January 2014

Area-Based Poverty And Community Associated Clostridium Difficile Infection In New Haven County, 2011-2013

Ranjit Dhaliwal
Yale University, dhaliwalranj@gmail.com

Follow this and additional works at: http://elischolar.library.yale.edu/ysphtdl

Recommended Citation
http://elischolar.library.yale.edu/ysphtdl/1065

This Open Access Thesis is brought to you for free and open access by the School of Public Health at EliScholar – A Digital Platform for Scholarly Publishing at Yale. It has been accepted for inclusion in Public Health Theses by an authorized administrator of EliScholar – A Digital Platform for Scholarly Publishing at Yale. For more information, please contact elischolar@yale.edu.
Area-based poverty and community associated *Clostridium difficile* infection in

New Haven County, 2011-2013

By: Ranjit Dhaliwal
Abstract

BACKGROUND: The relationship between socioeconomic status and CA-CDI incidence has not been examined. I hypothesize that there will be higher incidence rates of CA-CDI in areas of higher socioeconomic status, where individuals are more likely to have health insurance, better access to care and are more educated.

METHODS: Community onset (CO) cases from Emerging Infections program surveillance were defined as those with a CDI positive specimen sample less than four days after admission to a health care facility. Community associated CO cases were defined as those that did not have a healthcare exposure in the prior three months. Unadjusted CA-CDI incidence rates by sex, race, spatial location, and poverty rate were calculated. A spatial analysis of CA-CDI was conducted in SatScan9.3. Using Epi Info 7, chi-square test for trend was conducted to assess the relationship between CDI incidence and percent below poverty by census tract.

RESULTS: 1106 cases of CA-CDI occurred in New Haven County from 2011 to 2013. CA-CDI incidence was between 44 and 50 cases per 100,000 population for these three years. When cases for all three years were aggregated, a significant trend was revealed, where CA-CDI incidence increased as census tract poverty decreased. Similarly, age 5-17 CA-CDI incidence decreased as census tract poverty increased, but age 45-64 CA-CDI incidence increased as census tract poverty increased. A significant spatial cluster was revealed near Wallingford.

CONCLUSIONS: Incidence appears to be highest in the census tracts with the highest socioeconomic status, but data were inconclusive. Adjusted rates as well as additional surveillance data will help reveal the true relationship between socioeconomic status and CA-CDI. Spatial clusters will help direct future interventions that aim to reduce CA-CDI incidence.
Acknowledgements

I would like to thank everyone at Connecticut Emerging Infections Program for their contributions to this project, for graciously allowing me to use their surveillance data, and for their friendship. I especially would like to thank Kim Yousey-Hinde and Robert Heimer for their patience, dedication and mentorship. I would like to thank the faculty and my peers at YSPH for their friendship, assistance, and dedication to public health. I am thankful for having been a part of such a great community of scholars.
Table of Contents

Abstract 2
Acknowledgements 3
Introduction 5
Methods 11
Results 14
Discussion 18
Tables and Figures:
  Table 1 23
  Figure 1 24
  Figure 2 25
  Table 2 26
  Figure 3 27
  Table 3 28
  Figure 4 29
  Figure 5 30

References 31
Introduction

*Clostridium difficile* infection (CDI) is a growing public health concern. Traditionally CDI was thought to be nosocomial in origin, since it was the leading cause of infectious diarrhea and pseudomembranous colitis in a healthcare setting (Barbut, Corthier et al. 1996). In the last decade, the epidemiology of CDI changed. Researchers in Quebec examined surveillance data and suggested that incidence had increased from 35.6 cases per 100,000 population in 1991 to 156.3 cases per 100,000 population in 2003 for that catchment area (Pépin, Valiquette et al. 2004, Loo, Poirier et al. 2005). The increased incidence was not limited to Canada, as outbreaks were also reported in the USA (Dallal, Harbrecht et al. 2002, McDonald, Killgore et al. 2005). In these outbreaks, a larger proportion of infections progressed to more severe symptoms, such as toxic megacolon, intestinal perforation, necessity of colectomy, and death (Dallal, Harbrecht et al. 2002, Pépin, Valiquette et al. 2004, McDonald, Killgore et al. 2005).

A large proportion of infections that occurred in outbreaks across North America were caused by the North American Pulse Field Gel Electrophoresis Type 1 (NAP1) strain. This strain produces increased amounts of the two toxins, TcdA and TcdB, and also produces a binary toxin. Increased toxin production occurs because of mutations in genes involved in toxin expression (McDonald, Killgore et al. 2005). Infection by the NAP1 strain is a significant predictor of severe CDI, which can result in some of the more severe symptoms mentioned above (See, Mu et al. 2014). However, others have suggested that strain type does not predict outcome, so results are mixed at best (Walk, Micic et al. 2012). Research regarding the relationship between community onset, community associated CDI (CA-CDI) and strain type
suggested that a majority of infections that originate in the community are caused by the NAP1 strain (Limbago, Long et al. 2009).

