Geographic determinants of colorectal cancer in Louisiana

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Received: 26 May 2021 / Accepted: 20 December 2021 / Published online: 7 January 2022 © The Author(s) 2022

Abstract
Purpose Currently, rural residents in the United States (US) experience a greater cancer burden for tobacco-related cancers and cancers that can be prevented by screening. We aim to characterize geographic determinants of colorectal cancer (CRC) incidence in Louisiana due to rural residence and other known geographic risk factors, area socioeconomic status (SES), and cultural region (Acadian or French-speaking).

Methods Primary colorectal cancer diagnosed among adults 30 years and older in 2008–2017 were obtained from the Louisiana Tumor Registry. Population and social and economic data were obtained from US Census American Community Survey. Rural areas were defined using US Department of Agriculture 2010 rural–urban commuting area codes. Estimates of relative risk (RR) were obtained from multilevel binomial regression models of incidence.

Results The study population was 16.1% rural, 18.4% low SES, and 17.9% Acadian. Risk of CRC was greater among rural white residents (RR Women: 1.09(1.02–1.16), RR Men: 1.11(1.04–1.18)). Low SES was associated with increased CRC for all demographic groups, with excess risk ranging from 8% in Black men (RR: 1.08(1.01–1.16)) to 16% in white men (RR: 1.16(1.08–1.24)). Increased risk in the Acadian region was greatest for Black men (RR: 1.21(1.10–1.33)) and women (RR: 1.21(1.09–1.33)). Rural–urban disparities in CRC were no longer significant after controlling for SES and Acadian region.

Conclusion SES remains a significant determinant of CRC disparities in Louisiana and may contribute to observed rural–urban disparities in the state. While the intersectionality of CRC risk factors is complex, we have confirmed a robust regional disparity for the Acadian region of Louisiana.

Keywords Colorectal cancer · Rural · Socioeconomic status · Geographic disparities

Introduction
Geographic disparities in cancer incidence and outcomes can be due to numerous factors. At the individual level, demographic factors, occupation, poverty, and health behaviors or beliefs can contribute to cancer risk [1–3]. Additionally, there are many well-established cancer risk factors beyond the individual level, including healthcare access, living environment (social and physical), and large-scale policy and systems [2]. Currently, in the United States (US) residents in rural or non-metropolitan areas experience greater cancer burden for tobacco-related cancers and cancers that can be prevented by screening [4]. While national trends show the rural–urban disparity in colorectal cancer (CRC) incidence has narrowed greatly over several decades, disparities remain [4–7]. However, there is variation in geographic disparities, which underscores the need for cancer reporting at the regional level [8].

In the US, the risk of colorectal cancer has also been associated with low socioeconomic status (SES), both at the individual and area level [9–11]. Reasons for this association are complex and include higher prevalence of modifiable CRC risk factors among individuals of low SES, such as poor diet, low physical activity, and tobacco use [12, 13]. SES gradients in CRC are also influenced by healthcare access and setting, insurance status, and the ability to attend routine or follow-up medical appointments [9]. Further evidence supports spatial clustering of CRC incidence and mortality in areas of high poverty and thus may play an important role in geographic disparities in CRC [12, 14, 15].

The National Cancer Institute (NCI) has now validated small area-based measures of rural residence and SES for cancer reporting in the Surveillance, Epidemiology, and
End Results (SEER) program [16, 17]. Previously, these measures were reported at the county level which has been shown to be vulnerable to aggregation and misclassification bias [18]. Importantly, small area-based measures of exposures enable the use of multilevel or hierarchical modeling, which accounts for interdependence of individuals in shared environments or systems and is well suited but underutilized in the study of rural cancer disparities [2, 18, 19]. A national assessment of CRC risk for rural residential status using small area-based measures (census tract) has not yet been reported. While a census tract-level analysis of cancer incidence found higher SES was associated with increased breast and prostate cancer incidence and lower SES was associated with increased lung cancer risk, there was no clear association between SES and colorectal cancer incidence at the national level [16].

