Original Article

State Disparities in Colorectal Cancer Rates: Contributions of Risk Factors, Screening, and Survival Differences

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BACKGROUND: Northeastern states of the United States have shown more progress in reducing colorectal cancer (CRC) incidence and mortality rates than Southern states, and this has resulted in considerable disparities. This study quantified how the disparities in CRC rates between Louisiana (a Southern state) and New Jersey (a Northeastern state) would be affected if differences in risk factors, screening, and stage-specific CRC relative survival between the states were eliminated. **METHODS:** This study used the Microsimulation Screening Analysis Colon microsimulation model to estimate age-adjusted CRC incidence and mortality rates in Louisiana from 1995 to 2009 under the assumption that 1) Louisiana had the same smoking and obesity prevalence observed in New Jersey, 2) Louisiana had the same CRC screening uptake observed in New Jersey, 3) Louisiana had the same stage-specific CRC relative survival observed in New Jersey, or 4) all the preceding were true. **RESULTS:** In 2009, the observed CRC incidence and mortality rates in Louisiana were 141.4 cases and 61.9 deaths per 100,000 individuals, respectively. With the same risk factors and screening observed in New Jersey, the CRC incidence rate in Louisiana was reduced by 3.5% and 15.2%, respectively. New Jersey's risk factors, screening, and survival reduced the CRC mortality rate in Louisiana by 3.0%, 10.8%, and 17.4%, respectively. With all trends combined, the modeled rates per 100,000 individuals in Louisiana became lower than the observed rates in New Jersey for both incidence (116.4 vs 130.0) and mortality (44.7 vs 55.8). **CONCLUSIONS:** The disparities in CRC incidence and mortality rates between Louisiana and New Jersey could be eliminated if Louisiana could attain New Jersey's levels of risk factors, screening, and survival. Priority should be given to enabling Southern states to improve screening and survival rates. ***Cancer* 2015;121:3676-83**. © *2015 American Cancer Society.*

KEYWORDS: colorectal cancer, computer simulation, prevention and control, screening.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States. An estimated 132,700 CRC cases will be newly diagnosed, and 49,700 persons will die of the disease in 2015.[1] Although age-standardized CRC incidence and mortality rates have been decreasing in the Northeastern states of the United States since the late 1970s and early 1980s, the decreases began later and have been slower in the Southern states.[2] As a result, CRC incidence and mortality rates are now higher in Southern states than Northeastern states; this is opposite of the patterns observed before 1980.[2]

Most cancer control plans and policies that affect cancer prevention and access to screening in the United States are designed and implemented at the state level. The observed variation in CRC incidence and mortality trends between states provides important information for policymakers on the success of the implemented interventions and provides evidence that interventions in some states can be improved. Differences in risk factors, screening, and treatment are the most likely candidates to explain the observed disparity in CRC incidence and mortality trends.[3] Screening has been hypothesized to be the most important driver.[2] However, the individual contributions of these factors to disparities have never been evaluated, and doing so could inform the design of future cancer control policies and interventions.

In this analysis, we determined to what extent improving risk factor prevalence, screening uptake, and CRC relative survival could reduce observed disparities in CRC incidence and mortality rates between states. We chose Louisiana as an exemplary Southern state with unfavorable trends in CRC incidence and mortality and New Jersey as an exemplary Northeastern state with more favorable trends because for both states, long-term, high-quality cancer registry data are

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TABLE 1. Main Natural History Assumptions in the Microsimulation Screening Analysis Colon Model

Model Parameter	Value	Source
Distribution of risk for adenomas over the general population	γ-distributed; mean, 1; variance, 1.98	Fit to multiplicity distribution of adenomas in autopsy studies[5]: Age of 60 y ≥1: 20% ≥2: 6% ≥3: 2% Age of 90 y ≥1: 37% ≥2: 17% ≥3: 9%
Adenoma incidence per year	Age- and race-dependent and varying from 0% to 10%/y	Fit to adenoma prevalence in autopsy studies[a] and cancer incidence in SEER registry in 1995[6]
Probability of a new adenoma being progressive	Dependent on age at onset and varying from 0% to 89%	Fit to adenoma prevalence in autopsy studies[a] and cancer incidence in SEER registry in 1975–1979 (prescreening era)[6]
Regression of adenomas	No significant regression	Expert opinion
Mean duration of preclinical cancer	6.7 years	Estimated from large randomized controlled fecal occult blood test trials[7]
Proportion of nonprogressive adenomas staying 6–9 mm and becoming ≥10 mm	25% and 75%, respectively	Fit to size distribution of adenomas in colonoscopy trial (percentages corrected for colonoscopy sensitivity)[8]: ≤5 mm: 73% 6–9 mm: 15% ≥10 mm: 12%
Proportion of CRCs developing from 6- to 9-mm adenomas and ≥10-mm adenomas	30% and 70%, respectively	Expert opinion
Localization distribution of adenomas and cancer	Dependent on state and race	Directly estimated from SEER in 1995[6]
10-year relative survival after clinical diagnosis of CRC	Dependent on period, stage, state, and race[b]	Directly estimated from SEER in 1995–2008[6]

