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# Associations of County-Level Social Determinants of Health with COVID-19 Related Hospitalization Among People with HIV: A Retrospective Analysis of the US National COVID Cohort Collaborative (N3C)

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**ORIGINAL PAPER** 



### Associations of County-Level Social Determinants of Health with COVID-19 Related Hospitalization Among People with HIV: A Retrospective Analysis of the U.S. National COVID Cohort Collaborative (N3C)

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#### Abstract

Individually, the COVID-19 and HIV pandemics have differentially impacted minoritized groups due to the role of social determinants of health (SDoH) in the U.S. Little is known how the collision of these two pandemics may have exacerbated adverse health outcomes. We evaluated county-level SDoH and associations with hospitalization after a COVID-19 diagnosis among people with (PWH) and without HIV (PWOH) by racial/ethnic groups. We used the U.S. National COVID Cohort Collaborative (January 2020-November 2023), a nationally-sampled electronic health record repository, to identify adults who were diagnosed with COVID-19 with HIV (n = 22,491) and without HIV (n = 2,220,660). We aggregated SDoH measures at the county-level and categorized racial/ethnic groups as Non-Hispanic (NH) White, NH-Black, Hispanic/Latinx, NH-Asian and Pacific Islander (AAPI), and NH-American Indian or Alaskan Native (AIAN). To estimate associations of county-level SDoH with hospitalization after a COVID-19 diagnosis, we used multilevel, multivariable logistic regressions, calculating adjusted relative risks (aRR) with 95% confidence intervals (95% CI). COVID-19 related hospitalization occurred among 11% of PWH and 7% of PWOH, with the highest proportion among NH-Black PWH (15%). In evaluating county-level SDoH among PWH, we found higher average household size was associated with lower risk of COVID-19 related hospitalization across racial/ethnic groups. Higher mean commute time (aRR: 1.76; 95% CI 1.10-2.62) and higher proportion of adults without health insurance (aRR: 1.40; 95% CI 1.04–1.84) was associated with a higher risk of COVID-19 hospitalization among NH-Black PWH, however, NH-Black PWOH did not demonstrate these associations. Differences by race and ethnicity exist in associations of adverse county-level SDoH with COVID-19 outcomes among people with and without HIV in the U.S.

**Keywords** Social determinants of health  $\cdot$  Race and ethnicity  $\cdot$  HIV  $\cdot$  COVID-19 hospitalization  $\cdot$  SARS-CoV-2 infection  $\cdot$  Pandemic  $\cdot$  Access to care  $\cdot$  Area-level  $\cdot$  County-level

#### Introduction

In the United States (U.S.), people with HIV (PWH) have been disproportionately impacted by the Coronavirus Disease 2019 (COVID-19) pandemic due to multiple,

Jessica Y. Islam and Eric Hurwitz have contributed equally to this work.

The members of the N3C consortium are listed in Acknowledgements.

Extended author information available on the last page of the article

interconnected factors stemming from the historical social marginalization of minoritized people. PWH in the U.S. are disproportionately Black or African American and Hispanic/Latinx adults, with significant inequities in risk of exposure, access to care, and mortality [1–3]. For example, in 2019, Black adults accounted for 41% of HIV infections, however, they only comprised 13% of the U.S. population [4]. The COVID-19 pandemic also exacerbated inequities among minoritized populations in health outcomes, leading to higher rates of hospitalization, severe disease, and death due to COVID-19 among racial and ethnic minority PWH and in the general population

[5–8]. We have previously shown that minoritized PWH were more likely to develop COVID-19 infection, hospitalization, and death compared to people without HIV (PWOH) [5, 6, 9]. Minoritized PWH were also likely to be inequitably impacted by HIV care interruptions during COVID-19 [10, 11]. Given the disproportionate impact of the pandemic on minoritized PWH, understanding the role of social determinants or drivers of health (SDoH) is critical to elucidate potential opportunities to alleviate inequities. As defined by the World Health Organization, SDoH are the conditions in which people are born, grow, work, live, and age, and the wider set of economic policies and systems shaping the conditions of daily life [12].

