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Colorectal Cancer Incidence Rates in the Louisiana Acadian Parishes Demonstrated to be Among the Highest in the United States

Jordan J. Karlitz, MD[1], Christine Blanton, MD[1], Patricia Andrews, MPH[2], Vivien W. Chen, PhD, MPH[2], Xiao-Cheng Wu, MD, MPH[2] and Elizabeth Fontham, DrPH, MPH[2]

OBJECTIVES: Determine whether colorectal cancer (CRC) rates are disproportionately high in the French-Acadian region (population 1.2 million) of Louisiana, home of the Cajuns, a founder population.
METHODS: 2005–2009 cancer incidence rates were stratified by age/race/gender in the 18 Acadian parish region and 9-parish subgroup with higher proportions of French speakers and compared with Louisiana and United States rates. Parishes were identified through language census data. A total of 3,288 CRC cases were identified in the Acadian region and 11,737 in Louisiana.
RESULTS: CRC rates in whites and white males in the 18 parishes were statistically significantly higher than both Louisiana and US rates. In the 9 parishes, rates increased further; whites had an incidence of 56.1/100,000, 13% higher than Louisiana ($P < 0.0003$) and 23% higher than US rates ($P < 0.0001$). In white males, incidence was 72.6/100,000, 19% higher than Louisiana ($P < 0.0002$) and 37% higher than US rates ($P < 0.0001$). If the 9-parish regions were considered a "state," white males would have the highest CRC incidence in the United States by 11% ($P < 0.0175$) compared with other white male populations.
CONCLUSIONS: CRC rates are among the highest in the United States, increasing with the proportion of French speakers, a marker for the Cajun population. This appears to be the first study identifying a high rate of cancer in a large, regional, US founder population, raising the possibility of a genetic predisposition. Alternatively, an unidentified, robust environmental risk factor may be present. Future studies are needed to identify genetic and/or other risk factors in this population.

INTRODUCTION

The Acadian Parishes of Louisiana (LA) are currently home to 1.2 million inhabitants and to the majority of Cajuns, approximately 500,000–700,000, in the state (Figure 1).[1] The Cajun population was established in the 1700s when French settlers (Acadians) in Nova Scotia, Canada, left the region due to oppressive English rule. Many Acadians settled in LA and were joined by others who emigrated from France. Compared with other US populations, Cajuns have had strong geographic ties to a specific region and have maintained a distinct community with a preserved language, Cajun French. According to ancestry survey data from 1990, Vermilion parish, one of the centrally located parishes in the Acadian region, reported 69.2% of the total population was of French ancestry (54.7% French Canadian and 14.5% French), highlighting the increased concentration of those with French descent in the region.[2]

Founder effects have been demonstrated in the Cajun population for several genetic diseases including Tay-Sachs, Oculopharyngeal Muscular Dystrophy, and Usher syndrome type 1C.[3–5] A founder effect occurs when a new population originates from a small subgroup of a larger population.[6] This can result in de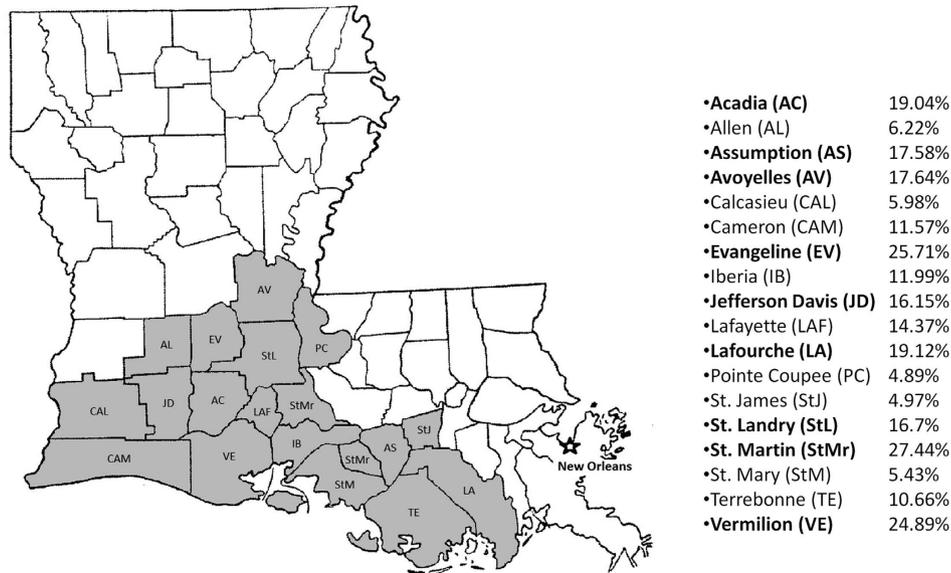creased genetic variation in the new population, which may have a nonrandom sample of genes from the original population. If a mutation associated with disease is introduced into the founder population, this can lead to an unusually high frequency of disease. Founder populations are important to study as cancer susceptibility genes, potentially novel, may be discovered that may be important not only for the population in question, but for others worldwide who may share a similar remote ancestry.

