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Short communication

Association of *Clostridioides difficile* infection rates with social determinants of health in Denver area census tracts, 2016–2019

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ABSTRACT

We evaluated the association between census tract measures of socioeconomic status and *Clostridioides difficile* infection (CDI) rates in the Denver metro area from 2016 to 2019. Social vulnerability index, poverty, and race were associated with CDI. Findings may relate to differences in chronic disease prevalence, antibiotic exposure, and access to quality care.

1. Introduction

Clostridioides difficile is an urgent public health threat that caused more than 460,000 infections, 223,900 hospitalizations, and 12,800 deaths in the United States in 2017 (Centers for Disease Control and Prevention (U.S.), 2019; Guh et al., 2020). Infection occurs when antibiotics disrupt the colonic microbiome followed by exposure to, and colonization by, *C. difficile* spores in a person who is susceptible. Host risk factors include older age and underlying illness (Longo et al., 2015). While traditionally a health care-acquired pathogen, nearly half of infections have onset in the community (Guh et al., 2020). Most efforts toward *C. difficile* infection (CDI) prevention have focused on antimicrobial stewardship and infection prevention in health care (Kociolek et al., 2023 Apr). Much less is known about whether health disparities exist at the population level, and whether public health efforts should address underlying social determinants of health.

For many health conditions, it is recognized that socioeconomic status plays a role in disease acquisition and outcomes. However, data demonstrating an association between SES and healthcare-associated infections are limited. Centers for Disease Control and Prevention's Emerging Infections Program conducted an analysis to examine the association between community-level SES variables and community-associated CDI. Using data collected from 10 states in 2014–2015, they found that communities with lower SES had a higher CA-CDI incidence (Skrobarcek et al., 2021). Census tract level data collected by the New Mexico Emerging Infections Program (EIP) indicated that CA-CDI rates were associated with health insurance coverage and educational attainment. In addition, they found that non-white races were significantly more likely to acquire CA-CDI (Hudspeth et al., 2019). An Australian study examined the role of neighborhood socioeconomic disadvantage using an index of SES and found socioeconomic disadvantage to be associated with CDI (Spatial clusters of Clostridium difficile infection and an association with neighbourhood socio-economic disadvantage in the Australian Capital Territory, 2023). We used surveillance data to map neighborhood rates of CDI in the Denver metro area in order to define local variation in disease burden, identify whether neighborhood (defined as a census tract) social vulnerability index was associated with increased CDI rates, and compare SVI to other measures of SES from the U.S. census as a risk factor for CDI.

2. Materials and methods

We conducted an ecological study of 2,532,982 persons living in the Denver metro area. The unit of analysis included the 587 census tracts in Adams, Arapahoe, Denver, Douglas, and Jefferson counties. The study design was similar to analogous published studies (Skrobarcek et al., 2021; Czaja et al., 2020).

The outcome of interest was census tract rates of CDI for the period of

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2016–2019. The Colorado Department of Public Health and Environment is an EIP site and conducts population- and laboratory-based surveillance for CDI, (Guh et al., 2020) which is a reportable condition in the five-county area. A case of CDI was defined as a positive *C. difficile* toxin assay or a positive *C. difficile* molecular assay on an incident stool specimen from a resident of the catchment area aged 1 year or older who did not have a positive *C. difficile* test in the prior eight weeks. Cases were geocoded to census tract of residence using 2010 U.S. census boundaries. All cases were included in our analysis. Cases were aggregated into observed counts within census tracts according to sex (female or male) and age (0–19, 20–39, 40–59, or ≥60 years) strata. Expected counts for each census tract were calculated by applying sex- and age-stratified rates for the catchment area to the corresponding age- and sex-stratified population counts for each census tract. Observed and expected counts within census tracts were used in statistical analyses to calculate standardized morbidity ratios (SMR). Population denominators were taken from the 2015–2019 American Community Survey (ACS) to calculate the person-time for the standardized morbidity ratios in the five-county area. Chart review was not possible for all cases, so we did not stratify rates by epidemiologic classification as healthcare facility-onset, community onset-healthcare facility-associated, or community-associated.

The primary explanatory variable was social vulnerability index. SVI is a variable developed by the CDC/Agency for Toxic Substances and Disease Registry that indicates the relative vulnerability of every U.S census tract ranked on 15 social factors. The overall ranking taken from the 2018 CDC/ATSDR is provided on a 0 to 1 score, indicating lowest vulnerability to highest vulnerability (CDC SVI Documentation, 2018). We separately evaluated explanatory variables taken from 2015–2019, including percent living below the federal poverty level, percent of non-white race, percent of Hispanic ethnicity, and percent without health insurance (Data and February 2023). ACS covariates included established population risk factors for infectious disease (Data and February 2023). Covariate data were linked to outcome data by census tract geocode. Census tract boundaries were taken from the U.S. Census 2010 Tiger/Line files (Data and February 2023).

Statistical analyses included smoothing methods developed to address rate instability due to small numbers within areal units and spatial autocorrelation. Global spatial autocorrelation of CDI rates was evident in maps of census tract SMR and confirmed using Moran's I statistic ($P < 0.001$). We, therefore, used two Bayesian conditional autoregressive models to estimate parameters from median and 95% credible intervals (Elliott et al., 2001). The parameter of interest for Model One was the beta coefficient for SVI. For Model Two, the parameters of interest were the beta coefficients for the ACS variables with or without adjustment for covariates (Elliott et al., 2001). We used the Spearman coefficient to evaluate correlation between SVI and ACS variables. Analyses were conducted using SAS 9.4, RStudio 4.1.2, ArcGIS Pro 2.8.7, and OpenBUGS 3.2.3 software. The study was approved by the Colorado Multiple Institutional Review Board and Institutional Review Board at CDPHE.