Racial and ethnic inequities in health care outcomes in the U.S. occur likely due to a systemic network of factors, collectively known as SDoH, that may function at multiple levels including individual-level or at a geographic area or contextual level. In the context of either HIV or COVID-19, the potential role of SDoH in adverse health outcomes has been explored, though not at the intersection of these two conditions. For example, racial and ethnic minorities living in areas or neighborhoods with a high burden of adverse SDoH, such as a large proportion of people living below the federal poverty level, are at higher risk of incident HIV [13, 14]. Further, SDoH factors at the individual level, such as socioeconomic factors or health insurance status, lower access to health care; societal and community level factors, such as housing policies and the built environment (e.g., higher levels of exposure to pollution and environmental hazards), and interpersonal factors (e.g., residence in multi-generational and multifamily households) contribute to disparities we observe in both the HIV and COVID-19 context [15–19].

To date, the role of SDoH-especially area-level factors-have not been examined at the intersections of HIV and COVID-19, both epidemics with marked racial/ethnic inequities, despite the established role of the built environment. In the present analysis, we focus on SDoH measured at the county-level given counties are directly responsible for implementing state-level COVID-19 policies and dictate how policies operate based on multi-level factors, including for allocation of funding and other resources [20]. Focusing on state-level SDoH ignores the high level of heterogeneity within states across counties, suggesting that SDoH identified at the county-level may provide more impactful opportunity for future, tailored interventions. Our objective was to evaluate the associations of countylevel SDoH with hospitalization after a COVID-19 diagnosis among PWH and PWOH by race and ethnicity, leveraging the National COVID Cohort Collaborative (N3C), the largest and most comprehensive clinical COVID-19 database in the U.S.

#### Methods

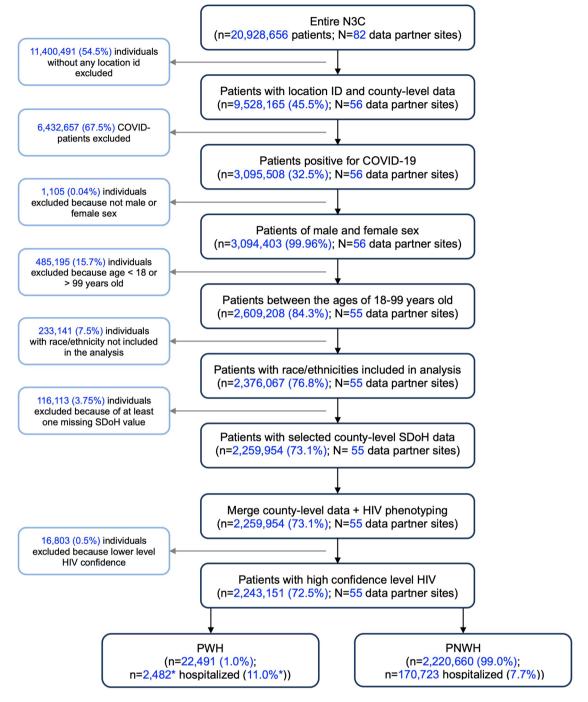
#### **Study Population**

The N3C is a nationally sampled database of people with COVID-19 infection and outcomes, containing harmonized electronic health record (EHR) data from clinical centers across the U.S., and sponsored by the U.S. National Institutes of Health (NIH). N3C's data storage platform, called the Enclave, currently contains data for approximately 21 million COVID-19 positive and negative people beginning on January 1, 2020, with inclusion of previous medical record data at the same data partner site through January 1, 2018. Data are collected during regular healthcare encounters and ingested into the Enclave from data partners. Data come from TriNetX, ACT, PCORnet, or Observational Medical Outcomes Partnership (OMOP) common data model (CDM) before being harmonized on OMOP 5.3.1 CDM, with additional quality control checks described previously [21-23]. Data updates are released regularly. This analysis used data from the Enclave release as of November 2, 2023. Individual data partner sites received approval for the data transfer agreement through their local Institutional Review Board (IRB) or via a centralized review via an agreement between the NIH and the Johns Hopkins University. Individual investigators obtained IRB approvals through their respective institutions.

## Cohort Definitions, Including for COVID-19, HIV, and Race/Ethnicity

For this analysis, we included all patients captured in N3C with a COVID-19 diagnosis with available countylevel SDoH data (Fig. 1). Supplementary Fig. 1 summarizes percentage of adults from each participating N3C data partner site by HIV status. Our study included only COVID-19 positive people, who were identified in the N3C Enclave using either: (1) one or more lab test with a positive result, (2) one or more "strong positive" diagnostic ICD-10 or SNOMED codes, or (3) two or more "weak positive" diagnostic ICD-10 or SNOMED codes [24]. The index date was the date of diagnosis or positive test result from the initial COVID-19 infection.