Abbreviations: CRC, colorectal cancer; SEER, Surveillance, Epidemiology, and End Results.
[a] References to autopsy studies are provided in Supporting Material 1 in the online supporting information.
[b] See Supporting Material 2 in the online supporting information.

available through the Surveillance, Epidemiology, and End Results (SEER) program and the National Program of Cancer Registries.

MATERIALS AND METHODS

We used the Microsimulation Screening Analysis (MISCAN) Colon microsimulation model[4] of the Cancer Intervention and Surveillance Modeling Network to quantify how the disparity in observed CRC rates between Louisiana and New Jersey would be affected if Louisiana were to attain risk factor prevalence (ie, smoking and obesity), screening uptake, and stage-specific relative survival for CRC as observed in New Jersey. Stage-specific survival was used as a proxy for differences in treatment between the states. This study did not include patient-specific information and was exempt from institutional review board review.

MISCAN Colon Model

Supporting Material 1 describes the MISCAN model (see online supporting information). Briefly, the model simulates the life histories of a large population of individuals from birth to death and has a natural history component that tracks the progression of underlying colorectal disease in the absence of screening. As each simulated individual ages, there is a chance that 1 or more adenomas may develop; this depends on age, sex, race, and individual risk. Adenomas can progress in size from small (≤5 mm) to medium (6-9 mm) to large (≥10 mm), and some may eventually become malignant. A preclinical (ie, not yet detected) cancer has a chance of progressing through stages I to IV and may be detected because of symptoms at any stage. With screening, adenomas and preclinical cancers may be detected; this depends on the sensitivity of the test and, for endoscopic tests, on whether the lesion is within reach of the endoscope.

The natural history part of the model was calibrated to prescreening data from autopsy studies and the 1995 age-specific CRC incidence from the Louisiana Tumor Registry (the main assumptions are presented in Table 1).[9] We included only first primary cases. Autopsy-only and death certificate–only cases as well as tumors of the appendix were excluded. The model used state-specific all-cause mortality life tables from the Cancer Survival in Five Continents study (CONCORD).[10] Stage-specific relative survival after a CRC diagnosis from 1995 to 2009 for Louisiana and New Jersey was obtained from SEER

data (Supporting Material 2 [see online supporting information]).[6] The prevalence of smoking and obesity over time by state and by age was obtained from the Behavioral Risk Factor Surveillance System.[11] Smoking prevalence data were available from 1955 onward, and obesity prevalence data were available from 1970 onward (Supporting Material 3 [see online supporting information]). We assumed smoking and obesity prevalence before these years to be equal to the 1955 and 1970 levels, respectively. The relative risk of smokers versus nonsmokers was estimated to be 1.6, and the relative risk for obese individuals (body mass index $\geq$ 30 kg/m^2) versus nonobese individuals was estimated to be 1.4.[12,13] The prevalence of risk factors affected the risk for developing adenomas; subsequently, an increase in the risk factor prevalence would affect the CRC incidence after an average lag time of approximately 20 years.[14]

The estimates for screening uptake over time were also obtained from Behavioral Risk Factor Surveillance System data (Supporting Material 4 [see online supporting information]).[11] We assumed no screening before 1978. For years for which no data were available, rates were extrapolated linearly. An overview of the test characteristics of the screening tests used is provided in Supporting Material 1 (see online supporting information).

