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Cancer Epidemiology, Biomarkers & Prevention

Where Can Colorectal Cancer Screening Interventions Have the Most Impact?

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Abstract

Background: Although colorectal cancer death rates in the United States have declined by half since 1970, large geographic disparities persist. Spatial identification of high-risk areas can facilitate targeted screening interventions to close this gap.

Methods: We used the Getis-Ord Gi* statistic within ArcGIS to identify contemporary colorectal cancer "hotspots" (spatial clusters of counties with high rates) based on county-level mortality data from the national vital statistics system. Hotspots were compared with the remaining aggregated counties (non-hotspot United States) by plotting trends from 1970 to 2011 and calculating rate ratios (RR). Trends were quantified using joinpoint regression.

Results: Spatial mapping identified three distinct hotspots in the contemporary United States where colorectal cancer death rates were elevated. The highest rates were in the largest hotspot, which encompassed 94 counties in the Lower Mississippi Delta [Arkansas (17), Illinois (16), Kentucky (3), Louisiana (6), Mississippi (27), Missouri (15), and Tennessee (10)]. During 2009 to 2011, rates here were 40% higher than the non-hotspot United States [RR, 1.40; 95% confidence interval (CI), 1.34–1.46], despite being 18% lower during 1970 to 1972 (RR, 0.82; 95% CI, 0.78–0.86). The elevated risk was similar in blacks and whites. Notably, rates among black men in the Delta increased steadily by 3.5% per year from 1970 to 1990, and have since remained unchanged. Rates in hotspots in west central Appalachia and eastern Virginia/North Carolina were 18% and 9% higher, respectively, than the non-hotspot United States during 2009 to 2011.

Conclusions: Advanced spatial analysis revealed large pockets of the United States with excessive colorectal cancer death rates.

Impact: These well-defined areas warrant prioritized screening intervention. *Cancer Epidemiol Biomarkers Prev; 1–6. ©2015 AACR.*

Introduction

Tremendous progress against colorectal cancer has been achieved in the United States over the past several decades. Overall, colorectal cancer death rates have declined by 47% since the mid-1970s (1). This reduction has been attributed to increased population screening (53%), as well as changing patterns in risk factors (35%), and improvements in treatment (12%; ref. 2). However, geographic trends vary substantially. We previously reported that since the early 1990s, colorectal cancer death rates had declined by ≥30% in northeastern states, but remained virtually unchanged in Mississippi and Alabama, shifting the burden of disease from the Northeast to the South in little more than a decade (3). This pattern is consistent with the historical shift in the socioeconomic gradient of colorectal cancer. Prior to the late 1980s, colorectal cancer death rates were highest among those with higher income and education levels (4, 5). However, by 2007, colorectal cancer death rates among individuals with the least education were double those of the most educated (6). Geographic differences both in the burden of colorectal cancer and the pace of the downward trend reflect this crossover.

The majority of colorectal cancer deaths are preventable through healthy behaviors, like maintaining a healthy body weight, consuming a healthy diet, being physically active, and engaging in appropriate screening (7). Screening reduces mortality by reducing incidence through the detection and removal of precancerous adenomas, and by detecting malignancies at an early stage, when treatment is most successful. Herein, we extend our previous state-level analysis (3) to the county in order to more precisely highlight high-risk areas where targeted screening programs could have the greatest impact.

Materials and Methods

We accessed colorectal cancer death data from 1970 through 2011 for all counties in the United States using SEER*Stat software, version 8.1.5 (8). SEER*Stat is a product of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. The SEER program annually obtains mortality files containing all deaths in the United States from the National Center for Health Statistics (numerator data) and population estimates from the Population Estimates Program of the U.S. Census Bureau (denominator data). Following the convention of the National Center for Health Statistics, analysis was limited to those counties with a minimum of 10 deaths per decade to minimize the relative standard error in the calculation of rates. Death rates were expressed per 100,000 person-years and weighted to the 2000 U.S. standard population by the direct method using 5-year age groups to allow for comparison across time and space. County-level rates were

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calculated for 10-year intervals (1970–79, 1980–89, 1990–99, 2000–09) for stability.