PWH were identified using a combination of one or more of OMOP concepts corresponding with HIV diagnosis (via ICD-10, SNOMED), medication (via RxNorm), and laboratory (via LOINC) measurements (Supplementary Table 1) [25]. Levels of confidence were defined in collaboration with study clinicians to outline four different definitions of PWH. Patients using pre-exposure



\*approximate value due to limited sample size in NH-AIAN PWH to mitigate risk of reidentification

Fig. 1 Flowchart summarizing the inclusion and exclusion criterion of our study population and final totals to evaluate county-level SDoH among people with and without HIV in the U.S. National COVID Cohort Collaborative (N3C) (Jan 1st, 2020–Nov 2nd, 2023)

prophylaxis (PrEP), only with hepatitis B (HBV, thus receiving some HIV-related medications for treatment of HBV), or using post-exposure prophylaxis (PEP) were excluded from the cohort of PWH (Supplementary Table 1) [25]. For this analysis, we included only PWH

meeting our highest two levels of confidence to minimize potential misclassification of HIV status (Supplementary Table 1).

We defined race/ethnicity for each person by combining race and ethnicity variables. Individuals were classified as either: non-Hispanic (NH)-Black, Hispanic/Latinx of any race, NH-Asian American, Native Hawaiian or Pacific Islander (AANHPI), NH-American Indian or Alaskan Native (NH-AIAN), and NH-White. People with either missing, multiple categories, or race/ethnicity classified as "Other" were excluded from the main race/ethnicity stratified analysis (n=233,141).

## Exposures of County-Level Social Determinants of Health (SDoH)

Our analysis included a set of SDoH measures derived at the county-level from publicly available data sources ingested into N3C and included continuous variables in the following constructs: resource deprivation, access to care/health resources, population characteristics, traveling behavior, vulnerable populations, and health status as described in prior work leveraging N3C [20]. The following countylevel SDoH were available for use in N3C and incorporated in this analysis: average household size, social deprivation index (SDI) score [26], unemployment rate, poverty rate, low food access percentage, area deprivation index (ADI) [27], foreign born percentage, Black-white segregation score [28], Supplemental Nutrition Assistance Program (SNAP) rate [29], percent without health insurance, adult population density, rural designation [30], percent of Black adult residents, percent of Hispanic/Latinx adult residents, percent adults who smoke, and mean commute time within a specific county based on the geographic identifier of each person's address. These county-level SDoH variables were derived from the latest versions (as of 2021) of the following data resources: the Food Access Research Atlas [31], Social Capital Index [32], the ADI [33], SDI [26], the US Census County Business Patterns dataset [34], and Rural-Urban Continuum Codes (RUCC) [30].

#### Outcome of Hospitalization After a COVID-19 Positive Diagnosis

We operationalized COVID-19 related hospitalization as a binary outcome if the patient was hospitalized in the day prior to up to 16 days following the date of COVID-19 diagnosis, as described in prior work [21, 35]. This time frame is aligned with the windows used by the Centers for Disease Control and Prevention (CDC) [36].

#### Covariates

Covariates included in the analysis consisted of age, sex, body mass index (BMI), Charlson Comorbidity Index (CCI), and doses of COVID-19 vaccinations based on prior work establishing their role in COVID-19 related hospitalization consistent with previous studies [5, 23]. Age was defined by calculating the number of years from the date of COVID-19 diagnosis to birth date for each patient. We used an adjusted CCI score (excluding HIV status) using a combination of binary flags for comorbidities prior to each patient's date of COVID-19 diagnosis, where comorbidities have been phenotyped and harmonized using N3C-vetted and -recommended concept sets. The weights for calculating CCI score follow the same definition as described in Charlson et al. [37]. BMI was calculated based on the participant's last recorded height and weight before the date of COVID-19. If this variable was unavailable, the maximum BMI post-COVID was used, given that BMI is relatively stable during this short timeframe. We included CCI and BMI as covariates given the increasing risk of poor COVID-19 outcomes among those with multiple comorbidities [38] and better outcomes with COVID-19 vaccinations [23].