The validity of the model had been tested previously with data from several large randomized screening and surveillance studies, such as the 3 large randomized controlled trials for fecal occult blood testing,[7] the Colon Cancer Prevention Program sigmoidoscopy study (CoCap),[15] and the National Polyp Study.[16] In addition, the model was able to reproduce the observed CRC incidence and mortality trends in the United States while accounting for secular trends in risk factor prevalence, screening practice, and chemotherapy treatment.[17]

Study Population

We used the model to simulate the Louisiana population from 1995 to 2009 (corrected for the impact of Hurricane Katrina) for both sexes and all races combined. In a secondary analysis, we also simulated the black and white Louisiana populations separately. We did not analyze other racial groups or Hispanics separately because of the small numbers in Louisiana. We restricted our analysis to the population aged 50 years and older because this is the group for which screening is recommended.[18,19]

Base Case Analysis

We simulated the Louisiana population with the CRC risk factor prevalence, CRC screening uptake, and stage-specific CRC relative survival observed in Louisiana (run 1). Alternatively, we modeled the Louisiana population under the assumption that it had the same risk factors (run 2), same screening (run 3), and same CRC survival (run 4) as observed in New Jersey and a combination of all 3 (run 5).

We did not incorporate all known risk factors for CRC into the model because data were not available. Therefore, the simulated CRC incidence (mortality) rates do not fully correspond with the observed rates in Louisiana in 2009. Instead, we assumed that the simulated relative benefit of New Jersey risk factors, screening, and CRC survival versus those of Louisiana would be applicable to the observed CRC incidence and mortality. This assumption seems reasonable: 3 randomized controlled trials of biennial guaiac fecal occult blood test screening found similar percent mortality reductions ranging from 15% to 21%, even though they were performed in populations with a different background CRC incidence level.[20]

We calculated the expected CRC incidence (mortality) rates in Louisiana for the scenarios by applying the percent difference in age-standardized incidence (mortality) rates between run 1 and run 2, 3, 4, or 5 to the observed CRC incidence and mortality rates for Louisiana in 2009.

The observed excess CRC risk was calculated as the absolute difference in the observed CRC incidence (mortality) rates between Louisiana and New Jersey in 2009 (formula 1 in Supporting Material 5 [see online supporting information]).[21] Subsequently, the expected excess risk from each of the modeled scenarios was calculated as the absolute difference between the expected CRC incidence (mortality) rate from each scenario and the observed incidence (mortality) in New Jersey (formulas 2-5 in Supporting Material 5 [see online supporting information]).

Sensitivity Analyses

We performed 4 sensitivity analyses. First, we performed an analysis in which Louisiana residents received not only less screening but also lower quality screening; 25% lower adenoma detection rates with endoscopy were assumed. Assuming New Jersey screening adherence, we then re-estimated the reduction in excess CRC risk due to differences in screening. Second, we explored the robustness of our results for the assumption that equal access to care would result in the same stage-specific relative CRC survival for Louisiana and New Jersey; we assumed that 25% of the difference in relative survival between states could not be taken away with equal access to care. Third, we evaluated the impact on the mortality disparity if equal

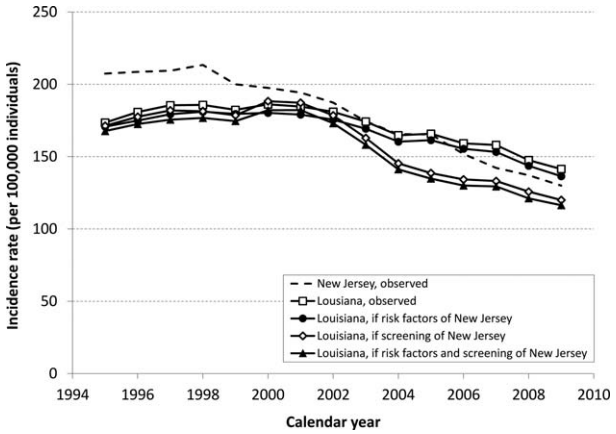

Figure 1. Age-standardized colorectal cancer incidence rates (per 100,000 individuals) in the population aged 50 years and older from 1995 to 2009 as observed in Louisiana and New Jersey and as expected in Louisiana if it had the same risk factors and/or screening pattern observed for New Jersey.