Given the establishment of the Cajuns as a founder population, we sought to determine whether rates of colorectal cancer (CRC) are higher in the Acadian region compared with statewide and US rates as this may imply an increased frequency of hereditary CRC. As CRC is one of the few malignancies in which Mendelian inheritance is common, this would be an appropriate cancer to study in a founder population. Lynch syndrome (LS) or hereditary non-polyposis colorectal cancer, is an autosomal dominant form of CRC that may account for up to 5% of all CRC cases.[7] The penetrance for development of malignancy is up to 68.7% in males and 52% in females.[8] Founder effects for LS have been discovered in several populations, including Newfoundland, Canada.[9] It is believed that the increased rates of CRC in this province, which are among the highest in the world, may be attributable

[1]Division of Gastroenterology, Tulane University School of Medicine, New Orleans, Louisiana, USA and [2]Epidemiology Program, Louisiana State University (LSU) Health Sciences Center, School of Public Health, New Orleans, Louisiana, USA
Correspondence: JJ Karlitz, MD, Division of Gastroenterology, Tulane University School of Medicine, 1430 Tulane Avenue, SL 35, New Orleans, Louisiana 70112-2699, USA. E-mail: jkarlitz@tulane.edu

•**Acadia (AC)**	19.04%
•Allen (AL)	6.22%
•**Assumption (AS)**	17.58%
•**Avoyelles (AV)**	17.64%
•Calcasieu (CAL)	5.98%
•Cameron (CAM)	11.57%
•**Evangeline (EV)**	25.71%
•Iberia (IB)	11.99%
•**Jefferson Davis (JD)**	16.15%
•Lafayette (LAF)	14.37%
•**Lafourche (LA)**	19.12%
•Pointe Coupee (PC)	4.89%
•St. James (StJ)	4.97%
•**St. Landry (StL)**	16.7%
•**St. Martin (StMr)**	27.44%
•St. Mary (StM)	5.43%
•Terrebonne (TE)	10.66%
•**Vermilion (VE)**	24.89%

18 Acadian parishes with 5% or more of the population (age 5 and older) speaking French at home were identified. A 9 parish subgroup of the 18 parishes with 15% or more of the population speaking French at home has text highlighted in bold.

Figure 1   French spoken at home in the Acadian region according to 2000 census data.

to a high rate of familial cancer in the population and possibly to the presence of novel susceptibility genes.[10,11] Familial adenomatous polyposis is another autosomal dominant inherited syndrome that greatly increases the risk of CRC and founder effects have been established.[12–14]
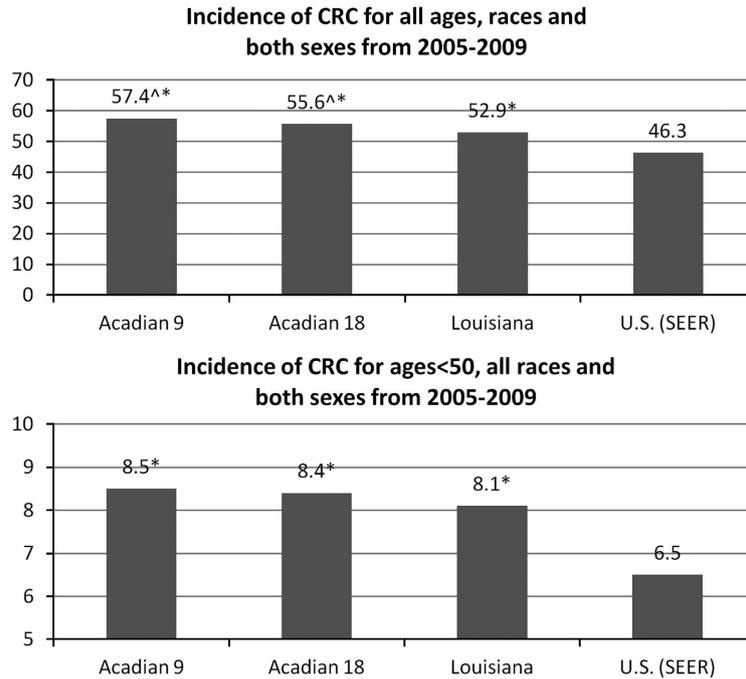
We also sought to examine the rates of non-colonic cancers in the Acadian region to see if these are disproportionately high. Breast cancer shares similarities with CRC including a high Mendelian heritable burden. Up to 10% of cases are attributable to BRCA1 and BRCA2 mutations and conceivably, there could be a founder effect in the Acadian region.[15] Uterine cancer rates were studied as it is the most common extra-colonic malignancy associated with LS. Cancers that share environmental risk factors with CRC are also important to consider. If rates of both CRC and non-colonic malignancies are high in the Acadian region, it may suggest a shared environmental predisposition for the development of malignancy. In addition to genetic predisposition, breast cancer and CRC share risk factors of obesity and smoking.[16–18] Other malignancies sharing environmental risk factors with CRC include lung cancer (smoking) and pancreatic cancer (smoking and alcohol), both of which were analyzed.[19,20]

METHODS

Study population. We identified 18 Acadian parishes (Acadian 18) by incorporating both the consensus of what has defined "Acadiana" historically and by 2000 US Census data that provides parish data on the percentage of those who consider French as their "home language" (Figure 1).[21,22] As an initial cut off, we included parishes with greater than 5% of the population speaking French at home (range is 5–27%).