A case of CA-CDI is defined as a toxin positive assay for an individual without a documented healthcare exposure in the last twelve weeks. A healthcare exposure is defined as a hospital or long term care facility stay. CDI incidence and severity have clearly increased, but more specifically, CA-CDI has also become more common. Recently, it has been estimated that approximately 25% of all total CDI cases are defined as CA-CDI, though the percentage tends to vary depending on the population (Norén, Åkerlund et al. 2004, Kutty, Woods et al. 2010, Lessa 2013). The incidence of CA-CDI has been estimated to be as high as 40 cases per 100,000 population (Khanna, Pardi et al. 2011, Lessa 2013).

CA-CDI incidence also increased in individuals not considered to be high risk for the disease, including younger individuals and individuals without underlying illness (Pituch 2009, Kuntz, Chrischilles et al. 2011). Risk factors for CA-CDI and modes of acquisition of the pathogen may be different compared to that of nosocomial CDI. Some individuals with CA-CDI have displayed traditional risk factors for CDI, such as increased age and prior antibiotic use (Kutty, Woods et al. 2010). In other instances, only a subset of individuals displayed risk factors that are unique to CA-CDI, including exposure to a hospitalized individual, outpatient surgical procedure, or antibiotic use greater than four weeks prior to onset of symptoms (Fellmeth, Yarlagadda et al. 2010). Similarly, proton pump inhibitor was considered by some to be a risk factor for CA-CDI (Dial, Delaney et al. 2005). Others insisted that proton pump inhibitor use is not a risk factor for CA-CDI (Wilcox, Mooney et al. 2008, Naggie, Miller et al. 2011). Relying on
traditional risk factors to identify new CA-CDI cases may result in missed diagnoses (Wilcox, Mooney et al. 2008).

Modes of pathogen transmission and acquisition might differ for individuals with CA-CDI. Toxigenic strains have been isolated from infected individuals, their homes, asymptomatic healthcare personnel, sewage, soil, domesticated animals, and store-bought meat products (Hafiz 1974, Kim, Fekety et al. 1981, Songer and Anderson 2006, Songer, Trinh et al. 2009, Hoover and Rodriguez-Palacios 2013). Infected individuals may acquire the pathogen via contact with one or more of these potential sources, leading to CA-CDI. Increased asymptomatic carriage of the pathogen in the community may be another cause of increased CA-CDI incidence (Bauer, Goorhuis et al. 2008).

Present Study

The goal of this study is to characterize CA-CDI in New Haven County, Connecticut. In addition to providing census tract level incidence of CA-CDI, geospatial clusters of infection, if present are also revealed. A demographic description of CA-CDI by census tract will be provided. Combining surveillance and socioeconomic data will improve understanding of the economic contribution to health. To my knowledge, the relationship between socioeconomic status and CA-CDI incidence has not been examined. Area-based socioeconomic factors can also be powerful predictors of health outcomes. Areas of high socioeconomic status will have the lowest proportion of individuals living in poverty and a higher proportion of individuals with advanced education. Uneducated individuals are more likely to be uninsured and thus less likely to receive adequate healthcare (Monheit and Vistnes 2000). Although the risk factors of CA-CDI and non-CA-CDI may differ, prior antibiotic use is still a significant predictor of CA-CDI
Use of prescribed antibiotics such as fluoroquinolones clindamycin, and penicillins may be higher in individuals with increased healthcare access. Individuals living in wealthier census tracts have better access to healthcare, and have the insurance that enables affordable access to care (Monheit and Vistnes 2000, Adler and Newman 2002). I hypothesize that there will be higher incidence rates of CA-CDI in areas of higher socioeconomic status.

Microbiologic Review

Pathogenesis

An exhaustive review of *Clostridium difficile* was completed in 1974, though its relevance as a human pathogen was still not understood (Hafiz 1974). It was not until 1978, after an extensive four year study, that *Clostridium difficile* infection (CDI) in humans was linked to pseudomembranous colitis (PMC) (Bartlett, Chang et al. 1978). Initially, *Staphylococcus aureus* was believed to be the cause of antibiotic associated PMC, but, after the discovery of cytotoxicity in tissue cultures and reproduction of colitis in hamster models, CDI was confirmed to be the cause (Bartlett, Chang et al. 1978). After the link between CDI and PMC was revealed, research on CDI in humans increased dramatically. Within the next decade, clinical features and toxigenesis had been carefully described (Tedesco, Gurwith et al. 1978, Burdon, Brown et al. 1979, Mogg, Burdon et al. 1979, Peikin, Galdibini et al. 1980, Lyerly, Krivan et al. 1988)