County-level death rates were used as input for cluster analysis with the Getis-Ord Gi* statistic within ArcGIS, version 10.2 (Environmental Science and Research Institute). The Getis-Ord Gi* statistic identifies statistically significant clusters of high and low values based on the "neighborhood" of each county as derived from modeling the spatial relationship among counties. To account for the variation in county size and the exclusion of some counties due to suppression or missing data, we used a Spatial Weight Matrix that quantifies the spatial relationships among counties based on user-defined distance (100 kilometers) or number of neighbors (minimum of 2). The ability to incorporate underlying spatial relationships that take into account the heterogeneity in county location and size is a unique advantage of advanced spatial analysis over the simple mapping commonly used to present cancer surveillance data. In addition, spatial analysis derives clusters based on statistical significance, whereas the interpretation of simple mapping is more prone to bias because cut points can be subjectively defined based on a variety of methodologies (quantiles, standard deviation, etc.). The result of the cluster, or hotspot, analysis includes the associated Z score and *P* value, indicating the statistical significance of the cluster. We considered statistical significance at the confidence level of 95% or higher, associated with P value < 0.05 and Z score > 1.96.

Death data were also analyzed using Anselin local Moran's I statistic of spatial association (9), available within ArcGIS, and the spatial analysis software tool SaTScan, version 9.3 (10), to validate cluster results. SaTScan analysis was performed using adjusted mortality counts and the spatial, discrete Poisson model. The maximum scan window was adjusted based on the population size, and results were tested for 5% and 10% of the population.

Three-year moving average annual death rates from 1970–72 through 2009–11 were calculated separately for identified hotspots and for the remaining United States counties as a whole, heretofore referred to as the non-hotspot U.S. Trends were quantified using joinpoint regression analysis (11). Rate ratios (RR) with 95% confidence intervals (CI) were calculated to quantify the risk of colorectal cancer death in hotspots versus the non-hotspot U.S.

Results

The age-standardized colorectal cancer death rate per 100,000 Americans decreased from 29.2 in 1970 to 15.1 in 2011. The magnitude of this decline accelerated over time, from 4% during the 1970s to 27% during the 2000s (Fig. 1). Prior to 1990, colorectal cancer death rates were highest in the northeast and mid-central United States and lowest in the South (Fig. 2). However, by the 2000s, rates were generally homogeneous across the country with the exception of three distinct spatial clusters, or hotspots. These hotspots were located in the Lower Mississippi Delta (Hotspot 1), west central Appalachia (Hotspot 2), and eastern North Carolina/Virginia (Hotspot 3) and included 238 counties in 12 states (Supplementary Table S1). Kentucky had counties in both Hotpot 1 and Hotspot 2. These same three, primarily rural areas were similarly identified by all three spatial analysis tools (data not shown).

The highest death rates were in the Lower Mississippi Delta. This hotspot, which had a population of 3.7 million in 2011, encompassed a 94-county area that spanned parts of Arkansas (17 counties), Illinois (16), Kentucky (3), Louisiana (6), Mississippi (27), Missouri (15), and Tennessee (10). During 2009 to 2011, the population was 61% white and 37% black, a slight shift from 67% and 32%, respectively, during 1970 to 1972. Colorectal cancer death rates in the Delta were 18% lower than the non-hotspot U.S. during 1970 to 1972 (RR, 0.82; 95% CI, 0.78–0.86), but 40% higher during 2009 to 2011 (RR, 1.40; 95% CI, 1.34–1.46). This crossover occurred around 1990 in both whites and blacks (Fig. 3). While the contemporary race-specific disparity was slightly smaller for whites (RR, 1.26; 95% CI, 1.20–1.33) than for blacks (RR, 1.37; 95% CI, 1.28–1.47), the difference was not statistically significant. Notably, the trend based on joinpoint regression analysis indicated that while rates are declining in the Delta among white men and women and black women, they have