#### **Statistical Analysis**

We used descriptive statistics to summarize patient characteristics and county-level SDoH measures. We transformed each SDoH variable from continuous to quartile categories for ease of interpretation, where those in the highest quartile were considered the exposed group in regression models. We examined potential collinearity amongst all county-level SDoH variables available in N3C. We applied variance inflation factor (VIF) for SDoH measures to avoid multicollinearity issues by removing some of highly correlated SDoH variables, using VIF value of 5 as a cutoff (Supplementary Table 2) [39]. We removed unemployment rate, poverty rate, snap rate, population density, percent of Black adults, percent of foreign born adults, and ADI due to their multicollinearity with other SDoH measures (VIF > 5). We excluded Non-Hispanic American Indian and Alaskan Native adults from multivariable analyses due to small sample sizes and the infeasibility of conducting multivariate exact modeling within current N3C Enclave's computational environment.

We conducted stratified analyses among PWH and PWOH to identify associations of SDoH with COVID-19 related hospitalization. Acknowledging significant heterogeneity exists within racial/ethnic groups, we stratified our models by race and ethnicity (NH-AANHPI, NH-Black, Hispanic/Latinx of any race, NH, NH-White, and NH-AIAN) to evaluate inequities within each subgroup. We performed multilevel, multivariable logistic regression modeling in conjunction with the delta method [40] to estimate adjusted prevalence risk ratios (aRR) with 95% confidence intervals (95% CI) to assess the associations between COVID-19 related hospitalization with each county-level SDoH measure. To account for potential clustering by participating data partner site, we estimated cluster-robust standard errors to allow for correlation between observations within a cluster [41]. In each model, we compared those in the highest quartile (Q4) of each SDoH measure to the first, second, and third quartiles combined. Finally, we further evaluated each county-level SDoH found to be significantly associated with COVID-19 related hospitalization in the multivariable predictive models by running individual models of each SDoH by quartiles, where the lowest quartile was considered the reference group to assess any potential gradient effects of the county-level SDoH. All models were adjusted for age, sex, CCI, BMI, and doses of COVID-19 vaccination. All data management and analyses were conducted in the N3C Data Enclave using Python and Spark R.

#### Results

#### General Characteristics by HIV Status, Race/ Ethnicity, and COVID-19 Related Hospitalization

Overall, our study population included 2,243,151 people from 55 clinical partner sites, where 22,491 and 2,220,660 were PWH and PWOH, respectively (Fig. 1). The proportion of minoritized people were higher among PWH: 8362 (37.2%) were Black among PWH vs. 431,179 (19.4%) among PWOH (Table 1). Additionally, the median, IQR, and percentage of people in the fourth quartile for each SDoH variable were similar across racial/ethnic groups in both PWH and PWOH (Table 1). Overall, 2482 (11.0%) PWH and 170,723 (7.7%) PWOH were diagnosed with COVID-19 related hospitalization over the study period, with 8–15% of people with a history of a COVID-19 related hospitalization across all racial/ethnic groups among PWH, and 4–10% among PWOH (Table 1, Fig. 2).

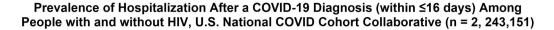
#### Area-Level SDoH and COVID-19 Related Hospitalization Across Racial/Ethnic Groups by HIV Status

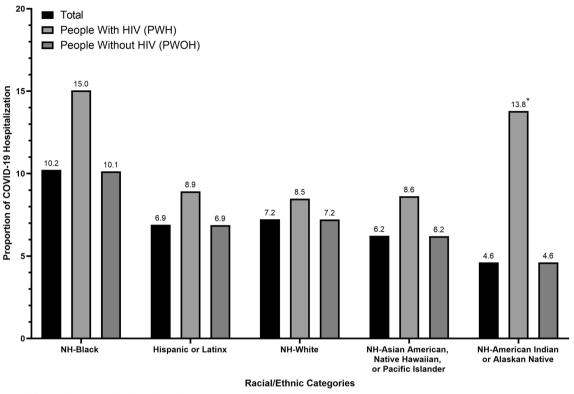
Figure 3 summarizes the associations of county-level SDoH with COVID-19 related hospitalization across racial/ethnic groups among PWH and PWOH separately. Among PWH, we observed that a higher (Q4) county-level average household size was associated with lower risk of COVID-19 related hospitalization among all racial/ethnic groups, including NH-AANHPI (aRR: 0.21; 95% CI 0.08-0.53), NH-Black (aRR: 0.39; 95% CI 0.16-0.93), Hispanic/Latinx (aRR: 0.23; 95% CI 0.07–0.76), and NH-White (aRR: 0.62; 95% CI 0.43-0.88) PWH. We observed similar associations among PWOH, excluding NH-White PWOH. Among NH-Black PWH, living in a county with a higher (O4) median commute time (aRR: 1.76; 95% CI 1.10-2.62) and living in a county with a higher (Q4) percentage of adults without health insurance (aRR: 1.40; 95% CI 1.04-1.84) was positively associated with COVID-19 related hospitalization. Among NH-White PWH, living in a county with a higher