Louisiana ranks 4th in the US for CRC incidence, with significantly greater rates of CRC among all race and sex groups when compared to national rates. Recent research has identified two distinct geographically determined risk factors for CRC in Louisiana. First, the Acadian region of south Louisiana has been shown to have experienced significantly higher rates of CRC incidence compared to state and national rates, which have motivated theories of genetic risk among the Acadian founder population [20]. Acadian settlers arrived in Louisiana in the late-18th century after being exiled from present day Nova Scotia [21]. Acadians are a subset of Louisiana Creole which is a broad term that refers to the blend of ancestry and culture (European, West African, and Native American) in the state during this period [22]. During Segregation and the Jim Crow era, white Acadian Creoles began to distance themselves from the broader mixed-race Louisiana Creole label by identifying only as Acadian or ‘Cajun’ [22]. In the 1920’s, in a push for Americanization, Louisiana school children began to be punished for speaking French at school which marked a decline in the use of Cajun and Creole dialects [23]. An ecological analysis of CRC rates during 2005–2009 found that Louisiana counties in which at least 10% of the population were French or Cajun French-speaking (excluding French Creole) had greater risk than the state average [20]. This risk was most pronounced for white men, where the incidence of CRC was 37% greater than national rates [20]. Additionally, previous research also reported a significant association between neighborhood-concentrated disadvantage, an index of socioeconomic disadvantage, and the incidence of CRC in the state [11]. In this study, we aim to characterize multiple geographic determinants of colorectal cancer incidence in Louisiana. We will examine risk differences by residential location (urban/rural), area socioeconomic status, and cultural region using multilevel analysis. Continued monitoring of geographic CRC disparities will provide insight into how the state compares to national trends and support longitudinal reporting for CRC awareness and prevention in Louisiana.

Methods

Data

Data on primary colorectal cancer diagnosed in Louisiana residents, 30 years and older, between 1 January 2008 and 31 December 2017 were obtained from the Louisiana Tumor Registry, a participant of the NCI’s SEER Program and the Centers for Disease Control and Prevention’s National Program of Cancer Registries. Cases were identified by the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) site codes C180-C189, C199, and C209. Histology codes (9050-9055, 9140, 9590-9992) were excluded. Age was categorized into 5-year groups beginning at 30 years old. Early onset colorectal cancer (EOCRC) included cases diagnosed before 50 years old, while average-onset colorectal cancer (AOCR) included cases in residents 50 and older. Patients were geocoded to 2010 US Census tracts by address at the time of diagnosis. Population at risk for each age, race, and sex group was determined by census tract using US Census American Community Survey (ACS) 2012 5-year population estimates. Geographic determinants were linked to patients by 2010 US Census tract. Census tracts with missing geographic data were excluded (n = 52). This research was approved by Louisiana State University Health Sciences Center, New Orleans Institutional Review Board.

Geographic Determinants

All geographic determinants were observed at the census tract level. An indicator of rural residence was derived from US Department of Agriculture 2010 rural–urban commuting area (RUCA) codes (2019 revision), with metropolitan cores and associated commuting areas (secondary codes 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, 10.1) classified as urban and all other areas classified as rural (Fig. 1a). While this definition of rural is consistent with the NCI’s SEER working group census tract-level study [17], a sensitivity analysis was designed to investigate the effect of metropolitan status to facilitate a comparison between our results and studies that use county-level US Department of Agriculture Rural Urban Continuum codes [4, 6-8]. For the sensitivity analysis, census tracts within metropolitan cores were identified by RUCA primary code 1 and all other census tracts were classified as non-metropolitan. An index of socioeconomic status was developed using US Census ACS 2012 5-year estimates and includes measures of occupation, unemployment, poverty, income, education, and home and rent values [24].
This index was validated by NCI and described as having a more consistent interpretation across geographic regions when compared to a competing composite index [16]. Low SES was defined as census tracts in the lowest quartile of the SES index (Fig. 1b). The Acadian region of Louisiana was defined as census tracts with more than 5% of households speaking French or Cajun French at home (Fig. 1c), based on the US Census ACS 2012 5-year estimates [20].