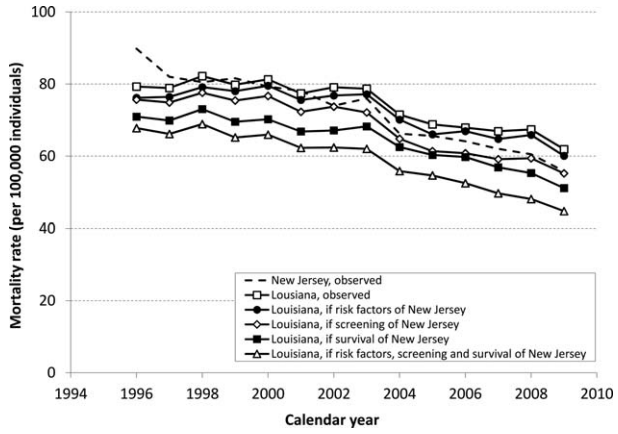

Figure 2. Age-standardized colorectal cancer mortality rates (per 100,000 individuals) in the population aged 50 years and older from 1995 to 2009 as observed in Louisiana and New Jersey and as expected in Louisiana if it had the same risk factors, screening pattern, and/or survival pattern observed in New Jersey.

access to care resulted not only in the same stage-specific relative CRC survival for Louisiana and New Jersey but also in the same stage distribution. Finally, in the base case, CRC relative survival estimates by state were estimated with SEER*Stat.[6] SEER*Stat uses US life tables to estimate expected mortality in the absence of cancer. Louisiana death rates are higher than overall US death rates, whereas New Jersey rates are lower. Therefore, we performed a sensitivity analysis in which we corrected the CRC relative survival for the differential background mortality in each state.

RESULTS

In 1995, the observed Louisiana CRC incidence rate (167 cases per 100,000 persons aged 50 years and older) was approximately 19% lower than the New Jersey CRC incidence rate (205 cases per 100,000; Fig. 1). By 2009, the ordering had reversed, with the CRC incidence in Louisiana being almost 10% higher than that in New Jersey. For CRC mortality, a similar pattern was observed (Fig. 2). The observed excess in age-standardized CRC incidence and mortality rates in 2009 in Louisiana versus New Jersey was 11.5 cases and 6.1 deaths per 100,000, respectively (Tables 2 and 3).

If Louisiana had the same smoking and obesity prevalence observed in New Jersey, the expected CRC incidence rate would have been 136.5 per 100,000 in 2009, which is 3.5% lower than the observed rate for Louisiana (Fig. 1 and Table 2). The expected CRC mortality rate in 2009 would have been 60.1 per 100,000 (3.0% lower than the observed rate; Fig. 2 and Table 3). In this scenario, Louisiana would still have an excess of 6.5 cases and 4.3 deaths per 100,000 in comparison with New Jersey.

If Louisiana had the same screening uptake or stage-specific relative CRC survival as New Jersey, CRC mortality would have dropped to 55.2 and 51.1 per 100,000, respectively, in 2009 (ie, 10.8% and 17.4% lower than the observed rates in Louisiana). With the combination of the same trends in smoking and obesity, screening, and stage-specific relative CRC survival observed in New Jersey, CRC mortality in Louisiana would have been 27.8% lower than the observed rate of 61.9 per 100,000 in Louisiana. In addition, this reversed the disparity between the states; in comparison with the rates currently observed in New Jersey, Louisiana would have 13.6 cases and 11.1 deaths fewer per 100,000.

The observed disparity in CRC incidence and mortality between Louisiana and New Jersey was considerably higher for blacks (42.2 excess cases and 8.4 excess deaths per 100,000 persons) versus whites (0.5 excess cases and 1.2 excess deaths per 100,000 persons; Tables 2 and 3). Interestingly, the potential reduction in CRC mortality if Louisiana had risk factors, screening, and survival similar to those of New Jersey was lower for blacks than whites (18.3% and 23.2%, respectively).

Sensitivity Analyses

Our findings were robust for assumptions concerning quality of endoscopy, residual survival differences, and stage distribution (Table 4). Lower quality endoscopy slightly attenuated the potential reduction in excess mortality from 27.8% (base case) to 26.8%. The residual

TABLE 2. Base Case Analysis: Disparities in Colorectal Cancer Incidence in Individuals Aged 50 Years and Older in Louisiana and New Jersey in 2009

Scenario	All Races			Blacks			Whites		
	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[b]
New Jersey, observed	130.0			132.0			131.2		
Louisiana, observed	141.4		11.5	174.2		42.2	131.7		0.5
Louisiana, if risk factors of New Jersey	136.5	3.5	6.5	171.3	1.6	39.3	128.4	2.5	−2.8
Louisiana, if screening of New Jersey	120.0	15.2	−10.0	153.8	11.7	21.8	112.3	14.7	−18.9
Louisiana, if risk factors, screening, and survival of New Jersey	116.4	17.7	−13.6	151.1	13.2	19.1	110.3	16.2	−20.8

Abbreviation: ASR, age-standardized rate per 100,000 individuals (2000 US standard population).
[a] Percent reduction in comparison with the incidence rate observed in Louisiana.
[b] Excess colorectal cancer incidence rate in Louisiana versus New Jersey.