*Clostridium difficile* spores, like many other bacterial spores, survive a variety of environmental conditions and chemical treatments, but are inactivated by sporicidal agents (Lawley, Clare et al. 2009). Ingestion of spores, passage through the acidic environment of the stomach, and passage into the intestinal column results in the development of microfilimental
projections on the normally smooth outer surface of the spore, which promotes attachment to
the intestinal microvilli (Panessa-Warren, Tortora et al. 2007). Spores then germinate, allowing
vegetative cells to multiply. The mucus layer is penetrated and these cells eventually adhere to
enterocytes via a combination of flagellation and adhesins. At this stage colonization begins
and virulence factors that promote colonization, such as cysteine protease, s-layer proteins,
and flagellar components, are released by the bacteria. Sooner after, toxin production begins.
Study of the toxins has either confirmed or built upon previous studies (Snyder 1937, Hafiz
1974, Lyerly, Krivan et al. 1988). Both Toxin A (TcdA) and Toxin B (TcdB) are
glucosyltransferases, which act to transfer a UDP-glucose to GTPases in the cell. Action of TcdA
and TcdB induces morphological changes in the cell by disrupting cell signaling (Dawson,
Valiente et al. 2009). The fluid secretion and mucosal damage that occurs due to TcdA and TcdB
can result in diarrhea and PMC.

In addition to these two toxins, an additional factor has been identified. Binary toxin,
also referred to as Clostridium difficile transferase (CDT), is found in a smaller proportion of
strains. CDTa and CDTb, the two components of the toxin, combine cytotoxicity in vitro (Geric,
Carman et al. 2006). Although the binding site of CDT in the human body is unknown, the toxin
has been found in several epidemic strains. It has been suggested that the toxin may improve
bacterial adherence to the intestinal epithelium by increasing the presence of microtubules on
the surface of the bacterial surface (Schwan, Stecher et al. 2009).

Diagnosis

After initial disease manifestation, symptoms such as multiple aqueous diarrhea episodes per
day, fever, abdominal cramps, dehydration, and malnourishment can occur. The first test for
presence of CDI used was a tissue culture that utilized antitoxin to neutralize TcdA and TcdB. Since this test is highly sensitive and specific, it was considered one of the best methods for detecting CDI (Bartlett, Chang et al. 1978). Unfortunately it was time and labor intensive, so alternative methods were eventually developed. Stool culture is highly effective, though it is cost and labor-intensive. When possible, it is the preferred method of diagnosis because, when conducted on selective media, the infecting strain can be recovered and analyzed. This may become increasingly important as we try to understand the incidence and prevalence of infection by the NAP1 strain. Immune enzyme assays are a quick diagnosis method though there is high variability in the sensitivity and specificity of this method (Walker, Ruane et al. 1986). The test is simple, so it is often used, though in combination with a more robust detection method. Polymerase chain reaction is a highly sensitive and specific method that can also be used. Laboratory findings must always be considered with the prevailing symptoms for the patient in mind.

*Treatment*

Due to success with the use of oral vancomycin in treating enterocolitis, it was and continues to be used to treat PMC (Cohen, Gerding et al. 2010). The drug was approved by the Food and Drug Administration in the 1980’s and approved for use in the treatment of CDI (Wilson, Silva et al. 1981). It has since remained the only FDA approved drug for the treatment of CDI. Side effects of vancomycin use, including kidney damage, can be serious and more likely in the elderly.

Since there is a risk of becoming infected by vancomycin-resistant enterococcus species as a result of treatment, injected metronidazole has become the treatment of choice for
individuals with less severe CDI (Bartlett 2002). Oral metronidazole is also preferred for its reduced cost in comparison to oral vancomycin (Bartlett 2002). The effectiveness of metronidazole versus vancomycin has been researched. Some suggest that there is no significant difference between the effectiveness of the two treatment methods (Zar, Bakkanagari et al. 2007). Others suggest that vancomycin is a more effective treatment option (Musher, Aslam et al. 2005). However, vancomycin resistant enterococcal infection may occur (Gerding 1997). In addition, individuals who took metronidazole were more likely to have recurrent infections (Musher, Aslam et al. 2005). Even though these two methods have proven viable, there are instances in which both drugs may prove ineffective. Individuals with severe symptoms may not respond appropriately to therapy (McPherson, Rees et al. 2006). Strains resistant to at least one of these two drugs have been discovered. In these instances, failure of initial therapies may necessitate hospitalization, where fidaxomicin or intravenous immunoglobulin can be administered (McPherson, Rees et al. 2006, Louie, Miller et al. 2011).