Statistical Analysis

CRC incidence was analyzed as a rate of cases out of the total person-years at risk and modeled using multilevel binomial regression, with individuals nested within census tracts. Age was included in the model as a covariate and a random intercept for census tracts was used to account for correlation among residents living in the same tract. Models were stratified by race and sex. Races other than white and Black or African American were excluded due to insufficient numbers. We provide age-adjusted risk estimates for each geographic risk factor separately (rural residence, low socioeconomic status, Acadian) and then provide risk estimates conditioned on all three factors. Multilevel models were executed using GLIMMIX procedure in SAS version 9.4.

Results

The study included 23,345 incident cases of CRC among residents in 1,096 census tracts. Characteristics of the at-risk study population and cases are presented as Table 1. Overall, the study population was 47.5% male and 29.8% Black or African American, while cases of CRC were 53.5% male and 32.4% Black or African American. Regarding geographic risk factors, 16.1% resided in rural census tracts and 18.4% resided in low-SES areas, with 6.1% of residents were in rural, low-SES tracts. Many of the rural, low-SES areas were located in the Mississippi Delta region of the state (Fig. 1a and b). 17.9% of the study population resided in Acadian or French-speaking areas (Fig. 1c).

The study population included individuals 30 years or older, 55.3% of which were 50 or older. The majority of CRC cases in the study (90%, n = 21,009) were diagnosed in patients 50 or older and were considered average-onset colorectal cancer (AOCRC). The remaining 10% of cases were early-onset colorectal cancer (EOCRC).

Estimates of risk from multilevel models of incidence are provided in Table 2. Age-adjusted risk estimates are provided in Fig. 2. For all CRC, rural–urban disparities were observed in white women and men, where the relative risk (RR) and 95% confidence interval for rural areas compared to urban was 1.09 (1.02–1.16) and 1.11 (1.04–1.18), respectively. There were no significant rural–urban disparities in Black or African American women or men. Low SES was associated with increased CRC in all race and sex groups, with the excess risk ranging from 8% in Black men [RR: 1.08 (1.01–1.16)] to 16% in white men [RR: 1.16 (1.08–1.24)] when compared to residents of moderate-to-high-SES areas. The increase in risk observed for the Acadian or French-speaking region was greatest for Black or African American men [RR: 1.21 (1.10–1.33)] and women [RR: 1.21 (1.09–1.33)]. There was also significant regional risk among white men [RR: 1.18 (1.11–1.25)] and white women [RR: 1.16 (1.09–1.23)]. Conditioned on other risk factors, rural–urban disparities in CRC among whites were no longer statistically significant [Women RR: 1.05 (0.98–1.12), Men RR: 1.06 (1.00–1.13)]. However, risk associated with low SES remained significant with risk ratios ranging from 1.10 (1.02–1.18) in Black men to 1.14 (1.07–1.23) in Black women. Similarly, Acadian or French-speaking areas had significantly increased risk, with risk ratios ranging from 1.15 (1.08–1.22) in white women to 1.22 (1.11–1.35) in Black women and men.
Table 1  Characteristics of colorectal cases and population controls included in the study, Louisiana 2008–2017