 Table 1
 Summary characteristics of people with and without HIV with a COVID-19 diagnosis captured in the National COVID Cohort Collaborative (N3C), (Jan 1st, 2020–Jan 21st, 2023)

	All adults		People with HIV		People without HIV	
	n	%	n	%	n	%
Race ethnicity						
NH-Black	439,541	19.59	8362	37.18	431,179	19.42
Hispanic/Latinx	297,044	13.24	3436	15.28	293,608	13.22
NH-White	1,409,756	62.85	9725	43.24	1,400,031	63.05
NH-Asian American and Pacific Islander	81,481	3.63	823	3.66	80,658	3.63
NH-American Indian or Alaskan Native	15,329	0.68	145	0.64	15,184	0.68
County level social determinants of health	Median (IQR)	% <sup>a</sup>	Median (IQR)	% <sup>a</sup>	Median (IQR)	% <sup>a</sup>
Average household size	2.55 (2.42-2.69)	22.37	2.54 (2.42-2.70)	25.66	2.55 (2.42-2.69)	22.34
Social deprivation index score	51 (22.0-76.0)	21.71	66.00 (28.00–79.00)	26.38	51.00 (22.00-76.00)	21.66
Percent of the population without health insurance	10.4 (7.50–13.40)	24.95	10.40 (8.00–13.50)	26.62	10.40 (7.50–13.40)	24.93
Percent of the population who smoke	16.19 (13.83–18.68)	25.06	16.18 (13.82–18.70)	25.37	16.19 (13.83–18.68)	25.06
Mean commute time	5.40 (4.10-12.10)	22.41	5.30 (3.80-11.80)	21.48	5.40 (4.10-12.10)	22.42
Rurality (based on Rural–Urban Continuum Codes or RUCC)	0.87 (0.13–1.46)	24.75	0.66 (-0.04–1.22)	15.74	0.88 (0.13–1.46)	24.84
Percent of Hispanic/Latinx people	8.20 (4.60–16.10)	21.74	8.60 (5.10-19.40)	27.81	8.20 (4.60–16.10)	21.68
Black, White segregation score	0.43 (0.37-0.52)	21.99	0.45 (0.39-0.55)	28.08	0.43 (0.37-0.52)	21.93
Percent of people with limited food access	0.22 (0.13-0.29)	25.63	0.21 (0.13-0.27)	20.30	0.22 (0.13-0.29)	25.68

<sup>a</sup>Proportion of people within the fourth quartile of each SDoH measure (i.e., exposed group)





\*Cell count is set to < 20 observations to suppress small cell counts.

Fig. 2 Prevalence of Hospitalization After a COVID-19 Diagnosis Among People with and without HIV in the U.S. National COVID Cohort Collaborative (N3C) (Jan 1st, 2020–Nov 2nd, 2023) (n=2,243,151)

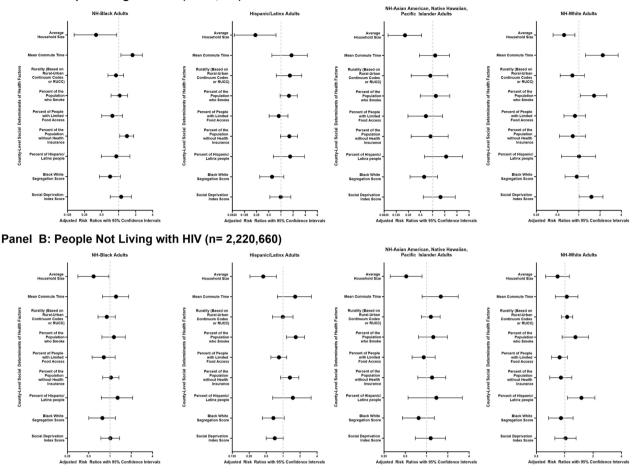
(Q4) median commute time (aRR: 2.18; 95% CI 1.24–3.60) was associated with higher risk of hospitalization. These associations were not observed among NH-Black PWOH. Among Hispanic/Latinx populations, living in an area with a higher (Q4) percentage of adults who smoke was associated with a higher risk of COVID-19 hospitalization among PWOH (aRR: 1.67; 95% CI 1.14–2.40). Among NH-White PWH, living in an area with a higher (Q4) percentage of adults who smoke (aRR: 1.65; 95% CI 1.05–2.49) was associated with a higher risk of COVID-19 hospitalization.