TABLE 3. Base Case Analysis: Disparities in Colorectal Cancer Mortality in Individuals Aged 50 Years and Older in Louisiana and New Jersey in 2009

Scenario	All Races			Blacks			Whites		
	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[b]
New Jersey, observed	55.8			71.5			55.3		
Louisiana, observed	61.9		6.1	79.9		8.4	56.5		1.2
Louisiana, if risk factors of New Jersey	60.1	3.0	4.3	77.8	2.6	6.3	54.8	3.0	−0.5
Louisiana, if screening of New Jersey	55.2	10.8	−0.6	73.1	8.5	1.6	49.3	12.7	−6.0
Louisiana, if survival of New Jersey	51.1	17.4	−4.7	71.3	10.8	−0.2	49.5	12.4	−5.8
Louisiana, if risk factors, screening, and survival of New Jersey	44.7	27.8	−11.1	65.3	18.3	−6.2	43.4	23.2	−11.9

Abbreviation: ASR, age-standardized rate per 100,000 individuals (2000 US standard population).
[a] Percent reduction in comparison with the mortality rate observed in Louisiana.
[b] Excess colorectal cancer mortality rate in Louisiana versus New Jersey

difference in stage-specific relative CRC survival and correction for differential background mortality between Louisiana and New Jersey decreased the potential reduction in CRC mortality to 24.0% and 25.0%, respectively. The stage distribution had virtually no effect.

DISCUSSION

This study shows that removing differences in smoking and obesity prevalence, screening uptake, and stage-specific relative CRC survival would eliminate observed disparities in CRC incidence and mortality rates between Louisiana and New Jersey. Screening had the biggest impact on CRC incidence: the observed CRC incidence in Louisiana could be reduced by 15.2% if CRC screening were increased up to the level of New Jersey. Stage-specific CRC relative survival had the largest impact on CRC mortality: the observed CRC mortality could be reduced by 17.4% if the survival were improved to the level of New Jersey. Eliminating differences in the prevalence of smoking and obesity had a relatively modest impact on CRC incidence (3.5% reduction) and mortality (3.0% reduction).

The impact of smoking and obesity is modest because of the relatively small impact of the individual risk factors on CRC incidence and mortality (relative risks of 1.6 and 1.4, respectively) and because the prevalences of these risk factors were similar between the 2 states (Supporting Material 3 [see online supporting information]).

Eliminating differences in risk factors, screening, and survival not only completely eliminates the excess CRC incidence and mortality in Louisiana but reverses the pattern. This may sound surprising, but because in the early 1990s New Jersey had higher incidence and mortality rates than Louisiana,[2] it makes sense that the background CRC risk in Louisiana is actually lower than that in New Jersey.

The disparity in CRC incidence and mortality rates between Louisiana and New Jersey mainly exists for blacks and not for whites (Tables 2 and 3). When simply looking at the 2009 rates, one could argue that the disparity

TABLE 4. Sensitivity Analyses: Disparities in Colorectal Cancer Mortality in Individuals Aged 50 Years and Older in Louisiana and New Jersey in 2009 Under Alternative Model Assumptions

	Lower Quality Endoscopy			Residual Survival Difference			Same Survival and Stage Distribution			Survival Corrected for Background Mortality		
Scenario	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[a]	ASR	% Reduction[a]	Excess Rate[b]	ASR	% Reduction[a]	Excess Rate[b]
New Jersey, observed	55.8			55.8			55.8			55.8		
Louisiana, observed	61.9		6.1	61.9		6.1	61.9		6.1	61.9		
Louisiana, if risk factors of New Jersey	60.2	2.7	4.4	60.1	3.0	4.3	60.1	3.0	4.3	60.0	3.0	4.2
Louisiana, if screening of New Jersey	56.1	9.3	0.3	55.2	10.8	−0.6	55.2	10.8	−0.6	54.6	11.7	−1.2
Louisiana, if survival of New Jersey	50.7	18.1	−5.1	53.6	13.3	−2.2	50.8	17.9	−5.0	53.4	13.7	−2.4
Louisiana, if risk factors, screening, and survival of New Jersey	45.3	26.8	−10.5	47.0	24.0	−8.8	44.6	27.9	−11.2	46.4	25.0	−9.4

