, -0.12), p=.02) and MSS at baseline (b=-0.28, 95% CI (-0.52, -0.04), p=.02). There was no main effect of Case Rates on change in MSS (b=38.4, 95% CI (-19.6, 96.4), p=.19). This model also showed evidence of suppression effects for % crowded housing (β=-.59 vs r=-.36), and Case Rates (β=.33 vs r=-.10).

Given the size of the subset sample with change in MSS scores (n=34), we conducted a multiple imputation using the same methodology as listed above (See 2.8 Handling Missing Data) to account for potential influence of missingness on our results. MSS values at baseline were imputed for 95 individuals and MSS values at follow-up were imputed for 29 individuals to then create a new change in MSS score. Months between visits was imputed for individuals not seen for a follow-up visit. Age, years of education, employment and AIDS status at baseline were included in the imputation to at least partially account for missingness. Convergence was checked for the 100 imputed datasets (all rhat values < 1.01). Multivariable regression models were run on change in MSS across the 100 imputed datasets, and estimates pooled.

Table 18 depicts the results of iterative multivariable regression models on change in MSS (Model 1). The first iterative regression model included % crowded housing as the main predictor of interest, covarying for months between visits and MSS at baseline. After removing non-significant terms (i.e., months between visit p=.20), unlike the non-imputed results, there was no significant association between % crowded housing and change in MSS (p=.49). Higher MSS at baseline remained statistically significantly related to more decline in MSS scores at follow-up (p<.001).

Table 18, Model 2 depicts results from the iterative multivariable regression models investigating the relationship between % crowded housing on change in MSS, moderated by COVID-19 case rates. Initial covariates were the same as stated above. After removing non-significant terms (i.e., months between visit p=.18), the final pooled estimates (Table 15, Model 2) indicated a non-significant interaction effect between % crowded housing and Case Rates on change in MSS (p=.35), with different parameter estimates compared to the non-imputed results. Table 18, Model 3 replicates the subset regression which included only the main effects % crowded housing and Case Rates, covarying for MSS at baseline. This model showed non-significant associations between change in MSS and both % crowded housing (p=.23) and Case Rates (p=.35).

The significant negative association between baseline MSS and change in MSS seen in the non-imputed results also emerged in the pooled estimate results (p<.001). Upon further investigation of this relationship in the non-imputed dataset, this relationship was no longer significant when one individual was excluded due to having a MSS change score greater than three standard deviations above the sample mean.

Table 18. Pooled estimates of multivariable regressions on change in MOS-HIV mental health summary score (MSS) by % crowded housing, moderated by COVID-19 case rates (N=180 per dataset)

	Estimate (95% CI)	***t*-ratio**	***df***	***p*-value**
MSS Change				
Model 1				
MSS at baseline	-0.37 (-0.56 to -0.17)	-3.74	35.6	<.001**
% Crowded housing	-0.12 (-0.48 to 0.23)	-0.69	35.6	.49
MSS Change				
Model 2				
MSS at baseline	-0.36 (-0.56 to -0.16)	-3.71	35.1	<.001**
% Crowded housing	-0.26 (-0.77 to 0.25)	-1.02	43.2	.31
Case Rates	35.0 (-17.2 to 87.2)	1.34	58.2	.18
% Crowded housing x Case Rates	-1.25 (-3.91 to 1.41)	-0.94	88.3	.35
Model 3				
MSS at baseline	-0.36 (-0.56 to -0.16)	-3.71	35.1	<.001**
% Crowded housing	-0.30 (-0.80 to 0.20)	-1.22	43.2	0.23
Case Rates	21.6 (-24.7 to 68.0)	0.94	43.2	0.35

Note: Computed across 100 datasets; **: *p*-value<.001, *: *p*-value<.05; MSS = MOS-HIV Mental Health Summary Score; CI = Confidence Interval

Associations between neighborhood factors and cognition and mood at baseline. We were interested in the potential cross-sectional relationships between neighborhood factors and both cognition and mood. We first examined the association between global mean scaled scores at baseline with Sociodemographic, Economic, and Neighborhood factors. As this outcome was significantly different between non-Hispanic Whites and minoritized groups (i.e., Blacks and Latinos, *p*<.001), we stratified analyses by non-Hispanic Whites (n=101) and minoritized groups (n=79), in order to prevent confounding associations between race and ethnicity and neighborhood factors. To identify potential covariates, univariable associations between global mean scaled scores and sample characteristics at baseline were run per racial and ethnic group. For minoritized groups, age (*p*<.01), years of education (*p*=.04) estimated duration of HIV infection (*p*=.02), hypertension (*p*=.01), and employment status (*p*=.02) were significantly related to global mean scaled scores. Hypertension (p=.02), PAOFI Total score (p=.03), and employment status (p<.001) were significantly related to global scaled score at baseline for Whites. All models were adjusted for demographics (i.e., age, sex, years of education), and non-significant terms (p>.05) removed and the models re-run. There were no associations between any of the neighborhood factors and global mean scaled score at baseline (ps>.10) for either Whites or minoritized groups, and all possible subset regression models reflected evidence of suppression effects (i.e., βs were not between 0 and r value).

We repeated these analyses using global mean T-scores at baseline, for which scaled scores for each test were corrected for demographic effects on cognitive test performance (i.e., age, sex, years of education) based on published normative data for non-Hispanic Whites, non-Hispanic Blacks, and Spanish-speaking Latinos (references to the respective normative adjustments for the administered comprehensive cognitive battery are listed in (Kamalyan et al., 2021). Normative data for English-speaking Latinos was only available for three subtests of the Weschler Adult Intelligence Scale – 3rd Edition (WAIS-III): Digit Symbol, Symbol Search, and Letter Number Sequencing tests (Taylor & Heaton, 2001). Otherwise, norms for English-speaking Whites were used to convert raw scores for English-speaking Latino into T-scores. Individual test T-scores were then averaged to create a global mean T-score. This outcome did not significantly differ by racial/ethnic group. Thus, in the overall sample, covariates included sex (p=.007), years of education (p=.003), hypertension (p=.02), PAOFI Total score (p<.001), IADL dependence (p=.02), and employment status (p<.001). Once again, we did not find statistically significant associations between any of the neighborhood factors and global mean T-scores at baseline (ps>.10), with continued evidence of suppression effects for the predictors of interest.