Figure 4 summarizes our examination of individual SDoH, based on statistically significant results of the above multivariable models. On further examination, increasing household size (Panel A) was no longer significantly associated with lower risk of COVID-19 hospitalization among racial/ethnic groups or those with and without HIV. However, we did observe that across racial/ethnic groups, living within the highest quartile of average household size at the county-level was negatively associated with hospitalization although not statistically significant. Among Hispanic/Latinx adults PWH, we observed that living in quartile 2

(aRR: 2.03; 95% CI 1.33–2.97) and three (aRR: 2.49; 95% CI 1.23–4.46) versus quartile 1, was associated with higher risk of COVID-19 hospitalization. Although not always statistically significant, it is also notable that the point estimates of each quartile of increasing percentage of adults who smoke were consistently positively associated with COVID-19 hospitalization.

#### Discussion

Our analysis evaluating associations between county-level SDoH measures and COVID-19 related hospitalization, stratified by racial/ethnic groups and HIV status, revealed noteworthy insights. Across racial/ethnic groups and living with HIV, most county-level SDoH measures were not consistently associated with increased risk of COVID-19 related hospitalization with a few exceptions. We observed that across racial/ethnic groups, living in a county with higher average household was associated with lower risk of COVID-19 hospitalization, which may suggest a positive



Panel A: People Living with HIV (n= 22,491)

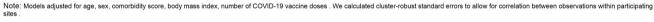
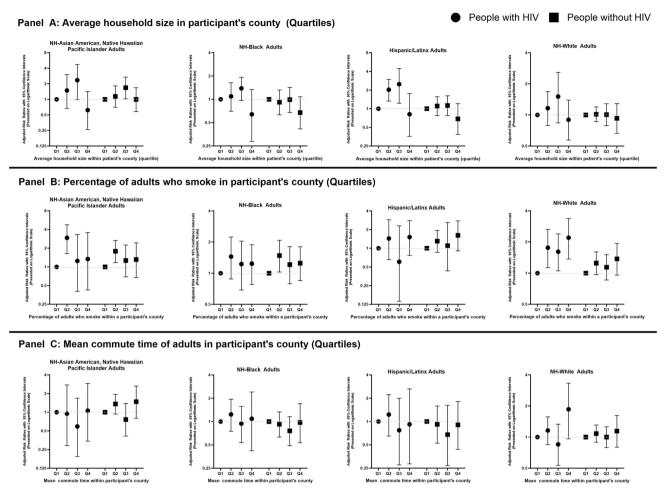


Fig. 3 Associations of county-level SDoH with COVID-19 hospitalization among people with HIV (A) and people without HIV (B) stratified by race/ethnicity (National COVID Cohort Collaborative, Jan 1st 2020–Nov 2nd, 2023)

role of familial or social support, for example, in promoting prompt care-seeking behavior, resulting in decreased poor COVID-19 outcomes. Also, among NH-Black adults with HIV, living in a county with a higher percentage of people without health insurance was associated with higher risk of COVID-19 related hospitalization, where people without health insurance are more likely to experience worse COVID-19 health outcomes. Further, living in a county with higher percentage of adults who smoke displayed increased risk for COVID-19 hospitalization, consistent with prior studies [42]. Overall, our results suggest that living in a socially deprived area leads to poorer COVID-19 outcomes among people with and without HIV alike, though varies in association by race/ethnicity. These findings require further research to validate them in other datasets or populations, and likely suggest new areas of interventions at the area or structural levels for the U.S. to reach its Ending the HIV Epidemic (EHE) goals.