Methods

At the Connecticut Emerging Infections Program (CT-EIP), active population-based CDI surveillance is ongoing. CT-EIP is one component of the Centers for Disease Control and Prevention (CDC) supported network of 10 surveillance sites scattered throughout the country. Active surveillance began at CT-EIP in 2009, with 23 towns in New Haven and Litchfield county serving as the catchment area. From 2011 to 2013, New Haven County served as the catchment area for CDI surveillance. Diagnostic tests for CDI were generally performed in individuals exhibiting symptoms such as diarrhea. Laboratory confirmed, toxin-positive CDI cases, excluding those in individuals under one year of age, were reported to the CT-EIP. Via medical
record review, several variables were collected for each patient, including medical history and
current underlying conditions, antibiotic use, demographic information, and full address.

CDI cases were classified as either incident or recurrent cases based on a basic set of
criteria. Incident CDI was either the first toxin positive CDI for a patient or subsequent CDI that
occurred at least eight weeks after the most recent CDI toxin-positive test. Recurrent CDI was a
case that occurred within 8 weeks of the most recent CDI toxin-positive test. CDI cases are
further classified by onset status as they are collected. Healthcare facility onset cases (HCFO)
were defined as those with a CDI positive specimen sample four or more days after admission
to an acute or long term healthcare facility. Community onset (CO) cases were defined as those
with a CDI positive specimen sample less than four days after admission to a health care facility.
CO cases were further characterized as community onset, healthcare facility associated (CO-
HFA) or community onset, community associated (CO-CA) cases. CO-HFA cases were defined as
those with a documented healthcare exposure (i.e. healthcare facility discharge or residence at
a long term care facility), and CO-CA cases were defined as those that did not have a healthcare
exposure in the prior three months. For the purposes of this study CO-CA cases will be referred
to as CA-CDI.

Demographic information for the population of New Haven County was downloaded via
the Factfinder portal of the United States Census Bureau (United States Census Bureau).
Datasets from the 5-year estimates of the 2012 American Community Survey and the 2010
Decennial Census Summary File 1 were obtained. Population by age, sex, and race/ethnicity as
well as total population figures per census tract in New Haven County were collected from the
decennial census. Poverty rate, or proportion of individuals that lived below the federal poverty
line in the last 12 months, were collected for each census tract from the American Community Survey. Health disparities, which impact disease burden, are often reflected in socioeconomic inequities. Census tract level data are thought to be most sensitive to socioeconomic gradients in health (Krieger, Chen et al. 2003, Krieger, Chen et al. 2005). Area-based socioeconomic status will be estimated using the proportion of individuals living under the federal poverty line. This variable, named percent below poverty for purposes of this study, is thought to accurately depict the relationship between socioeconomic status and many health outcomes for both the total population and by race group (Krieger, Chen et al. 2003, Krieger, Chen et al. 2005). The census tract level poverty rate was split into four groups: <5%, ≥5 to 9.99%, ≥10 to 19.99%, and ≥20% of the total population living under the poverty line (Krieger, Chen et al. 2003, Krieger, Chen et al. 2005). For the purposes of this study, these four groups will be referred to as census tract poverty groups.

This study used CDI surveillance data collected from January, 2011 to October, 2013. All recurrent CDI cases were excluded from the analysis, though additional cases that occurred in the same patient were not excluded if confirmations of toxin positivity were separated by more than eight weeks. Cases that were not classified as community associated were also excluded. Patients with incomplete or invalid demographic information were excluded.

To analyze these data, the home addresses of patients were geocoded using Arcmap 10.1. Geocoding was conducted to determine latitude and longitude coordinates and a spatial join was conducted to associate each patient with a census tract. Using SAS 9.2 (SAS Institute Inc, Cary, NC), the proportion of individuals living under the federal poverty line for each census tract was linked to each patient. Using population data from the 2010 decennial census, the
population of New Haven County was described by age, sex, race, and poverty. CA-CDI incidence rates were determined by census tract with 2010 decennial census data used as the denominator for incidence calculations. Unadjusted CA-CDI incidence rates by sex, race, spatial location, and poverty rate were also calculated.

A spatial analysis of CA-CDI was conducted in SatScan 9.3 (Martin Kulldorff, Harvard School of Medicine). Cartesian coordinates from geocoded cases were used in the analysis. A purely spatial, Poisson regression model was chosen. The shapefile output of the spatial analysis was joined to a Map of New Haven County to visualize the location of significant spatial clusters.