|                  | Cases         | Population controls | p value | Cases         | Population controls | p value | Cases         | Population controls | p value |
|------------------|---------------|---------------------|---------|---------------|---------------------|---------|---------------|---------------------|---------|
|                  | %  n          | %  n                |         | %  n          | %  n                |         | %  n          | %  n                |         |
| All              | 100.0 23,345  | 100.0 2,442,594     | <.0001  | 100.0 2,336   | 100.0 1,101,165     | 0.9036  | 100.0 21,009  | 100.0 1,341,429     | <.0001  |
| Sex              |               |                     |         |               |                     |         |               |                     |         |
| Female           | 46.5 10,845   | 52.6 1,284,036      | <.0001  | 50.6 1,183    | 50.8 559,034        | 0.9036  | 46.0 9,662    | 54.0 725,002        | <.0001  |
| Male             | 53.5 12,500   | 47.4 1,158,558      | <.0001  | 49.4 1,153    | 49.2 542,131        | 0.0018  | 54.0 11,347   | 46.0 616,427        | <.0001  |
| Race             |               |                     |         |               |                     |         |               |                     |         |
| White            | 67.6 15,773   | 70.2 1,714,398      | <.0001  | 63.9 1,493    | 66.9 737,210        | 0.0531  | 68.0 14,280   | 72.8 977,188        | <.0001  |
| Black            | 32.4 7,572    | 29.8 728,196        | <.0001  | 36.1 843      | 33.1 363,955        |         | 32.0 6,729    | 27.2 364,241        |         |
| Rural            |               |                     |         |               |                     |         |               |                     |         |
| No               | 82.0 19,149   | 83.9 2,050,134      | <.0001  | 83.2 1,943    | 84.6 931,821        |          | 81.9 17,206   | 83.4 1,118,313      | <.0001  |
| Yes              | 18.0 4,196    | 16.1 392,460        |         | 16.8 393      | 15.4 169,344        |          | 18.1 3,803    | 16.6 223,116        |         |
| Low SES          |               |                     | <.0001  |               |                     | <.0001  |               |                     | <.0001  |
| No               | 77.4 18,073   | 81.6 1,994,131      | <.0001  | 79.0 1,845    | 82.2 905,048        |          | 77.2 16,228   | 81.2 1,089,083      | <.0001  |
| Yes              | 22.6 5,272    | 18.4 448,463        |         | 21.0 491      | 17.8 196,117        |          | 22.8 4,781    | 18.8 252,346        |         |
| Acadian          |               |                     | <.0001  |               |                     |         |               |                     | <.0001  |
| No               | 80.1 18,703   | 82.1 2,006,182      | <.0001  | 79.7 1,862    | 81.9 902,245        | 0.0052  | 80.2 16,841   | 82.3 1,103,937      | <.0001  |
| Yes              | 19.9 4,642    | 17.9 436,412        |         | 20.3 474      | 18.1 198,920        |          | 19.8 4,168    | 17.7 237,492        |         |

SES socioeconomic status
Statistically significant results, at alpha = 0.05, are shown in bold
Table 2  Relative risk estimates and 95% confidence intervals from multilevel models of early and average-onset colorectal cancer incidence, Louisiana 2008–2017