As for the relationships between neighborhood factors and mood at baseline, we first chose to conduct these analyses with BDI-II as the outcome, as this questionnaire was the most commonly administered measure of depressive symptoms across studies at baseline (n=161) and was the originally proposed mood measure of interest. BDI-II values did not significantly differ by racial/ethnic group. Thus, in the overall sample, covariates included age (p=.01), AIDS status (p=.0), PAOFI Total (p<.001) and IADL dependence (p<.001). All substance use characteristics were significantly associated with BDI-II scores at baseline (ps<.03), aside from lifetime cocaine use disorder and lifetime other drug use disorder. Thus, we chose to include the encompassing category of lifetime any substance use disorder diagnosis as a covariate for a more parsimonious approach. Although it was significantly associated with BDI-II at baseline, we did not include current any substance use disorder, as this encompassed only 7 individuals. Lastly, both lifetime and current major depressive disorder were significantly associated with BDI-II at baseline (ps<.01), but given that our outcome was depressive symptoms, we did not include these two variables in our models. As such, after adjusting for age, AIDS status, PAOFI Total, IADL dependence, and lifetime any substance use disorder, we did not find any significant associations between any of the neighborhood factors and depressive symptoms at baseline (ps>.10). Subset regression models all showed evidence of suppression effects for the neighborhood factors.

To compare cross-sectional analyses with our results investigating change in mood, we also examined the associations between MOS-HIV Mental Health Survey T-scores at baseline with neighborhood factors. Among the overall sample at baseline, 85 individuals were administered this questionnaire. MOS-HIV Mental Health Survey T-scores did not significantly differ by racial and ethnic group, thus covariates included lifetime major depressive disorder diagnosis (p=.006), PAOFI Total (p<.001) and IADL dependence (p<.001). Similar to BDI-II analysis and change in

MSS, there were no significant associations between MOS-HIV Mental Health Survey T-scores at baseline and any of the neighborhood factors (*p*s>.10), with continued evidence of suppression effects.

4. DISCUSSION

This study investigated whether sociocultural and physical neighborhood vulnerabilities influenced neurocognitive and mental health decline in a diverse cohort of older people living with HIV (PWH) in southern California before and during the COVID-19 pandemic, and whether the impact of the pandemic on neighborhoods themselves moderated these relationships. Neighborhood composite measures of sociodemographic and economic vulnerabilities and access to resources were not related to significantly greater neurocognitive decline or worsened mood over two years in our sample of older diverse PWH. There was no evidence of a significant moderating effect of higher rates of COVID-19 case rates on the relationship between neighborhood vulnerabilities and cognitive or emotional decline for our sample.

4.1 Neighborhood Features Not Associated with Decline in Cognition or Mood

We hypothesized that neighborhood sociocultural and physical features would be related to change in cognition and mood among PWH, such that living in a more disadvantaged neighborhood before and during the COVID-19 pandemic would result in steeper neurocognitive decline and worsened mood. We did not find any significant associations between any of our neighborhood factors and either change in cognition or mood at follow-up.

Neighborhood Factors and Cognition. To our knowledge, our analyses were the first to investigate how physical and sociocultural neighborhood features may be associated with cognitive decline among older diverse PWH. Previous work among older adults living without HIV has reported that communities with poor physical/built neighborhood features or lower socioeconomic status have higher rates of neurocognitive impairment (Besser et al., 2017; Diez Roux & Mair, 2010; Finlay et al., 2021; Hunt et al., 2021; Sheffield & Peek, 2009; Tallon, 2017; Vassilaki et al., 2023) and are at higher risk of developing Alzheimer’s Disease (Powell et al., 2020). The pathways underlying these associations are likely multifactorial, as living in more disadvantage neighborhoods may contribute to increased sleep disruption due to increased noise pollution (Hunter et al., 2018); worse diet due to lower proximity to healthy food (Deary et al., 2009); lower levels of physical activity due to fewer built resources (Chen et al., 2022); increased systemic inflammation activated by higher levels of air pollution (Ilango et al., 2021; Kulick et al., 2020); as well as increased cardiovascular and metabolic dysregulation sustained by chronic stress (i.e., allostatic load) (Booth et al., 2015; Geronimus et al., 2006; Muñoz et al., 2021). Studies among PWH have shown associations between lower cognitive performance and poor sleep (Campbell et al., 2022; Mahmood et al., 2018); lower levels of exercise and poor diet (L. H. Rubin et al., 2021; N. Winston et al., 2020); higher levels of cardiovascular risk factors (McIntosh et al., 2021); and allostatic load (Fazeli et al., 2020). This body of literature suggested our hypothesis that specific neighborhood features may perpetuate these noted mechanisms and in turn impact cognition among PWH, but we did not find significant associations in our sample. Additional work among samples with sufficient statistical power is needed to clarify whether these findings are upheld, but it is possible that, for older diverse PWH, there is no significant relationship between neighborhood factors and cognition. Perhaps further research may provide evidence of a relationship, but that the effect size of the impact of neighborhood on cognition for this group is small, and therefore undetectable using our small sample size. Furthermore, if additional studies either replicate our lack of significant findings or show limited strength in the associations between neighborhood and cognition, this relationship may not be clinically meaningful.

In contrast, it is possible that our lack of significant associations between cognition and mood may be due to the fact that we did not have enough individuals living in neighborhoods with greater levels of sociodemographic and economic vulnerabilities or lower access to resources.

Though the range of the factor scores for the sample was adequate, the majority had neighborhood factor values between -1 and 0.5. This low variability in the distribution of neighborhood vulnerabilities for our sample may have contributed to our lack of associations between neighborhood factors and change in cognition or mood. Additionally, we designed our initial regression models by including more than one neighborhood factor as independent variables, as these neighborhood constructs are theoretically linked. However, even after investigating the factors individually due to continued evidence of suppression effects, there were no significant relationships with change in cognition.

Notably, in a systematic review, Besser and colleagues suggested that the evidence for the effects of neighborhood characteristics on cognition among older adults living without HIV in observational studies is modest at best (Besser et al., 2017). However, the most conservative sample size among the studies listed was an N of 412 (Tallon, 2017), a value over five times our current study's (N=79), and over double our imputed sample size (N=180). In the context of our smaller sample size of individuals at follow-up, the size of the regression estimates of the neighborhood factors on cognition was negligible to small. Thus, although the theoretical relationship may be warranted, we may have been underpowered to detect this potential small to moderate effect of neighborhood effects on cognition due to a higher attrition rate and restricted range of neighborhood vulnerabilities for our sample of PWH.