Using Epi Info 7 (Centers for Disease Control and Prevention, Atlanta, GA), chi-square test for trend was conducted to assess the relationship between CDI incidence and percent below poverty by census tract. Statistical analysis methods were in accordance with those of the Public Health Disparities Geocoding Project (Krieger et al). Statistical test results were considered significant if the p-value was less than 0.05.

Results

From August 1, 2009, to October 16, 2013, a total of 5607 incident cases of CDI were captured by Emerging Infections Program surveillance among New Haven County residents aged over 1 year. Of these 5607 incident cases, 5491, or 97.9% were successfully geocoded. Of these geocoded cases, 4342 occurred from 2011 to 2013. 1106 of those 4342, or 25.5% of all CDI, were classified as CA-CDI cases.

Table 1 lists descriptive features of the New Haven county population, including the distribution of race, sex, age groups and total population of individuals by census tract poverty
group. Mean annual CA-CDI incidence was significantly different for the five age groups. (ANOVA: P<0.01). Mean annual incidence by race/ethnicity was also significantly different (ANOVA: P<0.01). Hispanics had the lowest mean annual CA-CDI incidence at 19.84 per 100,000 individuals, and Non-Hispanic Whites had the highest incidence at 43.06 per 100,000 individuals. Mean Annual incidence was significantly different for females and males (53.21 per 100,000 individuals compared to 30.59 per 100,000 individuals, respectively, (T-test: P<0.01). Test for trend revealed that mean annual CA-CDI incidence increased as census tract poverty decreased (Chi-square test for trend: P=0.021).

CA-CDI annual incidence is given, stratified by census tract poverty group, in figure 1. Overall trends for incidence by census tract poverty were significant in 2011 (Chi-square test for trend: P=0.014), but not significant for 2012 (Chi-square test for trend: P=0.724) and 2013 (Chi-square test for trend: P=0.230). At 56.54 cases per 100,000 population, the highest incidence of CA-CDI occurred in 2013 among in census tract poverty group with less than 5% of the total population living in poverty. In 2012, CA-CDI incidence was also highest in the census tract poverty group with less than 5% of the total population living in poverty, with 51.91 cases per 100,000 population. In contrast, the census tract poverty group with the highest incidence in 2011 was the ≥5 to 10% group, with 52.80 cases per 100,000 population.

When CA-CDI incidence was further stratified by age, race-ethnicity, and sex, additional trends were revealed. In figure 2, age groups were further stratified by census tract poverty group. In the 45-64 years old age group, mean annual CA-CDI incidence increased as the proportion of individuals living under the federal poverty line per census tract increased (Chi-square test for trend P<0.01). In the 5-17 age group, mean annual CA-CDI incidence decreased
as the proportion of individuals living under the federal poverty line per census tract increased (Chi-square test for trend: all \( P<0.01 \)). Tests for trend were non-significant in the 1-4, 18-44, and 65+ age groups (Chi-square tests for trend: \( P=0.207 \), \( P=0.164 \), and \( P=0.224 \), respectively). CA-CIDI incidence was highest in the oldest individuals living in the census tracts with the highest proportion of individuals living under the federal poverty line at 149.34 per 100,000 individuals.

Table 2 describes the population distribution by age group, given in proportions of the total age group population, in the four census tract poverty groups. Chi-square tests for trend revealed that the proportion of total population decreased as census tract poverty increased (chi-square test for trend: all \( P<0.01 \)). The odds of living in the poorest census tract compared to the wealthiest census tracts was 0.173 for individuals aged 65 and above and 0.226 for individuals aged 45-64. The odds ratio was much higher in the youngest age group. Individuals aged 1-4 were only 0.823 times as likely to live in the poorest census tracts compared to the wealthiest census tracts.

In figure 3, race/ethnicity groups were further stratified by census tract poverty group. Due to missing data, only 1038 of the 1106 eligible CA-CIDI cases were used in this analysis. For Non-Hispanic Blacks, Non-Hispanic Whites, and Hispanics, CA-CIDI incidence increased as the proportion of individuals living under the federal poverty line per census tract increased; however, tests for trend revealed that relationships were non-significant (Chi-square test for trend: \( P=0.072 \), \( P=0.287 \), \( P=0.433 \), respectively). CA-CIDI incidence was highest in the Non-Hispanic Whites living in the census tracts with the highest proportion of individuals living under the federal poverty line at 48.66 per 100,000 individuals.
Table 3 describes the population distribution by race/ethnicity group, given in proportions of the total race/ethnicity group population, in the four census tract poverty groups. For Hispanic and non-Hispanic Black individuals, chi-square tests for trend revealed that the proportion of total population increased as census tract poverty increased (chi-square test for trend: all P<0.01). For non-Hispanic Whites, chi-square tests for trend revealed that the proportion of total population decreased as census tract poverty increased (chi-square test for trend: all P<0.01). Compared to living in the wealthiest census tracts, the odds of living in the poorest census tracts was 8.86 for non-Hispanic Blacks, 6.82 for Hispanics, and 0.091 for non-Hispanic Whites.