|                      | All colorectal cancer (Aged 30 and older) | Early onset colorectal cancer (Aged 30–49) | Average-onset colorectal cancer (Aged 50 and older) |
|----------------------|------------------------------------------|-------------------------------------------|--------------------------------------------------|
|                      | RR (95% CI)^a                            | RR (95% CI)^b                             | RR (95% CI)^a                                      | RR (95% CI)^b                             |
| **White females**    |                                          |                                           |                                                   |
| Rural                | 1.09 (1.02,1.16)                         | 1.05 (0.98,1.12)                         | 1.15 (0.93,1.43)                                  | 1.04 (0.83,1.29)                         | 1.08 (1.01,1.16)                         | 1.05 (0.98,1.13)                         |
| Low SES              | 1.14 (1.06,1.23)                         | 1.11 (1.03,1.20)                         | 1.45 (1.14,1.84)                                  | 1.40 (1.09,1.80)                         | 1.12 (1.03,1.21)                         | 1.09 (1.00,1.18)                         |
| Acadian              | 1.16 (1.09,1.23)                         | 1.15 (1.08,1.22)                         | 1.29 (1.07,1.56)                                  | 1.26 (1.05,1.52)                         | 1.14 (1.07,1.22)                         | 1.14 (1.06,1.21)                         |
| **White males**      |                                          |                                           |                                                   |
| Rural                | 1.11 (1.04,1.18)                         | 1.06 (1.00,1.13)                         | 1.18 (0.96,1.44)                                  | 1.13 (0.92,1.40)                         | 1.10 (1.03,1.18)                         | 1.05 (0.99,1.13)                         |
| Low SES              | 1.16 (1.08,1.24)                         | 1.12 (1.04,1.21)                         | 1.21 (0.95,1.53)                                  | 1.15 (0.90,1.48)                         | 1.15 (1.07,1.24)                         | 1.12 (1.04,1.21)                         |
| Acadian              | 1.18 (1.11,1.25)                         | 1.17 (1.10,1.24)                         | 1.07 (0.88,1.29)                                  | 1.05 (0.87,1.27)                         | 1.19 (1.12,1.27)                         | 1.18 (1.11,1.26)                         |
| **Black females**    |                                          |                                           |                                                   |
| Rural                | 1.02 (0.93,1.12)                         | 0.98 (0.89,1.07)                         | 1.07 (0.83,1.39)                                  | 1.06 (0.81,1.37)                         | 1.02 (0.92,1.12)                         | 0.96 (0.87,1.07)                         |
| Low SES              | 1.13 (1.05,1.21)                         | 1.14 (1.07,1.23)                         | 1.09 (0.90,1.32)                                  | 1.08 (0.89,1.31)                         | 1.14 (1.05,1.22)                         | 1.16 (1.07,1.25)                         |
| Acadian              | 1.21 (1.09,1.33)                         | 1.22 (1.11,1.35)                         | 0.94 (0.71,1.24)                                  | 0.94 (0.71,1.25)                         | 1.25 (1.12,1.38)                         | 1.27 (1.14,1.41)                         |
| **Black males**      |                                          |                                           |                                                   |
| Rural                | 1.00 (0.91,1.10)                         | 0.97 (0.88,1.06)                         | 0.95 (0.70,1.29)                                  | 0.92 (0.67,1.26)                         | 1.01 (0.91,1.11)                         | 0.97 (0.88,1.07)                         |
| Low SES              | 1.08 (1.01,1.16)                         | 1.10 (1.02,1.18)                         | 1.02 (0.81,1.29)                                  | 1.05 (0.83,1.33)                         | 1.09 (1.01,1.17)                         | 1.10 (1.02,1.19)                         |
| Acadian              | 1.21 (1.10,1.33)                         | 1.22 (1.11,1.35)                         | 1.31 (0.97,1.77)                                  | 1.32 (0.98,1.79)                         | 1.20 (1.08,1.32)                         | 1.21 (1.10,1.34)                         |

RR relative risk, CI confidence interval, SES socioeconomic status

^aAdjusted for age (5 year groups)

^bAdjusted for age (5 year groups) and other risk factors in the table (rural, low SES, Acadian)

Estimates that were statistically significant, at alpha = 0.05, are shown in bold.

Fig. 2  Age-adjusted relative risk (RR) estimates and 95% confidence intervals from multilevel models of colorectal cancer incidence, Louisiana 2008–2017
Risk patterns in overall CRC largely reflect risk observed for AOCRC (Table 2). Conditioned on other geographic risk factors, there was increased AOCRC in both low SES and Acadian or French-speaking areas for all four major race and sex groups. Risk factors for EOCRC were identified among white women only, where rates in low-SES areas were 45% greater than those in moderate- and high-SES areas [RR: 1.45 (1.14–1.84)] and the Acadian region exhibited 29% greater rates than other areas [RR: 1.29 (1.07–1.56)]. Conditioned on other geographic risk factors, these effects remained significant.

Results from sensitivity analyses with metropolitan status are provided as supplemental Table 1. Similar to the urban–rural classification, white residents in non-metropolitan areas had greater CRC risk compared to their counterparts in metropolitan areas [RR women: 1.13 (1.08–1.20), RR men: 1.16 (1.10–1.22)]. In contrast to the urban–rural classification, disparities by metropolitan status persisted among white residents after adjusting for low SES and Acadian or French-speaking areas for all four major race and sex groups. Risk factors for EOCRC was limited by relatively low incidence and thus less model precision when compared to AOCRC. Age-adjusted EOCRC incidence during the study period was 20.5 per 100,000 compared to 149.3 per 100,000 for AOCRC. However, we did report significant EOCRC risk among low-SES white females, who had 40–45% increased risk compared to their moderate- and high-SES counterparts. In the US, rates of EOCRC have been greatest in Southern states and among African Americans [8, 31]. While it is important to note that the absolute incidence of EOCRC is still low, evidence of significant birth cohort effects, and changes in behavioral risk factors such as diet, metabolic dysfunction, heavy alcohol consumption, and smoking indicate a need for continued research regarding the incidence of EOCRC [32, 33].