Our results provide insights into the potential role of county-level SDoH and its impacts on COVID-19 related hospitalization among PWH. We consistently observed across racial/ethnic groups that higher average household size was associated with lower risk of COVID-19 related hospitalization. However, when we operationalized average household size within quartiles, we no longer observed significant associations, excluding among Hispanic/Latinx adults. These observations suggest two things: (1) living in a county with larger households on average may have occurred in less dense housing areas, which is important given that prior research shows that housing density is more strongly associated with COVID-19 hotspots than population density [43]; and (2) living with more family members may improve social support and adherence to COVID-19 preventive behaviors to mitigate the spread of infection. Among Hispanic/Latinx adults, when examining quartiles of average household size, we observed that increasing



Note: Models adjusted for age, sex, comorbidity score, body mass index, number of COVID-19 vaccine doses. We calculated cluster-robust standard errors to allow for correlation between observations within participating sites.

Fig. 4 Individual examination of select county-level SDoH factors by quartiles with COVID-19 hospitalization among people with and without HIV stratified race/ethnicity (National COVID Cohort Collaborative, Jan 1st 2020–Nov 2nd, 2023)

number of residents was associated with a higher risk of COVID-19 hospitalization. Our finding among Hispanic/ Latinx people is similar to prior research that demonstrates living in multi-generational households, which is more common among communities of color, may lead to increased risk of COVID-19 and downstream outcomes [44]. Given that Hispanic/Latinx adults in the U.S. are more likely to be essential workers with greater exposure to SARS-CoV-2 and subsequent COVID-19 infection, living in more crowded households was an important risk factor [45]. Among Hispanic/Latinx populations we found that living in counties with a higher rate of smoking was associated with COVID-19 hospitalization. This may be attributable to the fact that areas with higher smoking rates generally are lower income areas or more socially deprived [46]. As such, multifactorial effects may be at play: (1) Hispanic/Latinx people living in lower income areas may be more likely to be essential workers leading to higher risk of exposure, as mentioned above, and (2) given we know that smoking increases risk of poor COVID-19 outcomes, including hospitalization [42], exposure to second-hand smoke or higher likelihood of smoking among adults living in these counties may have impacted risk of our hospitalization outcome. Interestingly, we observed that among NH-Black and -White PWH, living in counties with average higher commute time was associated with COVID-19 related hospitalization. Living in urban areas with public transportation frequently leads to longer commute times [47], which in the context of the pandemic may have led to higher chances of exposure to COVID-19, particularly at-risk groups such as essential workers without the privilege to work from home.

Despite the associations we found between select countylevel SDoH factors with COVID-19 related hospitalization, surprisingly, the majority did not seem to impact COVID-19 related hospitalization, including social vulnerability index scores. These results differ from prior national studies, which have demonstrated a significant role of social vulnerability index with COVID-19 case fatality and COVID-19 outcomes at an aggregate county level [48–50]. However, our results may suggest that individual-level COVID-19 related outcomes may be differentially impacted by countylevel exposures. A prior study leveraging N3C data which examined the association between area-level SDoH factors with COVID-19 incidence and mortality among all people and found that access to healthcare resources, vulnerable populations, traveling behaviors, and COVID-19 policies and related behaviors increased risk for adverse COVID-19 outcomes [20]. Of note, this study performed clustering at the state level compared to our study, which clusters at the level of data partner site and may contribute to the difference in results observed between the two studies given vast heterogeneity across counties within a state. Another study investigating the role of area-level SDoH measures on COVID-19 mortality in Canada demonstrated that racialized minorities, larger average household size, lower income, lower education, higher percentage of essential workers, and higher percentage of apartment buildings were positively associated with COVID-19 mortality [51]. Our results may have also differed from both aforementioned studies, given we evaluated within racial/ethnic categories rather than comparing across groups (i.e., using NH-White adults as the referent group). While most prior literature has compared outcomes of marginalized populations to NH-White adults, this analytic approach denotes underlying assumptions that living as a White adult is characterized by optimal health, despite significant heterogeneity within racial/ethnic groups. Future research should extend existing research, and within racial/ ethnic groups, examine the role of individual-level SDoH on COVID-19 outcomes. Growing evidence suggests that arealevel markers of socioeconomic status or contextual factors are not strong proxies for individual level SDoH when examining individual outcomes, due to the potential for ecologic fallacy [52, 53]. Despite the growing appreciation of the role of contextual or neighborhood level effects, linking arealevel factors to individual outcomes may lead to misclassification of the exposure and a potential underestimation of the impact of the SDoH under study [53].