In figure 4, sex groups were further stratified by census tract poverty group. For males and females, CA-CDI incidence decreased as the proportion of individuals living under the federal poverty line per census tract increased, though for both groups this trend was non-significant (chi square tests for trend: P=0.092, P=0.107, respectively). As mentioned previously, there was a significant difference in mean annual CA-CDI incidence for males and females (T-Test: P<0.01). Females had a higher mean annual incidence at 53.21 cases per 100,000 population. When CA-CDI was stratified by sex, the highest incidence of CA-CDI occurred in females living in census tracts with the lowest proportion of individuals living under the federal poverty line at 58.8 per 100,000 individuals.

Six spatial clusters of infection were discovered, though only one, the largest of all discovered, was statistically significant (p<0.05). This cluster had a 7.25 kilometer radius and covered 8 different census tracts within its border. 58.27 per 100,000 population CA-CDI cases were expected to occur per year within the borders of this cluster, but 67.9 cases per 100,000
individuals per year actually occurred, yielding a relative risk of infection of 1.59 for individuals living within this cluster compared to individuals not living in this cluster. Figure 5 overlays this cluster on a univariate choropleth map of census tract poverty in New Haven County, allowing for data visualization.

Discussion

The findings of this study have quantified the burden of CDI in New Haven County. This study appears to be the first of its kind to analyze the relationship between CA-CDI and area-based socioeconomic status. The burden of CDI on healthcare systems has been well established, causing massive increases in healthcare costs and straining resources (Kyne, Hamel et al. 2002, Miller, Hyland et al. 2002). Linking surveillance and census data will improve surveillance networks and better understand the burden of CA-CDI. Learning and understanding the incidence rate of nosocomial and CA-CDI will allow researchers to intervene in areas of high incidence and respond quickly when an outbreak may be occurring, and inform health policy decision-making at the local, state and federal levels.

The three-year range in which a variety of incidence calculations were made yielded important results. This analysis has also revealed the relationship between CDI incidence and census tract poverty measure, which acted as a proxy for socioeconomic status. I hypothesized that the census tracts with the highest socioeconomic status would have the highest CDI incidence. Mean annual incidence was indeed highest in the census tracts with the lowest proportion of individuals living under the federal poverty line, though the trend of increasing incidence with decreasing census tract poverty is not as clear as originally anticipated. When surveillance data from all three years were aggregated and analyzed, CA-CDI incidence
decreased significantly with increasing census tract poverty. The trend of decreasing CA-CIDI incidence with increasing census tract poverty was significant when restricted to 2011 surveillance data, but not when restricted to 2012 or 2013 surveillance data.

The relationship between area-based socioeconomic status and other health outcomes has been explored previously, but not for CA-CDI (Krieger, Chen et al. 2002, Yousey-Hindes and Hadler 2011). With other diseases such as influenza, incidence is expected to increase with increasing census tract poverty (Yousey-Hindes and Hadler 2011). That is not the case for CA-CDI. Increased access to broad spectrum prescription antibiotics due to better healthcare access in wealthier census tracts may indeed drive the trend of increased CA-CDI incidence as census tract poverty decreases. Additional research will be necessary to determine if prescription antibiotic use drives CA-CDI incidence in New Haven County.

Mean annual incidence for census tracts in which 5%-9.99% of individuals live under the federal poverty line was lower than expected for Non-Hispanic Blacks and non-Hispanic Whites. More importantly, a reversal of trend also occurred in which CA-CDI incidence increased with increasing census tract poverty for all three race/ethnicity groups. It should be noted, however, that these trends were not statistically significant. It is possible that the population distribution of non-Hispanic Whites may have played a role in the reversal of trend. Non-Hispanic Whites in the poorest census tract poverty group make up only 7.35% of the population. In the penultimate poorest census tract poverty group, non-Hispanic Whites make up only 19.53% of the population. The reduced number of individuals in the two poorer census tract poverty groups contributed to the increased CA-CDI incidence for non-Hispanic White individuals living in these two census tract poverty groups.
A substantial proportion of cases of CDI in New Haven County occurred in individuals aged 65 and above. These individuals made up 42.6% of infections, but only comprised 14.5% of the total population of New Haven County. The burden of CA-CDI in this segment of the population is immense. CA-CDI in the 45-64 and 65+ age groups differed from the trend of mean annual incidence of CA-CDI in that the incidence increases, not decreases, with decreasing socioeconomic status. Individuals above the age of 45 were much more likely to live in the wealthier census tracts, leaving a small population of individuals in the poorer census tract groups. The decreased population in the poorer census tract groups would drive up CA-CDI incidence. I believe this explains the reversal of trend witnessed in the older age groups and in non-Hispanic Whites. The impact this may have had on non-Hispanic Blacks and Hispanics is unknown, since their trends for population distribution differed from that of non-Hispanic Whites.