Results from this study also confirmed significantly high rates of CRC in the Acadian region of Louisiana. This region had 16–18% increase in CRC risk among white residents and 21% increase in risk among Black or African American residents, when compared to the rest of the state. This is in contrast to previous reports of elevated CRC risk in the region among white males only [20]. Differences in methodology of the present study include a census tract rather than county designation for Acadian communities, extended study period, and multilevel analysis of risk which is well suited for assessing geographic risk because it accounts for interdependence of individuals with shared environmental context [2, 18, 19]. Defining the Acadian region based on the proportion of French-speaking households was previously intended as a proxy for Cajun ancestry to investigate the hypothesis of hereditary CRC in the Cajun population [20]. However, with significant regional risk seen across all...
major demographic groups, it may be this definition serving as a proxy for other cultural or broad environmental factors in the area. The Acadian region did have a greater proportion of rural census tracts when compared to the rest of the state (23.8% vs 14.8%), but the regional disparity was robust after conditioning on rurality and SES.

**Limitations**

One limitation to the study is that there is no universal definition for rural in the US. In county-level studies, researchers often employed a metropolitan and non-metropolitan classification based on USDA Rural Urban Continuum codes and more nuanced categories of rural, urban or suburban, and metropolitan have been effective in characterizing geographic health disparities [4, 6–8, 18]. The urban and rural classification we used in the study were chosen to be consistent with SEER working group to support continuity in NCI cancer registry research [17]. Further, the study was limited to a 10-year period in a single state with a moderate rural population and thus lacked statistical power to sufficiently investigate the intersection of rurality, socioeconomic status, and region. Sensitivity analyses with effect interactions did not result in significant interactions and were not conclusive. While the use of cancer registry and other population-representative data sources enabled a comprehensive assessment of the population, the study concept did not include individual-level social and behavioral risk factors which may provide insight regarding mechanisms of geographic risk. Finally, the study did not include Hispanics, American Indian/Alaska Native, and Asian/pacific islanders as a subgroup for analysis due to relatively low numbers of residents in Louisiana.

**Conclusion**

SES remains a significant determinant of disparities in CRC incidence in Louisiana and may contribute to observed rural–urban disparities in the state. Results from this study support efforts for prevention and control that consider how these factors interact. For example, the Louisiana Colorectal Cancer Round Table, a coalition for colorectal cancer prevention and awareness, has conducted studies to better identify differential healthcare access in the state. One study estimated that over half of GI providers in Louisiana did not accept Medicaid in 2017, the time of the State Medicaid expansion, and that the geographic distribution of providers likely affected differential rates of screening and incidence for low income and rural populations [34]. Other research has also suggested that factors regarding patient volume or payer policies matter more than location alone [27, 35, 36]. Factors other than screening can also contribute to SES and regional disparities, such as diet, physical activity, tobacco and alcohol use, or environmental exposures [9]. While the intersectionality of CRC risk factors is complex we have confirmed a regional disparity for the Acadian or French-speaking region of Louisiana for all major demographic groups in the state.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s10552-021-01546-7.

**Acknowledgments** This research was supported by P20CA233374 from the National Cancer Institute.

**Author contributions** DD and CL contributed to the study conception and design. DD completed the data acquisition and analysis and wrote the first draft. All authors contributed to interpretation and read and approved the manuscript for intellectual content.

**Data availability** Data are maintained by Louisiana Tumor Registry and is not publicly available. Use of the data for research must be approved by the Louisiana Tumor Registry Board of Research.

**Code availability** SAS code for multilevel models of incidence is available upon request.

**Declarations**

**Conflict of interest** The authors have no conflict of interest to declare that are relevant to the content of this article.

**Ethical approval** This research was approved by Louisiana State University Health Sciences Center, New Orleans Institutional Review Board.

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