3. Results

During the 2016–2019 surveillance data period, there were 16,781 CDI cases in the Denver metro area. Of these, 16,097 (96%) were geocoded, and 16,781 (100%) had documented sex and age available for rate standardization and were included in the analysis. The overall crude CDI rate for the Denver metro area between 2016 and 2019 was 155 cases per 100,000 persons. Disease mapping indicated a heterogeneous distribution of age- and sex-adjusted rates of CDI with geographic clustering.

The median census tract SVI was 0.4 (range 0.2, 0.7). The median (range) percentage of the population living in poverty was 6.8 (3.7, 12.5), percentage without health insurance was 5.5 (3.0, 10.3), percentage of non-white was 14.3 (8.9, 24.7), and percentage of Hispanic was 15.7 (8.9, 30.7). SVI was correlated with poverty ($\rho = 0.79$), health insurance coverage ($\rho = 0.78$), non-white race ($\rho = 0.54$), and Hispanic ethnicity ($\rho = 0.80$). ACS variables were correlated with each other ($\rho =$ 0.41–0.75).

For every 0.1 unit increase in SVI, the rate of CDI increased by 5% (RR 1.05, 95% CI 1.04–1.06). In unadjusted models, poverty (RR 1.15, 95% CI 1.10–1.20, per 10% increase), uninsured status (RR 1.14, 95% CI 1.07–1.21, per 10% increase), non-white race (RR 1.09, 95% CI 1.05–1.12, per 10% increase), and Hispanic ethnicity (RR 1.04, 95% CI 1.01–1.06, per 10% increase) were associated with increases in CDI rates. In a multivariable model, poverty (aRR 1.10, 95 %CI 1.05–1.16, per 10% increase) and non-white race (aRR 1.05, 95% CI 1.01–1.09, per 10% increase) were associated with increases in CDI rates. (Table 1).

4. Discussion

We found lower neighborhood SES as indicated by an increase in SVI to be associated with elevated rates of CDI. We found similar associations between CDI rates, poverty, and race, which are components of SVI. Disease maps (not shown here) allow us to identify the location of neighborhoods with the highest CDI rates for potential future public health intervention. Our findings suggest that SVI may be a good single variable with which to identify neighborhoods at increased risk of CDI without the statistical issues associated with multiple correlated ACS variables, and that socioeconomic characteristics not directly related to health care are important risk factors for this healthcare-associated infection.

The modest association between neighborhood SVI and CDI rates suggests that the connection between exposure and outcome is likely indirect and complex. Skrobarcek *et al.* hypothesized that living in communities with high poverty levels may be a proxy for outpatient health care exposures that may increase CDI risk (Skrobarcek et al., 2021). Mechanisms that may be underlying the pathway between increasing SVI and elevated CDI rates include higher prevalence of chronic disease and population susceptibility to infection, reduced access to primary care or increased use of emergency care, differential exposure to antibiotics, differential care within the healthcare system, or increased community exposures. While SES is a defining factor of population health (Phelan et al., 2010), our findings add to a growing evidence base that supports the need for a more granular evaluation of the causal pathway between SES and CDI.

Strengths of this study include the use of population-based surveillance to define the health of a community on a scale relevant to state and local public health. Limitations include reliance on provider testing practices for case identification, which could lead to over or under diagnosis of CDI. Individuals may not have acquired CDI in the census tract of their residence. Zoning and scale of census tract boundaries can affect the classifications of exposures and outcomes (Elliott et al., 2001), an issue which we addressed through spatial modeling. Lastly, we were unable to separate community- from healthcare-associated cases due to sampling methods. This may have biased our risk estimate toward 1. Our findings may not be generalizable to other locations, though consistency

Table 1
Sex- and Age-Adjusted Rate Ratios for Reported Cases of *C. difficile* in 587 Denver Metropolitan Area Census Tracts, 2016–2019.

RR (95% CI)		
Characteristic	Univariable analysis	Multivariable analysis
Social Vulnerability Index, 0.1-unit increase	1.05 (1.04, 1.06)	————
Non-white race, 10% increase	1.09 (1.05, 1.12)	1.05 (1.01, 1.09)
Hispanic ethnicity, 10% increase	1.04 (1.01, 1.06)	0.99 (0.96, 1.02)
Poverty, 10% increase	1.15 (1.10, 1.20)	1.10 (1.05, 1.16)
Uninsured, 10% increase	1.14 (1.07, 1.21)	1.06 (0.97, 1.15)

with other studies is reassuring (Skrobarcek et al., 2021; Hudspeth et al., 2019; Spatial clusters of Clostridium difficile infection and an association with neighbourhood socio-economic disadvantage in the Australian Capital Territory, 2023).

This evaluation is a first step toward recognizing that root causes of healthcare-associated infections may extend beyond the healthcare environment. Future public health surveillance programs should collect data on social determinants of health in an effort to directly measure the nature of health disparities on disease risk and improve the health of vulnerable populations. Further research is needed to investigate the mechanistic pathways between SVI and CDI rates and other healthcare-associated and antimicrobial-resistant infections to ultimately translate findings into public health action at the community level.

CRediT authorship contribution statement

Jessica L. Butler: Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Reed Hranac:** Data curation, Writing – review & editing. **Helen Johnston:** Project administration, Resources, Writing – review & editing. **Mary Casey:** Project administration, Resources, Writing – review & editing. **Elizabeth Basiliere:** Writing – review & editing. **Alison G. Abraham:** Writing – review & editing, Methodology. **Christopher Czaja:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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