Limited Neurocognitive Decline. Another potential reason we did not find an association between sociocultural or physical neighborhood vulnerabilities and change in neurocognition may be due to cognitive test performances for our sample at follow-up revealing an average pattern of stability, even after adjusting for expected practice effects. These results are inconsistent with the handful of published studies investigating change in neurocognition during the COVID-19 pandemic (Amieva et al., 2022; Bakker et al., 2023; Borges-Machado et al., 2020; Hua et al., 2023; C. Li et al., 2023; Matsui et al., 2023; Menze et al., 2022; Tondo et al., 2021), noting accelerated cognitive decline among older adults. However, many of these studies have been conducted among older adults without HIV, with mild cognitive impairment and/or dementia, and/or using cognitive screeners as indicators of cognitive functioning (i.e., Mini-Mental State Examination, Telephone Interview for Cognitive Status). No published study has yet investigated changes in cognition among PWH during the COVID-19 pandemic, using a comprehensive battery of neurocognitive assessments. Our administered neuropsychological battery is sensitive to detect impairment due to HIV (Cysique et al., 2011) and equipped to measure longitudinal changes in global cognition as compared to quick screeners (Nakazato et al., 2014; Skinner et al., 2009). However, cognitive trajectories do not uniformly decline across virally suppressed PWH as opposed to those with neurodegenerative diseases such as Alzheimer's Disease and Related Dementias (Antinori et al., 2007; Milanini & Valcour, 2017). Accordingly, while higher rates of memory decline were noted among a mixed memory clinic population a year after the onset of the pandemic (Bakker et al., 2023), in HIV-associated neurocognitive impairment, typically a proportion of individuals decline over time, others improve, but most stay stable (Aung et al., 2023; Heaton et al., 2015). As previous studies have shown evidence of neurocognitive decline even over the course of two years (Watson et al., 2022), our cognitive outcome was conceptualized as a difference score between two time periods before and after the onset of the pandemic in attempt to identify whether a greater proportion of PWH cognitively declined during a historically high period of chronic stress. However, a difference score may not have been sufficient to capture the nature of cognition over time among PWH, as it can range between improvement, stability, subtle decline, sustained impairment, and abnormal cognitive aging (Aung et al., 2023; Qu et al., 2022; Tennant et al., 2022). Further investigations among this sample may consider incorporating additional timepoints before and after the onset of the COVID-19 pandemic to take advantage of more sophisticated methods of measuring change in neurocognition in HIV over time, such as linear mixed methods (Aung et al., 2023; Bakker et al., 2023; C. Li et al., 2023; Qu et al., 2022), growth-models (Sharifian et al., 2020), survey linear regression models (Duff, 2012; Mahanna-Gabrielli et al., 2023), or Cox proportional hazard models (Heaton et al., 2015; Watson et al., 2022).

Furthermore, receiving consistent and long-term treatment for HIV infection has been shown to contribute to stable HIV disease and minimize cognitive decline (Aung et al., 2023; Heaton et al., 2015; Hinkin et al., 2002; A. Winston et al., 2013). Our findings replicated this association by showing that greater years of antiretroviral therapy at baseline was significantly related to less cognitive decline at follow-up, perhaps reflecting longer duration of treatment, stable HIV disease, and greater access to healthcare for our sample (Al-Khindi et al., 2011; A. Winston & Vera, 2014). Though this association was no longer significant using imputed datasets, this may be a product of imputing cognitive data for 56.1% of the sample. Even just 50% of missingness in a sample size of 120 has shown to still result in a degree of bias after using multiple imputation regression methods (Mishra & Khare, 2014). In addition, the retention of baseline cognition in the imputed models may have explained more of the variance in change in cognition compared to years of antiretroviral therapy. Furthermore, it is possible that the method of imputation itself did not fit the true pattern of missingness (i.e., missing not at random), potentially contributing to biased results (Enders, 2017; D. B. Rubin, 1988). Our longitudinal analyses need replication in a larger sample of PWH to examine which of our results are supported.

Finally, of the studies reporting declines in cognition among older adults during the COVID-19 pandemic (Amieva et al., 2022; Bakker et al., 2023; Borges-Machado et al., 2020; Hua et al., 2023; C. Li et al., 2023; Matsui et al., 2023; Menze et al., 2022; Tondo et al., 2021), none of these studies incorporated the potential impact of one's neighborhood on cognitive trajectories during a period of confinement to our homes. What's more, most of these studies were conducted outside of the US (i.e., Slovenia, Japan, Italy, Germany, Portugal, France, Spain, and the Netherlands). If these associations had been investigated across multiple geographic regions, it would remain difficult to compare with any potential relationships found in the US, as there is no universal measure of neighborhood that quantifies information about varying environments and cultures around the globe in a standard way (D. Ding et al., 2013). Furthermore, the US has a practice of structural racism engrained in historic and ongoing policies that impact neighborhood composition and structure (Churchwell et al., 2020; Feagin & Bennefield, 2014; Krieger, 2020; Riley, 2018; Rothstein, 2017), which is quite distinct compared to other nations. Taken together, additional investigations must be conducted to determine whether neighborhood sociodemographic, economic, or access to resources are related to changes in cognition among older diverse PWH living in the US.

Neighborhood Factors and Mood. Similar to our results with cognitive decline, we did not find any significant associations between any of our neighborhood factors and change in mood at follow-up. Prior studies that report effects between neighborhood and depression or stress are among HIV- individuals, have larger sample sizes (i.e., $\geq$ 200), investigate individual variables of interest, and have implemented different statistical methods (i.e., logistic regression, growth-models, structural equational models), making it difficult to compare our own small to large regression estimates to effect sizes across these studies (Barnett et al., 2018; Berke et al., 2007; Ivey et al., 2015; Joshi et al., 2017; Kim, 2010). These previous findings appear to suggest that, for the general population, there are individual mechanisms that underly the relationships between each of our neighborhood features and changes in mental health. However, these specific relationships have not been studied for older PWH, therefore, further work is needed to understand if neighborhood pathways to mental health issues such as social connectedness, levels of crime and safety, access to mental health services and healthy coping (Bustamante et al., 2022; Diez Roux & Mair, 2010; Ivey et al., 2015; Joshi et al., 2017) would relate to rates of depression or other psychiatric outcomes for PWH. While we did explore whether individual neighborhood characteristics would be related to either mood or cognition in our exploratory analyses (see below), it is possible our smaller sample size of PWH precluded us from identifying reliable effects with each of our composites of neighborhood vulnerabilities. However, similar to cognition, our study may indicate that there is no significant impact of neighborhoods on mood, showing a consistent pattern for neuropsychiatric outcomes among older diverse PWH. There may be other more salient reasons for decline in mood in this population, such as individual health behaviors, aspects of social relationships and interactions, or impacts on physical health outcomes that may indirectly result in worsened mood, rather than the neighborhood environment. Thus, additional work is needed to clarify whether our findings reflect a true lack of additional influence of neighborhood sociocultural and physical features on worsened mood.