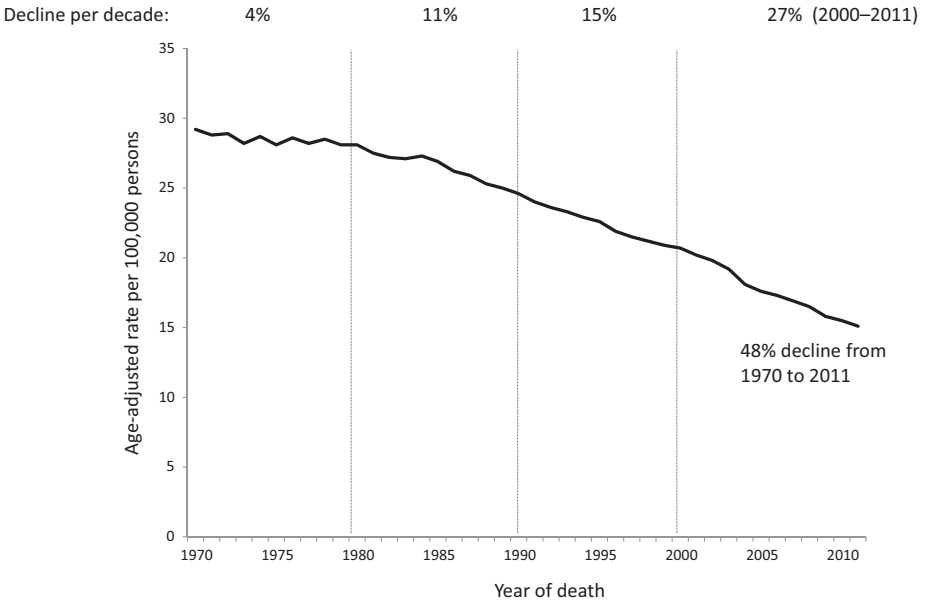

Figure 1.
Temporal trend in colorectal cancer death rates from 1970 through 2011.

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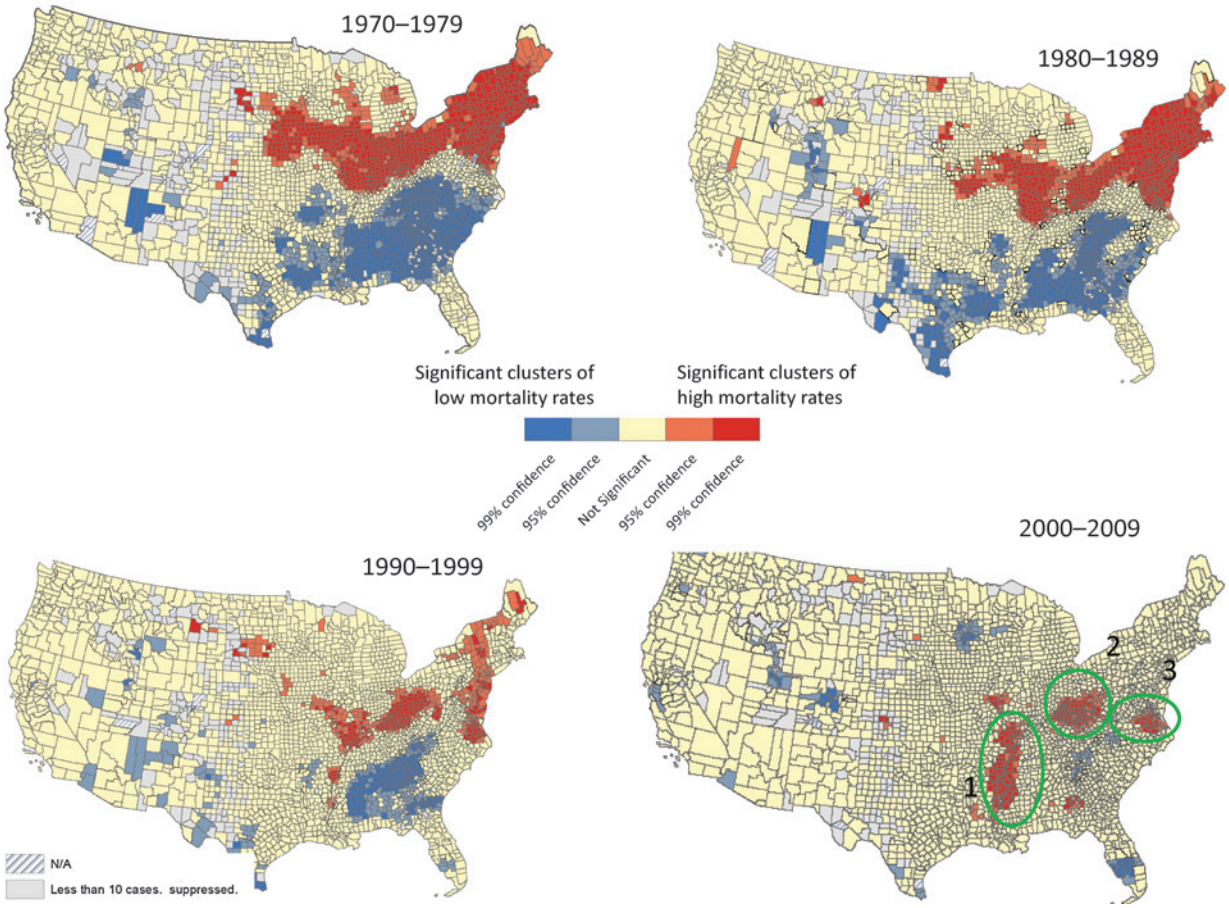