That certain SDoH factors' associations with COVID-19 related hospitalization varied by its significance among specific racial/ethnic groups is not surprising. The COVID-19 pandemic has disproportionately impacted racial/ethnic minorities in the U.S. differentially [54]. For example, in the domain of neighborhood and built environment, crowded living spaces with limited access to testing and treatment dramatically promoted increased spread of COVID-19 [55]. Furthermore, areas with high poverty and unemployment also have elevated COVID-19 exposure and transmission. It is well established that adverse SDOH, some rooted in long-standing impacts of structural racism in the U.S., impact adult health at the individual and population level [56]. Thus, our observations highlight the importance of examining the role structural racism plays in how SDoH factors may differentially impact different racial/ethnic groups through future work. In the context of HIV, it is particularly important to investigate the role of contextual SDoH given that the HIV epidemic in the U.S. is defined by inequities manifested as SDoH. For example, PWH are more likely to experience homelessness, poverty and food insecurity, which all contribute to significant barriers to care and consistent treatment, including prevention of HIV transmission [57–60]. In addition to their role in COVID-19, SDoH also play a prominent role in HIV incidence and outcomes [61]. Intervenable social factors such as low education and lowincome settings are associated with an increased risk in HIV incidence, especially among adolescents [62]. These structural determinants may also impact individual behavior, such as high-risk sexual behavior. Understanding the area-level SDoH factors that may have put these individuals at risk for acquiring HIV in the first place would be quite illuminating; however, this is not feasible currently in N3C as we do not have historical data prior to the occurrences of incident HIV.

When contextualizing the results of our analysis, it is important to consider potential limitations of the data we utilized. First, since the N3C is based on EHR data from multiple participating institutions, which are largely academic medical centers (though some data from community clinics are included), we may be missing data from the most vulnerable populations pertinent to our study question as those most marginalized by HIV may be less likely to be engaged in care. Second, the wider-spread availability of home-based COVID-19 testing may have led to under recording of hospitalizations due to COVID-19, as our definition of COVID-19 related hospitalization anchored first on having a COVID-19 diagnosis in the EHR; assuming this misclassification is non-differential would bias our findings towards the null. Importantly, we were unable to account for health care level factors such as capacity of the hospital (i.e., number of beds), availability of personal protective equipment (PPE), or number of ventilators. While we address variation within hospitals by clustering by participating data partner site, healthcare level factors may have played a significant role in COVID-19 hospitalization, though more so for outcomes downstream of hospitalization (e.g., ICU admission or in-hospital death). Third, this analysis was limited to the current county-level SDoH factors that were available in N3C for analyses. Fourth, area-level SDoH had to be aggregated from census tract, zip code level, and finally at the county level since only zip codes could be matched in N3C; greater granularity at the area levels may yield different insights than what we gained at the county level. Lastly, we acknowledge the problematic nature of grouping heterogenous minoritized groups, varying from Native Hawaiians to Alaska Natives to Asian Americans, into one group; given the number of factors in the models, we combined these

diverse communities into a single group and yet excluded smaller minoritized populations from analyses due to small sample sizes. In future, we hope a greater number of these individuals' data are included in N3C to allow meaningful comparisons. Future analyses should address additional SDoH measures as new data are constantly being ingested and harmonized into the N3C Enclave. Additionally, subsequent analyses should be performed using individual-level SDoH measures to better ascertain the association between SDoH and COVID-19 related hospitalization. With the ingestion of individual-SDoH and additional detailed arealevel SDoH measures, future analyses informed by our present findings can be conducted leveraging meaningful causal multi-level theoretical approaches. Notwithstanding the above limitations, this work is the most comprehensive to date to elucidate the potential role of area-level SDoH factors influencing COVID-19 risk among racial/ethnic PWH, and how HIV appears to play an outsized role in modifying those risks.

#### Conclusion

In conclusion, our results provide insights into the role of area-level SDoH, such as access to health insurance, commute time, household size, or smoking rates, on COVID-19 related hospitalizations among minoritized people with and without HIV. Insights gained from this analysis warrant further analyses at smaller geographic units or leveraging individual-level SDoH data to more granularly examine the effects of SDoH on HIV and COVID-19 outcomes. Our results are important as the pandemic has led to drastic economic, political, and societal disruption, prompting the need to incorporate SDoH variables into EHR datasets, like the N3C, and analyses, especially those pertaining to minoritized communities. The implications from this work shed light on the role of contextual health inequities, which may facilitate intervention development targeted at structural and social levels to address factors such as higher rates of being uninsured or smoking within U.S. counties.

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#### Declarations

Conflict of interest The authors have no conflict of interest to declare.

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