Limited Worsened Mood. In addition, given the recorded higher rates of depression among older adults, minoritized groups, and PWH respectively, even prior to a significant stressor (B. Brown et al., 2021; M. J. Brown & Weissman, 2020; May & Fullilove, 2022; Shiau et al., 2020), we hypothesized that older diverse PWH would experience elevated levels of poor mood after the onset of a global pandemic compared to before. Yet our sample of PWH showed relatively stable mood at follow-up when compared to baseline responses. However, in contrast to our results concerning cognitive decline, our results seem to be consistent with emerging literature investigating changes in mental health among people living with HIV during the COVID-19 pandemic (Brouillette et al., 2022; Kalichman & El-Krab, 2022; Koski et al., 2022; Manchia et al., 2022; Menze et al., 2022; Schaaf et al., 2022; Wang et al., 2021). One study showed evidence of similar rates of depressive symptoms between older PWH and HIV- individuals during this time period (Schaaf et al., 2022), while Brouillette and colleagues (2022) showed that a third of their sample of older PWH reported improvements in mental health during the first wave of the pandemic. Among these reports, there was additional evidence of a potential moderating impact of age, as younger individuals (i.e., ≤60 years old), regardless of HIV status, reported higher distress during the pandemic than older adults (Menze et al., 2022; Nguyen et al., 2021; Schaaf et al., 2022). In a critical review, Manchia and colleagues (2022) discuss how even though elderly people were more vulnerable to the physical effects of COVID-19, they reported lower psychopathology during the pandemic as compared to younger age groups, though those with cognitive impairment before the onset of the pandemic were at greater risk for worsened mental health outcomes (Manchia et al., 2022). However, a recent multisite study among Latinos living without HIV showed elevated depression and anxiety symptoms during the pandemic varied by sex and age group, with women and individuals 45 and older reported being most affected by psychosocial distress (Isasi et al., 2023). As our sample was on average 60 years old (range 50-90), male, and White, it is possible that our sample of older PWH benefitted from healthy coping strategies (Fuller & Huseth-Zosel, 2021; Whitehead & Torossian, 2021) or emotional resilience (Sterina et al., 2022), and the inclusion of a younger, more racially and ethnically diverse cohort may have elucidated how changes in mental health during pandemic impacted PWH.

Notably, the collection of mental health outcome data among published studies during the pandemic spanned a shorter timeframe (e.g., March 2020-June 2020, January 2020 to April 2021) than our study (e.g., March 2021 to June 2022 follow-up window) (Manchia et al., 2022). It is possible that we did not capture increased difficulties with mood among our sample potentially occurring during the heightened period of stress (Flaskerud, 2021; Ryan, 2021). Perhaps during the period that was prior to the widespread availability of the COVID-19 vaccine (i.e., prior to April 2021, (Painter, 2021)), during more strict stay-at-home orders (Newsom, 2020), peak unemployment rates (Kochhar, 2020), as well as additional stress and poor health related to racial protests (Eichstaedt et al., 2021) and the 2020 presidential election (Mefford et al., 2022; Panagopoulos & Weinschenk, 2022), we would have captured a greater degree of worsened mood in our sample of diverse older PWH. Though a significant relationship between higher baseline mood and worsened mood at follow-up emerged in non-imputed results, this may be due to outliers at the extreme ends of the distribution of the change score, which were then potentially extended into the imputation. It is also worth noting that the MOS-HIV Mental Health Summary T-scores needed to be imputed for 93 individuals (56.1%) at baseline and 45 participants (56.9%) at follow-up, thus the imputed estimates for the change in MSS, let alone the pooled results of the regression analyses, may still carry a substantial degree of bias (Mishra & Khare, 2014). Thus, further exploration of worsened mood among a larger sample of older diverse PWH during the COVID-19 pandemic is warranted.

Furthermore, literature that follows individuals longitudinally during the period of the pandemic is only just emerging (Bustamante et al., 2022; Ettman et al., 2020b; Kondo et al., 2022; Koski et al., 2022; K. W. Lee et al., 2022), of which Kondo et al, (2022) reported an important role of neighborhood features in distress. They described that among US adults aged ≥ 55 years, higher density of offsite alcohol outlets and walkable streets in neighborhoods were associated with an increase in distress, while access to neighborhood parks were associated with reduced distress between April and May 2020 (Kondo et al., 2022). Ma and colleagues (2022) found similar associations among a survey of the general population living in the Beijing metropolitan area, especially noting that the positive association between park accessibility and mental health was stronger for those with lower income compared to higher income (Ma et al., 2022). Of the handful of studies that investigated mental health among PWH and reported declines (Diaz-Martinez et al., 2021; K. W. Lee et al., 2022; Parisi et al., 2022; Wion & Miller, 2021), data were predominantly collected via surveys rather than psychometrically robust questionnaires, and no study considered neighborhood features as potential reasons behind exacerbated rates of mental health issues. Thus, additional research is needed to understand how confinement to and engagement with the neighborhood environment may have impacted neuropsychiatric outcomes among older diverse PWH after the onset of the pandemic.

4.2 No Moderation of the Impact of COVID-19 on the Neighborhood

Our analyses also investigated whether the impact of COVID-19 on the neighborhood would have resulted in steeper neurocognitive and emotional decline for those PWH living in more disadvantaged neighborhoods prior to the onset of the pandemic. Among our sample, there was no moderating impact of the cumulative case rates of COVID-19 on the association between neighborhood vulnerabilities and either worsened cognition or mood. This may be partially explained by the lack of decline in our sample, or due to no significant association between neighborhood factors and our outcomes of interest, as noted above.

COVID-19 Pandemic as an Additional Stressor. For our analyses, we conceptualized the impact of COVID-19 at the neighborhood level as an additional environmental stressor specific to this historic time. News reports had consistently indicated that those living in more disadvantaged neighborhoods in southern California were also grappling with higher case rates, deaths and lower rates of vaccinations (Bowman, 2021; de Joseph, 2020; Lauter, 2020; D. L. Oh et al., 2022). We had intended to capture the added stressor for these already vulnerable communities and measure that additional burden's impact on potential changes in cognition and mood. Our cumulative rate of COVID-19 cases was significantly related to our measures of sociodemographic and economic vulnerability, reflecting the reports in our area (Bowman, 2021; de Joseph, 2020), as well as spatial analysis of case rates in disadvantaged neighborhoods across the country (Bilal et al., 2020; Hu et al., 2020; Lamb et al., 2020; Mustanski et al., 2022; Zhong et al., 2022). However, further work is needed to understand if directly measuring regional COVID-19 case rates is related to individual cognitive and mental health.