Figure 2.
Hotspot analysis of county-level colorectal cancer death rates during the past four decades.

remained unchanged in black men since 1990. Prior to 1990, rates in black men increased steadily by 3.5% per year since at least 1970.

The hotspot in the west central region of Appalachia was comprised of 107 counties in Indiana (6), Kentucky (60), Ohio (22), and West Virginia (19). The population of more than 6.2 million was 89% white during 2009 to 2011. In contrast with the Delta, colorectal cancer death rates in this hotspot were higher than national rates in the 1970s, a disparity that widened over the next four decades (Supplementary Fig. S1). The RR increased from 1.10 (95% CI, 1.06–1.14) during 1970–1972 to 1.18 (95% CI, 1.14–1.22) during 2009–2011. Hotspot 3 consisted of 11 counties in northeastern North Carolina and 26 counties in southeastern Virginia and had a racial distribution and colorectal cancer pattern similar to that in the Delta, with an RR of 0.79 (95% CI, 0.71–0.86) during 1970 to 1972 and 1.09 (95% CI, 1.02–1.17) during 2009 to 2011.

Discussion

In contrast with the large decline in colorectal cancer death rates experienced by most of the nation, our study identified three distinct areas in Appalachia and the rural South where progress has lagged. These findings expand on previously reported state disparities in colorectal cancer death rates (3) and are consistent with recent research linking rural residence with increased risk of colorectal cancer death (12, 13). The trends in Hotspots 1 and 3 are also compatible with the historical shift in the burden of colorectal cancer from more to less affluent individuals (5). The patterns in colorectal cancer death rates in these high-risk areas are more similar to those in economically transitioning countries with limited health care resources, such as Romania, Russia, and Mexico (14), than to those in the United States.

The Lower Mississippi Delta and Appalachia are diverse geographic regions distinguished by longstanding challenges that include high unemployment, low levels of education and health literacy, and inadequate access to health care (15–18). The Lower Mississippi Delta has been classified as persistently poor (≥20% poverty) since 1970 by the U.S. Department of Agriculture's Economic Research Service and has county-level poverty rates that are two standard deviations above the national median (19, 20). High poverty similarly characterizes much of Appalachia and rural North Carolina and Virginia (21). In Appalachia, Central Appalachia is the most poverty-stricken subregion, where ≥20% of people live in poverty in most counties (22). Individuals who are economically disadvantaged have higher colorectal cancer death rates due to both higher incidence rates and poorer disease outcomes. Survival rates among low-income individuals are lower due to a variety of factors, including a higher prevalence of comorbidities, a lower likelihood of tumor resection and adjuvant