Abbreviation: ASR, age-standardized rate per 100,000 individuals (2000 US standard population).
[a] Percent reduction in comparison with the mortality rate observed in Louisiana.
[b] Excess colorectal cancer mortality rate in Louisiana versus New Jersey

between the 2 states is, therefore, a result of a difference in population distribution by race. However, when one looks at the patterns since 1995, it is clear that population distribution is not the explanation; for both races, the observed CRC incidence and mortality rates decreased less in Louisiana than New Jersey. This finding is corroborated by our modeling, which shows that CRC incidence and mortality rates in Louisiana could be reduced to a similar extent in blacks and whites if risk factors, screening, and survival were the same as those in New Jersey. Interestingly, the potential reduction was even somewhat higher in whites versus blacks. This finding is probably explained by the slight increase in CRC incidence and mortality in Louisiana blacks in the late 1990s, which cannot be explained by the factors investigated in this study. This means that other differences between Louisiana and New Jersey (eg, other lifestyle factors such as red meat consumption and physical inactivity, sex differences, or differences in the Hispanic proportion of the population) are contributing to the difference in CRC incidence and mortality between these 2 states. Consequently, some excess in CRC rates in blacks remained after the removal of differences in smoking, obesity, screening, and survival in Louisiana versus New Jersey.

In our primary analysis, we considered screening uptake and assumed equal access to screening and equal quality of screening in Louisiana and New Jersey. The lower population density and larger geographic area of Louisiana might make achieving equal access more difficult. In addition, quality of endoscopy has been shown to be dependent on the skill of the endoscopist performing the procedure, with colonoscopy being performed by gastroenterologists being more sensitive for cancer than colonoscopy by nongastroenterologists.[22] The number of certified gastroenterologists differs widely between states in the United States. In Louisiana, there were only 3.9 gastroenterologists per 100,000 residents in 2013, whereas there were 6.7 per 100,000 residents in New Jersey.[23] This pattern is mirrored in the other Southern and Northeastern states.[24]

Two limitations are noteworthy. First, we assumed that smoking and obesity prevalence affected the risk for CRC only by increasing the incidence of adenomas. This assumption is supported by the similar relative risks of these risk factors for developing adenomas and CRC.[12,13] However, greater adenoma progression may also play a role in the increased risk. In that case, eliminating differences in risk factors will have a larger impact on disparities in CRC rates, whereas eliminating differences in screening may have a smaller effect. Second, we did not explicitly consider state differences in treatment but used state differences in stage-specific relative CRC survival as a proxy. Data on the use and quality of CRC treatment by state are sparse, especially for the population less than 65 years old. One study suggested that Louisiana patients surgically treated for stage III colon cancer were significantly less likely to receive adjuvant chemotherapy than patients from other states.[25] However, if part of the state differences in survival cannot be explained by differences in (the quality of) treatment (eg, because Louisiana residents

could have more comorbidities and are, therefore, unable to receive guideline therapy), we have overestimated the potential for reducing disparities in CRC mortality. We explored the impact of our assumption in a sensitivity analysis and found that the effect was limited.

The Patient Protection and Affordable Care Act (Public Law 111-148, 2010) may be an important step toward the reduction of health disparities between states, although Louisiana has yet to expand the state Medicaid program. The Patient Protection and Affordable Care Act aims to improve access to quality health care for all Americans. Furthermore, all new health plans must cover certain preventive services, including CRC screening, without charging a deductible, copay, or coinsurance. Several studies have shown that in situations with equal access to care, such as military medical centers, Department of Defense facilities, and clinical trials, no differences in screening uptake or CRC treatments exist.[26-28] A notable example is universal CRC screening coverage in Delaware, which eliminated the black-white disparities in CRC mortality rates.[29]

In conclusion, this study shows that the disparities in CRC incidence and mortality rates between Louisiana and New Jersey could be eliminated if Louisiana were to attain New Jersey levels of risk factors, screening, and CRC relative survival. Priority should be given to enabling Southern states to improve screening and survival rates.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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