To date, no study has examined the direct association between the neighborhood impact of COVID-19 on cognition. There have been only two studies that investigated the direct association between the impact of COVID-19 on mental health, with conflicting results (Mamun et al., 2021; Okubo et al., 2021). Both studies considered geographical distributions of COVID-19 cases in relation to either depression (Mamun et al., 2021) or psychological distress (Okubo et al., 2021). Mamun and colleagues (2021) found that, in Bangladesh, the degree of depression was significantly higher in areas where the prevalence of COVID-19 cases was high. However, Okubo and colleagues (2021) reported no association between number of COVID-19 cases and mental health outcomes in Japan, but rather that higher levels of urbanization were associated with severe psychological distress. Therefore, additional research is needed to understand how best to measure the ways communities grappled with disruptions to resources due to precautionary restrictions, risks of transmission, and prolonged periods of isolation.

Use of COVID-19 Statistics. There is no gold standard method for measuring the impact of COVID-19 on the neighborhood. Studies have used positive case rates, number of tests administered, deaths and hospitalizations due to COVID-19 as individual outcomes and to track the spatial distribution of the pandemic (Bilal et al., 2020; K. M. Brown et al., 2021; Hu et al., 2020; Lamb et al., 2020; Mendoza et al., 2021; Mustanski et al., 2022; Zhong et al., 2022). Our COVID-19 impact on neighborhoods factor did not come to fruition. The correlations between cumulative case rates, rates of vaccinations and distance to COVID-19 testing centers across San Diego and Riverside County were weak, suggesting that each metric reflected a separate pandemic-related experience, rather than a proposed shared underlying construct. For instance, while case rates may represent the degree of transmission of the virus itself, rates of vaccinations may have been confounded by local preferences and political views (Kates et al., 2021; Millett, Honermann, et al., 2020), which may have resulted in varying levels of stress across communities. Furthermore, while disparities in available COVID-19 testing centers by racial/ethnic density were documented across the US (Bilal et al., 2020; Hu et al., 2020; Rubin-Miller et al., 2020; Wittenauer et al., 2022), this variable may have not been the best metric of how neighborhoods in this area of the country may have been receiving COVID-19 tests. Though we had hypothesized that greater access to a COVID-19 testing site may have reflected neighborhood structures or resources better able to serve their communities during a difficult time, distance to a center may not have been as important if vulnerable groups may not have had time away from work or transportation barriers to get tested (AuYoung et al., 2023; Bowman, 2021). Individuals may have also engaged with a COVID-19 testing center that was free, more convenient (e.g., shorter lines, quicker results, near a transportation stop), or supported by their medical coverage, rather than the closest testing center in their area.

Moreover, the available COVID-19 statistics are not uniformly distributed across the US, are likely underestimations (S. L. Wu et al., 2020) and subject to regional and demographic differences in adherence to public health guidelines (Lennon et al., 2020; Weiss & Paasche, 2020). In addition, the accessibility of these data for analysis can also vary by geographic region and by date of collection. For example, during the data collection period of this study (June 2022), San Diego County maintained both cumulative and past-7-day rates of positive COVID-19 cases and deaths per census tract and zip code, while Riverside County only collected data on cumulative case rates per zip code, updated weekly. Data collected at the zip code level are not as precise as census tracts, are susceptible to problems due to aggregating information into a larger area, and are less likely to be representative of true communities, as postal codes do not follow geographic boundaries (Din & Wilson, 2020). This may be one explanation for why COVID-19 case rates did not show a significant relationship with our neighborhood factors and contributed to increased suppression effects in our models. In addition, while our cumulative case rate captured the changing nature of the pandemic by incorporating the surge of cases due to different variants (Hadj Hassine, 2022; Ryan, 2021), this combined value may have smoothed over potential differences in how COVID-19 impacted neighborhoods across specific periods of the pandemic.

4.3 Evaluation of Created Neighborhood Factors

Our study operationalized the neighborhood environment by creating composite indices from specific publicly available social, economic, and environmental information. The quantification of neighborhood environment in previous studies has varied, with some analyzing individual variables (Bruce et al., 2015, 2015; Burke-Miller et al., 2016; Wright et al., 2022), whilst others creating indices or composites of neighborhood disadvantage (Brawner et al., 2022; Dawit et al., 2021; Kimaru et al., 2021) by using aggregated data for a geographic region (Brawner et al., 2022). Many of the individual variables that were included in our Sociodemographic and Economic factors were the same as those included in these listed studies (e.g., households with more than 1 person per room, lack of car ownership, single-parent households with children aged < 18, poverty level). However, we did not include other specific educational, occupational, or economic Census information that may be found in other published or developed neighborhood indices (e.g., median gross rent, median family income, % of the population aged ≥25 with at least a high school diploma, home ownership rate, unemployment) (Gallo et al., 2019; Kind et al., 2014; Singh, 2003). The specific variables chosen to represent constructs of a neighborhood may be critical in detecting the associations with cognitive and mental health, and the varied use across studies, including our own, may contribute to inconsistent findings.

As for our composite reflecting physical features of the environment, Undeveloped, it did not incorporate certain variables that have been associated with cognition or mood for individuals living in southern California. Notably, the values for living in a food desert and the Pollution Burden Index used were not originally created for the most up-to-date US Census boundaries like the other physical variables collected for this analysis. These two values had to be averaged to the overlapping 2020 population-weighted centroid's buffer, potentially introducing error into the estimated values of these two characteristics and contributing to their lack of sufficient communalities to the factor loadings in the first factor analysis. Additionally, distance to the nearest liquor store, a negative aspect of one's environment, loaded positively onto the Undeveloped factor, in the same direction as transit stops, parks, recreation and health centers, which may be grouped as positive resources. Higher density of alcohol outlets has been consistently shown to be related to increase in distress (Kondo et al., 2022), increased substance use (Theall et al., 2019), and greater neighborhood deprivation (Hay et al., 2009). Thus, rather than capture aspects of the physical environment that promote positive health outcomes, this unintuitive loading may reflect the underlying common metric among these variables, distance, particularly to centers of activity (Langdon, 2023; Rappaport, 2008), which have wide-ranging relationships with individual health. Furthermore, the relationship between cognition and air pollution and walkability has typically been found using much larger samples (i.e., N $\geq$500) (Gatto et al., 2014; Ilango et al., 2021; Jerrett et al., 2014; Kulick et al., 2020; Rosso et al., 2021; Zhao et al., 2021). Given these complications, as well as lacking walkability, transit stop, and recreation center data for Riverside County, using the individual variables of the Undeveloped factor in a larger sample of older PWH is warranted to understand whether access to physical/built resources in the environment are related to cognitive or emotional decline.