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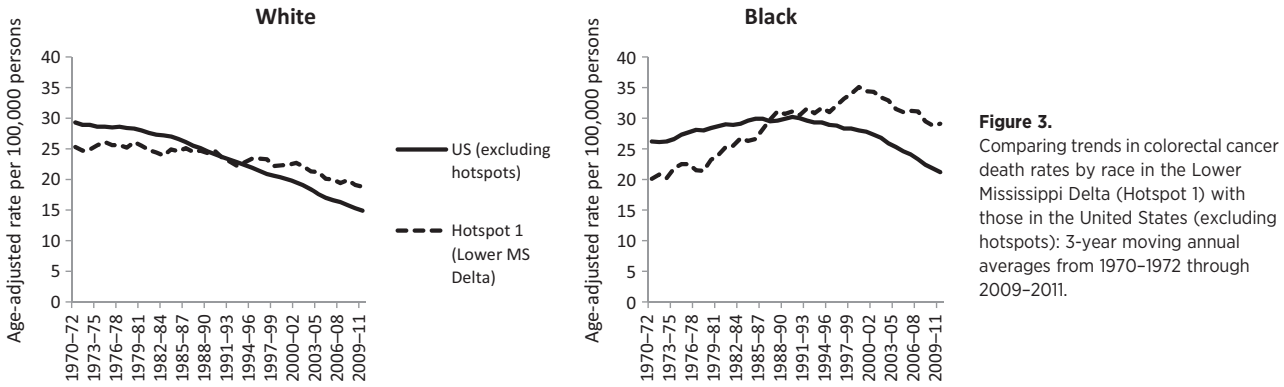

Figure 3.
Comparing trends in colorectal cancer death rates by race in the Lower Mississippi Delta (Hotspot 1) with those in the United States (excluding hotspots): 3-year moving annual averages from 1970–1972 through 2009–2011.

therapy, and more advanced disease stage (12, 23, 24). Later stage at diagnosis is largely a consequence of lower screening rates among people with lower socioeconomic status (25, 26), often as a result of obstacles in accessing health care. Notably, as of March 2015, only six of the 12 states found to contain high-risk counties have taken advantage of the federal funding opportunity offered by the Affordable Care Act to expand Medicaid coverage (Arkansas, Illinois, Indiana, Kentucky, Ohio, and West Virginia).

Research has demonstrated the efficacy of screening for reducing colorectal cancer mortality both by decreasing incidence through the removal of precancerous lesions and by detecting malignancy at an earlier, more treatable stage (27). Colorectal cancer screening rates have been increasing in the United States since at least 1987 (25, 28), but uptake has not been equally distributed and disparities by race, ethnicity, and socioeconomic status remain (25, 29). For example, in 2010, 40% of individuals with incomes less than 200% of the federal poverty threshold were current for colorectal cancer screening, compared with 66% of those with incomes of more than 500% of the poverty threshold (30). Area-level poverty is associated with screening behavior independent of individual factors; people who reside in communities with high poverty are less likely to be screened than those living in low-poverty settings even after controlling for income, education, and insurance status (31). The rural poor are at a particular disadvantage because of the low density of specialists for colorectal cancer screening and treatment (32, 33). Disparities by insurance status are even more striking. In 2010, just 19% of individuals without health insurance were current for colorectal cancer screening compared with 62% of those with coverage (34). The Delta Rural Poll found that 22% of Mississippi Delta residents were uninsured in 2009 (35), compared with 17% in the general U.S. population (36). In west central Appalachia, the uninsured rate is more than 19% in the majority of counties, and as high as ≥25% in many counties (22).