The hypothesized trend of increased CA-CDI incidence with decreased census tract poverty was again evident in males and females. An uneven population distribution by sex in the census tract poverty groups was not a concern, which further suggests that it may have impacted incidence calculations by race/ethnicity and age. To truly confirm that this is the case, adjusted incidence rates must be calculated. This is certainly a direction of future research in the topic of socioeconomic status and CA-CDI.

The significant cluster covered an area of New Haven County that includes most of Wallingford and parts of North Haven, Hamden, East Haven, North Branford, and Guilford. Risk for CA-CDI was elevated in this high wealth area of New Haven County. The greater Wallingford area is the site of many long term care facilities. The population in this area of New Haven
County may be older on average than the rest of the county, putting them at greater risk for CA-CDI. The discovery of this cluster may direct future interventions that aim to reduce the burden of CA-CDI and also direct future etiologic studies of CA-CDI.

Limitations

In this study antibiotic use among individuals who were infected was not examined. Prior antibiotic use is widely accepted as one of the primary risk factors for both nosocomial and community associated infection. Examining antibiotic use in New Haven County and its interaction with CDI incidence will help public health advocates and medical professionals make informed choices for diagnosis, treatment, and prevention of CDI. This type of analysis also did not allow for an examination of disease severity. Strain type was not analyzed, so we do not currently know if the infecting strain is the NAP1 strain. We also do not know the proportion of cases in which binary toxin is present, or the proportion of cases that become recurrent. In this study, the sample size of CA-CDI by census tract was limited, which limits the statistical power of the analysis conducted in this study. Additional surveillance data would improve statistical power, so chances are that our understanding of CA-CDI in New Haven County will improve as surveillance continues. The new Haven population is not a standard population. The uneven distribution of race ethnicity groups and of the elderly affected incidence calculations, clouding the true effect of socioeconomic status on CA-CDI incidence.

Conclusions and directions of future research

CA-CDI incidence may be higher in wealthier census tracts compared to poorer census tracts in New Haven County, but additional research using surveillance data is necessary to confirm that this is the case.
The uneven distribution of the New Haven County population may cloud the true relationship between area based socioeconomic status and CA-CDI incidence. Calculations of adjusted incidence rates may help reveal the true relationship.

A significant spatial cluster was discovered in the greater Wallingford area of New Haven County. CA-CDI incidence is higher than anticipated for that population, so it may prove beneficial to direct future interventions toward this area of New Haven County.
### Table 1
Demographic description of the New Haven County population

<table>
<thead>
<tr>
<th>Category</th>
<th>Group</th>
<th>Population</th>
<th>% of total</th>
<th># Cases</th>
<th>Mean Annual CA-CDI Incidence</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total at risk population</td>
<td></td>
<td>853257</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>410361</td>
<td>48.1</td>
<td>387</td>
<td>30.59</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>442896</td>
<td>51.9</td>
<td>719</td>
<td>53.21</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Race</td>
<td>Hispanic</td>
<td>127,163</td>
<td>14.9</td>
<td>80</td>
<td>19.84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>578,002</td>
<td>67.5</td>
<td>724</td>
<td>43.06</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>100,429</td>
<td>11.8</td>
<td>101</td>
<td>29.57</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Age</td>
<td>1 though 4</td>
<td>39,443</td>
<td>4.6</td>
<td>17</td>
<td>14.71</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 through 17</td>
<td>144,311</td>
<td>16.9</td>
<td>26</td>
<td>5.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18 though 44</td>
<td>307,590</td>
<td>36</td>
<td>187</td>
<td>20.19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45 through 64</td>
<td>237,941</td>
<td>27.9</td>
<td>404</td>
<td>60.44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>65 and up</td>
<td>123,972</td>
<td>14.5</td>
<td>472</td>
<td>129.71</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Census tract poverty</td>
<td>&lt;5%</td>
<td>308,237</td>
<td>36.1</td>
<td>442</td>
<td>51.72</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5%-9.99%</td>
<td>193,167</td>
<td>22.6</td>
<td>249</td>
<td>46.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥10%-19.99%</td>
<td>193,273</td>
<td>22.7</td>
<td>230</td>
<td>42.80</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>158,580</td>
<td>18.6</td>
<td>185</td>
<td>42.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P=0.021</td>
</tr>
</tbody>
</table>