4.4 Alternate Approaches

As our results did not show evidence of a significant relationship between neighborhood factors and emotional or cognitive decline via our proposed aims, we conducted additional exploratory analyses to understand the nature of these findings among our sample of diverse older PWH. We investigated an additive measure of functional decline, categorical change in outcomes, associations between neighborhood factors and our outcomes at baseline, as well as the potential relationships between individual neighborhood vulnerabilities and change in cognition and mood.

Categorical Change and Functional Decline. Of these analyses, we found a lack of variability in our sample using both an additive measure of functional decline and categorical changes in cognition and mood, with the majority of individuals not declining over time regardless of the method of quantification. Though the MOS-HIV Mental Health Summary Scale has been shown to be related to other measures of depression (Briongos Figuero, Bachiller Luque, Palacios Martín, González Sagrado, et al., 2011; Briongos Figuero, Bachiller Luque, Palacios Martín, Luis Román, et al., 2011), there was no single measure of mood, such as the Beck Depression Inventory-II, given across all studies at the HNRP during much of the follow-up window, contrary to its frequent administration prior to the pandemic. As these data were also not collected during the peak of the pandemic as the HNRP did not have clinical coverage, a significant limitation of our study is our inability to robustly measure depression and general mood through different periods of the pandemic, in a large sample size, potentially contributing to lack of variability in worsened moved over time.

Association between Neighborhood Factors and Cross-sectional Cognition. Our findings did not show a significant association between neighborhood factors and cognition or mood among our sample at baseline. This was surprising, as other ongoing cross-sectional work among a sample of older diverse PWH and HIV- individuals found that greater neighborhood socioeconomic deprivation was significantly associated with worse global scaled scores (Kamalyan et al., 2023). However, once those models were adjusted for demographics, particularly education, there was no longer a significant relationship. In addition, this ongoing work found different levels of global scaled scores and neighborhood socioeconomic deprivation between Whites, English-speaking and Spanish-speaking Latinos living with and without HIV in San Diego County. Notably, baseline global scaled scores in present analyses were significantly different between Whites and minoritized groups. Differences in US neighborhoods may be one of the underlying mechanisms of racial and ethnic disparities in cognition (Besser et al., 2017; Diez Roux & Mair, 2010; Glymour & Manly, 2008), as they purposefully separate people into social hierarchies and perpetuate disparate lived experiences. Race and ethnicity categorizations are often used in health outcome research as proxies for the deliberate discrepancy in the allocation of resources by identity group rationalized by white supremacist ideology, which is the upstream influence of racial and ethnic health disparities (Adkins-Jackson et al., 2023). However, there remain additional explanations for racial and ethnic disparities in cognitive test performance, such as discrimination and stereotype threat (Brondolo et al., 2009; Thames et al., 2013), language barriers (Rivera Mindt et al., 2021), and measurement invariance in neuropsychological tests (Avila et al., 2020). Taken together, race and ethnicity and place of residence in the US are confounded, and when neighborhood measures and sample race and ethnicity are included in models predicting cognitive test performance, it becomes nearly impossible to ascertain whether significant associations are due to the individual-level or environmental-level mechanisms. Thus, following procedures noted in previous studies (Besser et al., 2022; Meyer et al., 2021; D. L. Oh et al., 2022; Wong et al., 2023), we stratified our multivariable analyses by race and ethnicity. Nevertheless, we did not find an association between global scaled scores by ethnicity, nor demographically adjusted global mean T-scores in the whole sample and neighborhood factors at baseline. Additional work is needed among a larger sample of PWH to clarify these associations among a diverse group.

Association between Neighborhood Factors and Cross-sectional Mood. In terms of our lack of associations between neighborhood factors and mood at baseline, it is partially consistent with one cross-sectional study conducted in a population-based study of predominantly Mexican Americans in southern San Diego (Holmgren et al., 2021). Holmgren and colleagues (2021) used a similar Census-based composite of neighborhood socioeconomic deprivation and did not identify significant associations between neighborhood socioeconomic deprivation and depression symptoms after accounting for personal socioeconomic status. However, on the whole, our results do not fit with the consistent body of literature depicting higher rates of mental health issues for individuals living in more disadvantaged neighborhoods, greater neighborhood crime and safety, and lower social relationships (Barnett et al., 2018; Gan & Best, 2021; Ivey et al., 2015; Kim, 2010). What is more, the specific ways that neighborhoods impact mental health may differ for racial/ethnic group (Alegría et al., 2014; Diez Roux & Mair, 2010), and between PWH and HIV- individuals (Wright et al., 2022), and so larger studies that include participants with intersecting identities and healthy controls may better elucidate these relationships.

Crowded Housing and Worsened Mood. The only significant association identified in our exploratory analyses was that living in a neighborhood with a higher percentage of crowded households was related to greater decline in mood among our sample of older diverse PWH. The impact of crowded housing or urbanization on distress during the pandemic has been noted in a few studies (Bustamante et al., 2022; Okubo et al., 2021). This finding among our sample may be reflecting that those who live in more densely populated areas, such as downtown San Diego, or in close contact with essential workers (Bowman, 2021) may have had higher anxieties of getting infected with COVID-19. These worries are warranted as the COVID-19 virus has the potential to interact synergistically with HIV to worsen health outcomes (Barbera et al., 2021; Prabhu et al., 2020; Spinner, 2021). Of note, this finding among our small sample was not upheld after removing outliers on change in MOS-HIV Mental Health Summary score, as well as after multiple imputation procedures. As the majority of baseline and follow-up MOS-HIV Mental Health Summary scores needed to be imputed to create a change score, and the assumptions regarding missing data patterns and the variables chosen to impute missing data may have partially attributed to these lack of findings, replication among a larger sample of PWH is necessary to clarify these results. A larger sample size may also elucidate potential associations with other individual neighborhood vulnerabilities that have been noted to be associated with higher rates of depression and cognition, such as crime rates, social disorder, walkability and greenspace (Barnett et al., 2018; Berke et al., 2007; Ivey et al., 2015; Joshi et al., 2017; Kim, 2010; Ma et al., 2022).

4.5 Limitations and Future Directions

This study is not without limitations and reviewing them can best guide future studies.