Screening inequalities likely contribute to the disparities we observed. Screening in accordance with guidelines has been estimated at 49% in Appalachian Ohio (37), which has among the lowest rates of uninsured in Appalachia (22). Fleming and colleagues found that among Kentucky residents, those living in Appalachia were half as likely as non-Appalachians to report endoscopy screening for colorectal cancer in the past 10 years (38). While colorectal cancer screening rates for the Mississippi Delta are not available, breast cancer screening has been shown to be lower there than in the rest of the United States (39). In addition, a study of cancer incidence in Mississippi found that rural residence was associated with a later stage of disease, which is suggestive of lower screening prevalence in the predominantly rural Delta region (40). According to Behavioral Risk Factor Surveillance System data for 2010, colorectal cancer screening rates were below the national median (64.5%) in each of the 10 states represented in Hotspots 1 and 2, with West Virginia (54.5%), Mississippi (57.1%), and Arkansas (58.6%) ranking in the lowest quartile (41). It is noteworthy that none of the 12 states with counties identified as high-risk in our analysis are among the 25 states funded by the Centers for Disease Control and Prevention's Colorectal Cancer Control Program, which provides screening services to uninsured and underinsured low-income individuals.

Screening disparities primarily relate to cost and access to care. Income and education are strongly, positively associated with screening, even among insured individuals with a usual physician (42). Other factors associated with low screening rates include lack of knowledge about the importance of screening (43), not having a usual place for health care, and not having a physician recommendation for the test (44). However, a large proportion of underserved patients do not follow through with testing even after a provider recommendation (45). A common provider barrier to screening in underserved communities is an inadequate referral mechanism after an abnormal test (46). Patient navigators or community health workers are particularly beneficial for facilitating follow-up and treatment in underserved populations (47).

Obesity (body mass index $\geq$ 30 kg/m^2) increases the risk of colorectal cancer 2-fold in men and by 50% in women (48). With the exception of Virginia, all of the hotspot states are in the highest quartile for obesity prevalence among adults (49). Within Mississippi, which has the highest obesity prevalence of any state (35% vs. a national median of 27% in 2009), the highest county-level obesity rates (38% to 44%) are concentrated in the Mississippi Delta region (50). In addition, food consumption in the Delta, which is high in soft drinks, red meat, and salty snacks, differs from national patterns in a direction conducive to colorectal cancer development (51). Moreover, Mississippi and West Virginia residents are least likely to participate in leisure-time physical activity (67% vs. the U.S. median of 76%), which protects against colorectal cancer (52).

The primary strength of our study is the innovative use of advanced spatial analysis to analyze four decades of nationwide, county-level vital statistics data and pinpoint geographic disparities in colorectal cancer death rates. Although we were limited to the study of counties with a minimum of 10 deaths per decade in

order to produce reliable rates, this represented 93% of all counties during 2000 to 2009 and the Spatial Weight Matrix accounted for these missing data. Due to the nature of ecologic studies, we can only speculate about causes for the disproportionate burden of colorectal cancer. We are also somewhat limited in the interpretation of our results. For example, some portion of the increase in the risk of colorectal cancer death in the Lower Mississippi Delta hotspot is likely due to the shift in the racial distribution of the population, from 32% black in the early 1970s to 37% during 2009 to 2011. However, the effect of population migration on our results was likely minimal because both blacks and whites had similarly elevated risk. The interpretation of death data is also limited by inaccuracies in the underlying cause of death recorded on death certificates. However, misclassification for colorectal cancer is only about 10% (53).

Although the risk of death from colorectal cancer is at a historical low for most Americans, it is unnecessarily high among residents of the Lower Mississippi Delta, Appalachia, and other rural areas. Cancer prevention through lifestyle modification is the preferable mechanism for decreasing cancer occurrence; however, effecting change to reduce obesity and increase physical activity is extremely difficult. Moreover, the fruits of these efforts are not born at the population level for many years. Promoting and improving access to screening through patient navigation and outreach programs offers a more immediate return on investment. The state of Delaware effectively eliminated colorectal cancer disparities in less than a decade by implementing comprehensive statewide colorectal cancer screening (54). The rapid introduction of coordinated, targeted, community-based screening programs in these high-risk areas could be similarly successful.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: A. Robbins, A. Jemal
Development of methodology: R.L. Siegel, L. Sahar, A. Robbins, A. Jemal
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): R.L. Siegel
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): R.L. Siegel, L. Sahar, A. Robbins, A. Jemal
Writing, review, and/or revision of the manuscript: R.L. Siegel, L. Sahar, A. Robbins, A. Jemal
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): L. Sahar
Study supervision: A. Jemal

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