This table depicts the New Haven County population by sex, race, age group, and census tract poverty group. Census tract poverty groups are categorized by the proportion of individuals living under the federal poverty line in a given census tract. For every census tract that fell into one of four census tract poverty groups, population figures were aggregated to yield the values above. T-test revealed significant differences in CA-CDI incidence by sex. ANOVA revealed significant differences in CA-CDI incidence among race groups and age groups, respectively. Chi-square test for trend revealed significant trend in CA-CDI incidence, with incidence decreasing as census tract poverty increased.
Chi-square test for trend revealed a significant downward trend in incidence as census tract poverty increased for 2011 surveillance data (Chi-square test for trend: \( P=0.014 \)) but not for 2012 and 2013 surveillance data (Chi-square tests for trend: \( P=0.724 \) and \( P=0.23 \)).
In the 45-64 years old age group, mean annual CA-CDI incidence increased as census tract poverty increased (Chi-square test for trend P<0.01). In the 5-17 age group, mean annual CA-CDI incidence decreased as census tract poverty increased (Chi-square test for trend: all P<0.01). Tests for trend were non-significant in the 1-4, 18-44, and 65+ age groups (Chi-square tests for trend: P=0.207, P=0.164, and P=0.224, respectively).
Table 2: Population distribution by age group into census tract poverty groups

<table>
<thead>
<tr>
<th>Census Tract Poverty Group</th>
<th>1-4</th>
<th>5-17</th>
<th>18-44</th>
<th>45-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>0.29</td>
<td>0.37</td>
<td>0.30</td>
<td>0.41</td>
<td>0.44</td>
</tr>
<tr>
<td>5% -9.99%</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.25</td>
<td>0.24</td>
</tr>
<tr>
<td>10% -19.99%</td>
<td>0.25</td>
<td>0.21</td>
<td>0.26</td>
<td>0.20</td>
<td>0.20</td>
</tr>
<tr>
<td>20%+</td>
<td>0.25</td>
<td>0.21</td>
<td>0.23</td>
<td>0.14</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Table 2 describes the population distribution by age group, given in proportions of the total age group population, in the four census tract poverty groups. Chi-square tests for trend revealed that the proportion of total population decreased as census tract poverty increased (chi-square test for trend: all $P<0.01$). Older individuals were much less likely to live in the poorer census tracts.
Due to missing data, only 1038 of the 1106 eligible CA-CDI cases were used in this analysis. For Non-Hispanic Blacks, Non-Hispanic Whites, and Hispanics, CA-CDI incidence increased as the proportion of individuals living under the federal poverty line per census tract increased; however, tests for trend revealed that relationships were non-significant (Chi-square test for trend: P=0.072, P=0.287, P=0.433, respectively). The trend for Non-Hispanic Blacks is near, but not quite significant, perhaps due to a low number total number of cases.
Table 3 describes the population distribution by race/ethnicity group, given in proportions of the total race/ethnicity group population, in the four census tract poverty groups. For Hispanic and non-Hispanic Black individuals, chi-square tests for trend revealed that the proportion of total population increased as census tract poverty increased (chi-square test for trend: all P<0.01). For non-Hispanic Whites, chi-square tests for trend revealed that the proportion of total population decreased as census tract poverty increased (chi-square test for trend: all P<0.01). Only a tiny proportion of Non-Hispanic Whites lived in the poorest census tracts, but nearly half of Non-Hispanic Blacks and Hispanics lived in the poorest census tracts.

<table>
<thead>
<tr>
<th>Census Tract Poverty Group</th>
<th>Race/ethnicity Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-Hispanic Black</td>
</tr>
<tr>
<td>below 5%</td>
<td>0.09</td>
</tr>
<tr>
<td>5% to 10%</td>
<td>0.12</td>
</tr>
<tr>
<td>10% to 20%</td>
<td>0.30</td>
</tr>
<tr>
<td>above 20%</td>
<td>0.48</td>
</tr>
</tbody>
</table>
For males and females, CA-CIDI incidence decreased as the proportion of individuals living under the federal poverty line per census tract increased, though for both groups this trend was non-significant (chi square tests for trend: P=0.092, P=0.107, respectively). Females had a higher mean annual incidence at 53.21 cases per 100,000 population. Incidence among females in the poorest census tracts was still higher than that of men in the wealthiest census tracts.
Figure 5 displays the only statistically significant spatial cluster on a choropleth map of census tract poverty in New Haven County. Census tracts with the worst poverty tend to be aggregated around the New Haven and Waterbury urban areas. The spatial cluster, which is 7.25 kilometer in radius, covered 8 different census tracts within its border. Most of the town of Wallingford is included within the spatial cluster.
References