Sample Size and Composition. First and foremost, despite best efforts to adapt data collection procedures to a remote approach and continue to follow individuals over time (Kohli et al., 2023; Padala et al., 2020), there likely remained barriers to participants returning for a visit during this study's follow-up window. Notably, a portion of our sample was scheduled for follow-up visits in their parent study past the window for the current study's timeframe and thus had we been able to include their follow-up data, it may have influenced our results. Technological challenges, transportation access, and concerns about COVID-19 transmission may have resulted in a greater than expected decline in participation at follow-up (Abdulhussein et al., 2022), and perhaps those who were better equipped to manage these challenges were able to complete visits. Notably, our study had a similar sample size to two studies that investigated the impact on the pandemic among older adults living with HIV (Brouillette et al., 2022; Nguyen et al., 2021), however their work was focused on characterizing distress via surveys rather than neighborhood associations with longitudinal changes in this population. In addition, neighborhood studies typically require a large sample size (Besser et al., 2017), however, the annual rate of HIV infections is decreasing, with less than one percent of the US population in 2019 living with HIV (i.e., about 1.2 million) (*Basic Statistics | HIV Basics | HIV/AIDS | CDC*, 2022). It is for the greater good of public health that we do not have a larger pool of PWH to recruit into our studies, however, this limits the power needed to detect the impact of neighborhood on health outcomes in PWH. There are several potential ways to increase the sample size for future studies. For example, there are studies following persons living with HIV that have multiple sites (i.e., CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) study) from which longitudinal neurocognitive data can be leveraged (Heaton et al., 2015). However, difficulties do arise in receiving permission and access to personal address information across sites, as well as using neighborhood physical characteristic data that are uniformly collected and available. Another option may be to include all adults living with HIV and compare analyses by age group (Menze et al., 2022; Nguyen et al., 2021; Schaaf et al., 2022), as there are opposing relationships for cognition and mood by age among PWH (i.e., mood increases while cognition decreases with age). Third, as our sample was relatively healthy and virally suppressed for over a decade up to their baseline visit, it might be worth including HIV- individuals in future analyses and controlling for HIV status. Finally, using inverse probability weighting to adjust for the exclusion of individuals with missing data on multiple to all variables in combination with multiple imputation methods may be another potential direction (Seaman & White, 2013). These possible avenues can expand the current study's research questions and may increase the power needed to detect an association between neighborhood environment and health outcomes for PWH.

Gathering Additional Participant Information. We are additionally limited in the primary addresses that were collected for participants. Recruitment efforts only indicated their most recent address and were not updated at every visit. When they were updated, the older addresses were replaced with the new one, and not retained. For many of the participants at the HNRP, it was difficult to know if the address used for these analyses was their primary address at baseline. We anticipated that individuals do not typically move frequently over the course of two years, and if so, do not move to drastically different neighborhoods (S. (Alex) Li et al., 2022). Yet it is possible that the pandemic resulted in either greater numbers of relocation, as people moved into cheaper neighborhoods or with family members, or declines in residential mobility due higher economic uncertainty (Jones & Grigsby-Toussaint, 2020). As we were not able to track whether and where our participants moved to at the follow-up visit, this may have resulted in our quantified neighborhood environments to be less accurate for our participants and not related to cognitive performance. Furthermore, we did not have information on how long participants have lived at this primary address, why they self-selected into this area, nor how much time per day they spent at this address compared to other locations such as work, recreation centers, businesses, or friends and family member dwellings, and if that amount changed during the pandemic. These data are frequently not available in studies investigating the impact of the environment on cognition and mood, and their inclusion in future prospective studies can better describe potential associations between neighborhoods and health. Lastly, we did not know who in our sample was unhoused, as they would not necessarily have a primary address. The frequented areas for this vulnerable group may result in greater exposure to negative conditions and increased risky behaviors, leading to increased mental health burden (Latkin et al., 2013). Future studies should consider tracking all new and former addresses of participants, as well incorporate data on individual engagement with their environment using ecological momentary assessment and/or global positioning systems, which may provide additional granularity in the relationship between confinement and activity at home, neighborhood exposures, and health outcomes (De Silva et al., 2019; Johnson et al., 2020; Kamalyan, Yang, et al., 2020).

In addition, while we investigated unemployment status at baseline and education level as potential covariates, we did not collect markers of personal socioeconomic status such as individual income data, unemployment data, or information about how the pandemic uniquely impacted each individual financial situation consistently across our sample of PWH, and thus were unable to include in our analyses. There were no significant relationships between unemployment status or education and change in either cognition or mental health in our sample. With that in mind, the role of individual-level socioeconomic status remains unclear due to high correlations with neighborhood-level measures and low inter-neighborhood variability of personal socioeconomic status, as well as potential bi-directional relationships between individual socioeconomic status and mental health (Ridley et al., 2020).

Including Additional Neighborhood Information. Another limitation of this study is that not all physical neighborhood characteristics and COVID-19 case rates were available universally, in contrast to the reliable collection and accessibility of US Census data. Furthermore, by February 2023, neither San Diego nor Riverside County had any COVID-19 statistics available for download, thus we could not capture the impact of COVID-19 on the neighborhood during the peak period of the pandemic prior to vaccine availability (i.e., March 2020-March 2021). Given the limitations of accessing this data moving forward, and our lack of associations between COVID-19 case rates and change in certain health outcomes, quantifying the physical environment and the impact of COVID-19 at the neighborhood level for southern California may need to be reconceptualized. One potential method may be to measure how neighborhoods themselves changed during the pandemic, to then relate to cognitive and mental health outcomes. For example, noted reductions in traffic (Hudda et al., 2020), air pollution (Cicala et al., 2021; Venter et al., 2020), and increases in interacting with greenspace (Heo et al., 2021) may in turn have contributed to improvements in cognition and mood. However, closed local resources (E. K. Lee & Parolin, 2021), overburdened health care centers (French, 2021), and greater unemployment rates (Beer et al., 2022; Lupton-Smith et al., 2022) may have contributed to worsened health outcomes. Thus, measuring how aspects of the neighborhood changed may be a more fruitful approach in capturing both pre-existing resources and the added burdens and potential positive impacts after the onset of the COVID-19 pandemic.

Future work in a larger population is needed to understand interconnected yet heterogenous features of the environment and identify the salient processes that may lead to both positive and negative health outcomes for this population (Sharkey & Faber, 2014). Studies may also consider employing available indicators of neighborhood socioeconomic or physical features such as the Neighborhood Atlas (Kind & Buckingham, 2018; Singh, 2003), or the Healthy Communities Data and Indicators Project (*Healthy Communities Data and Indicators Project*, 2023), or identifying regional rather than national or state-based metrics of comparison, however these data are subject to less-frequent updates through local organizations and may not be generalizable to other sites. Alternatively, it may be fruitful to identify specific individual neighborhood factors that could be mediators between individual-level behaviors and cognition, for example, the role of the neighborhood environment linking social relationships and depression (Kim, 2010). There may also be protective aspects of neighborhoods that we did not assess in our study that may buffer the impact of notable risks and hazards (Finlay et al., 2022). Navigating environments enriched with opportunities for cognitive and social activity may be related to reduced cognitive decline (C. H. Tan & Tan, 2023) and depression (Berke et al., 2007), though protective effects may differ across race/ethnicity (Gallo et al., 2022) and gender (Berke et al., 2007). As our neighborhood factors may be incorporated into current and prospective datasets, prospective studies at our center may also investigate how neighborhood features may influence other health outcomes within PWH. For example, one study described that increased marijuana use among PWH was related to worsened mental health during the pandemic (Wang et al., 2021). Another study conducted prior to the pandemic detailed that there may be a relationship between living in dangerous environments and elevated marijuana use for PWH (Bruce et al., 2015). This emerging literature suggests that one way to capture potential changes in mental health while being confined to their surrounding environment may be through investigating changes in substance use during the pandemic for PWH.

4.6 Summary and Implications

Our study aimed to fill research gaps by using geospatial methods of combining US Census and satellite/imagery data to create composite indicators of neighborhood vulnerabilities in relation to health outcomes and understand how communities may be affected by particularly distressing events. We are among the first studies to operationalize the impact of the COVID-19 pandemic as a “natural stressor” at the neighborhood level, as well as the first to investigate potential associations between neighborhood vulnerabilities and neurocognitive decline and worsened mood among older diverse people living with HIV using comprehensive neurocognitive and psychiatric data. Though we did not find significant associations among our limited sample, our use of objective measures of neighborhood sociodemographic, economic, and accessibility to resources heightened the replicability of our work. Future studies focused on understanding the relationship between structural determinants of health and cognitive and mental health outcomes among vulnerable populations can draw from our work by including data from multiple sources and considering historic and geographic differences in policies and data accessibility. Placing the ways in which racial ideologies are sustained through economic, political, and social institutions at the center of disparities research is critical to elucidate specific individual and policy level interventions that impact the health of vulnerable groups.

APPENDIX

Appendix Table 1. Descriptive statistics of neighborhood factors in San Diego and Riverside County, CA (N=1255)

	Mean (SD)	Minimum	Median [IQR]	Maximum
Factors				
Sociodemographic	1.26e-16 (0.92)	-1.84	-0.17 [-0.71, 0.61]	3.27
Economic	-3.89e-17 (0.95)	-11.43	0.20 [-0.44, 0.63]	1.48
Undeveloped	-7.94e-17 (0.96)	-0.82	-0.22 [-0.43, -0.16]	16.4
Individual Variables				
Pollution Burden Index	4.63 (1.09)	1.81	4.53 [3.87, 5.40]	8.59
Living in a food desert[a]	18.2 (11.7)	0	16. 7 [10.53, 24.2]	100
Walkability index[b]	-0.40 (1.63)	-5.62	-0.35 [-1.33, 0.61]	7.30
Kilometers to nearest liquor store	0.97 (1.44)	0.02	0.71 [0.41, 1.15]	35.0
Kilometers to nearest health center	1.98 (3.00)	0.01	1.24 [0.72, 2.13]	45.6
Kilometers to nearest park	2.56 (3.98)	0	0.82 [0.32, 2.98]	27.0
Kilometers to nearest recreation center[b]	8.13 (10.40)	0.07	3.41 [1.37, 10.8]	69.9
Kilometers to nearest transit stop[b]	0.75 (0.95)	0.01	0.43 [0.24, 0.79]	7.40
% of the population under 18 years old	21.93 (8.12)	0	22.5 [17.7, 27.7]	51.7
% female headed households[c]	5.92 (4.88)	0	4.71 [2.24, 8.50]	31.5
% of the population Hispanic	39.25 (24.19)	0.42	35.9 [19.0, 57.1]	100
% of households without a computer	4.85 (4.79)	0	3.60 [1.60, 6.80]	35.9
% of households without internet	9.49 (7.61)	0	7.80 [4.10, 12.9]	100
% employed males in professional occupations[d]	48.94 (12.16)	0	49.3 [41.9, 56.3]	100
% of the population not born in the US	21.93 (10.79)	0	20.2 [13.6, 28.9]	77.5
% of households without a car	4.89 (5.87)	0	3.27 [1.25, 6.62]	100
% crowded households	7.33 (7.44)	0	5.10 [1.80, 10.4]	44.1
% poverty	11.30 (8.47)	0	9.34 [5.17, 15.2]	100

Note: a: n=915; b: only among San Diego County (n=736); c=with dependent children; d= over the age of 16 in management, business, science, and arts occupations; SD = Standard deviation, IQR = Interquartile Range

Appendix Table 2. Descriptive statistics of individual neighborhood variables of sample addresses in relation to census tracts in San Diego and Riverside County, CA (N=79)

	Mean (SD)	Minimum	Median [IQR]	Maximum
Pollution Burden Index	4.77 (0.91)	2.72	4.80 [4.38, 5.27]	6.55
Living in a food desert	16.7 (9.85)	0.48	13.4 [8.60, 24.0]	41.0
Walkability index	0.76 (1.30)	-3.06	1.03 [-0.28, 1.80]	3.06
Kilometers to nearest liquor store	0.52 (0.35)	0.18	0.42 [0.32, 0.65]	2.69
Kilometers to nearest health center	1.03 (0.92)	0.35	0.76 [0.62, 1.19]	8.07
Kilometers to nearest park	1.14 (1.93)	0.17	0.46 [0.33, 0.97]	13.7
Kilometers to nearest recreation center	3.06 (5.15)	0.47	1.26 [0.93, 2.09]	25.1
Kilometers to nearest transit stop	0.37 (0.27)	0.08	0.29 [0.23, 0.43]	2.13
% of the population under 18 years old	15.9 (6.53)	1.99	16.5 [10.0, 20.9]	30.8
% female headed households[a]	5.00 (3.41)	0.20	3.83 [2.63, 6.88]	15.1
% of the population Hispanic	33.6 (18.9)	7.54	28.0 [20.8, 43.1]	94.9
% of households without a computer	5.40 (2.91)	0.26	4.90 [3.14, 7.00]	15.0
% of households without internet	10.1 (4.69)	0.71	8.89 [7.00, 13.1]	22.6
% employed males in professional occupations[b]	50.6 (6.78)	34.5	50.8 [47.4, 54.3]	70.2
% of the population not born in the US	21.3 (9.03)	9.02	17.6 [14.8, 27.5]	44.4
% of households without a car	7.48 (4.47)	1.02	7.39 [5.03, 9.00]	29.5
% crowded households	6.65 (5.97)	0.86	4.22 [2.54, 9.03]	27.3
% poverty	11.9 (5.52)	1.92	10.0 [7.55, 15.7]	30.3

Note: a=with dependent children; b= over the age of 16 in management, business, science, and arts occupations; SD = Standard Deviation; IQR = Interquartile range

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