Five percent, as opposed to a higher percentage, was used in order to maximize the catchment population of those with French ancestry. With this criterion, a discrete, circumscribed geographical region was identified in southern LA that physically encompassed all 18 of the Acadian parishes and conformed well to the historical Acadian region. The total all-age population of the 18 parishes studied was 1,155,422 (according to 2000 census). Of 1,066,897 people who were age 5 and older, 149,158 (14%) regarded French as their home language. As many Cajuns no longer speak French as a first language and the accepted Cajun population in southern LA ranges from 500,000 to 700,000, 14% represents an underestimation of the number of Cajuns. Supporting this is the fact that census data in 1970 demonstrated that 572,264 people in LA spoke French at home but that number has steadily decreased, mainly due to conversion of households to speaking English.[23] Despite the decline in counts, the language data provide us with an objective way to identify parishes that have a large percentage of inhabitants with Cajun ancestry. We also conducted a more stringent analysis on a subgroup of the 18 parishes, in which >15% of the population of each parish regarded French as their "home language." With this threshold, 9 parishes (Acadian 9) were identified with a population of 470,663. In terms of race, according to US census data from 2000, ~71% of the Acadian 18 region is white.[24]

Data source and case definition/eligibility criteria. Data were obtained from the Louisiana Tumor Registry, a high-quality statewide population-based cancer registry, participant of both the NCI's Surveillance, Epidemiology, and End Results (SEER) program and one of the 10 Specialized Cancer Registries of the Centers of Disease Control and

Incidence of CRC for all ages, races and both sexes from 2005-2009

Incidence of CRC for ages<50, all races and both sexes from 2005-2009

^ indicates statistically significant higher rates with P<.05 than Louisiana and U.S. SEER rates

*indicates statistically significant higher rates with P<.05 than U.S. SEER

Note: There were no statistically significant differences between Acadian 9 and Acadian 18

SEER: Surveillence, Epidemiology, and End Results

Figure 2 Overall incidence rates of colorectal cancer (CRC) per 100,000 population in the Acadian parishes compared with Louisiana and US SEER rates.

Prevention's National Program of Cancer Registries. This study included cases of invasive primary CRC (ICD-0-3 codes: C18.0–C18.9, C19.9, C20.9, and C26.0). We excluded non-adenocarcinomatous, death certificate only and autopsy cases. The US data were from the 18 registries of the NCI's SEER program. As population based, de-identified data were used, this study was reviewed by the Institutional Review Board (IRB) and considered exempt.

Annual average, age-adjusted incidence rates of CRC per 100,000 individuals (2000 US standard population) in 2005--2009 were calculated using SEER*Stat software version 6.4.4 (Bethesda, MD, USA). We also analyzed subgroups by calculating age-adjusted rates (20–29, 30–39, 40–49, 20–49, 0–49, and all ages) by gender and race. As Cajuns are predominantly white and African Americans have higher rates of CRC than whites, race stratification was important. Given that the LA Cajun population has been estimated at 500,000--700,000 and that the total white population of the Acadian parishes is approximately 820,000, it is suggested that the majority of whites in the Acadian region have some degree of Cajun ancestry. We compared Acadian 18 rates and the Acadian 9 rates to similar subgroups in the state of LA as a whole and to the US SEER 18 population.

To determine whether other cancers may be disproportionately high, we analyzed age-adjusted incidence rates by gender and race for breast, uterine, lung, and pancreatic cancer. We also examined incidence rates of all reported malignancies in the region combined (CRC, breast, uterine, lung, pancreatic, and any other type of reported malignancy). We chose to analyze data from 2005 and later, when screening colonoscopy became more widely utilized on large segments of the population. Although Medicare began covering screening colonoscopy in 2001, there was a gradual increase in endoscopic screening utilization in LA over time.[25] Comprehensive cancer incidence data after 2009 were not available at the time of this study and hence 2005–2009 represents the most recent and complete data set.

RESULTS

From 2005 to 2009, 3288 cases of CRC were identified in the 18 Acadian parishes and 11,737 in the state of Louisiana. As depicted in Figure 2, the overall age-adjusted incidence rate of CRC for all races and both sexes combined in the Acadian 18 was 55.6 per 100,000 (95% confidence interval (CI), 53.2–57.2), 5% higher than LA (52.9, $P<0.0345$) and 20% higher than the US rate (46.3, $P<0.0001$). In the Acadian 9, the overall age-adjusted incidence rate rose to 57.4 (95% CI, 53.7–60.0), 9% higher than LA ($P<0.0149$) and 24% higher than the US rate ($P<0.0001$).

Age-adjusted incidence rates by race and gender for CRC in the Acadian 18 in 2005–2009 were compared with LA and the United States (Figure 3 and Acadian 18, Supplementary Data). As shown, CRC incidence for both whites and African Americans are generally higher than the US rate. However, in contrast to other subgroups, the all-age white population and
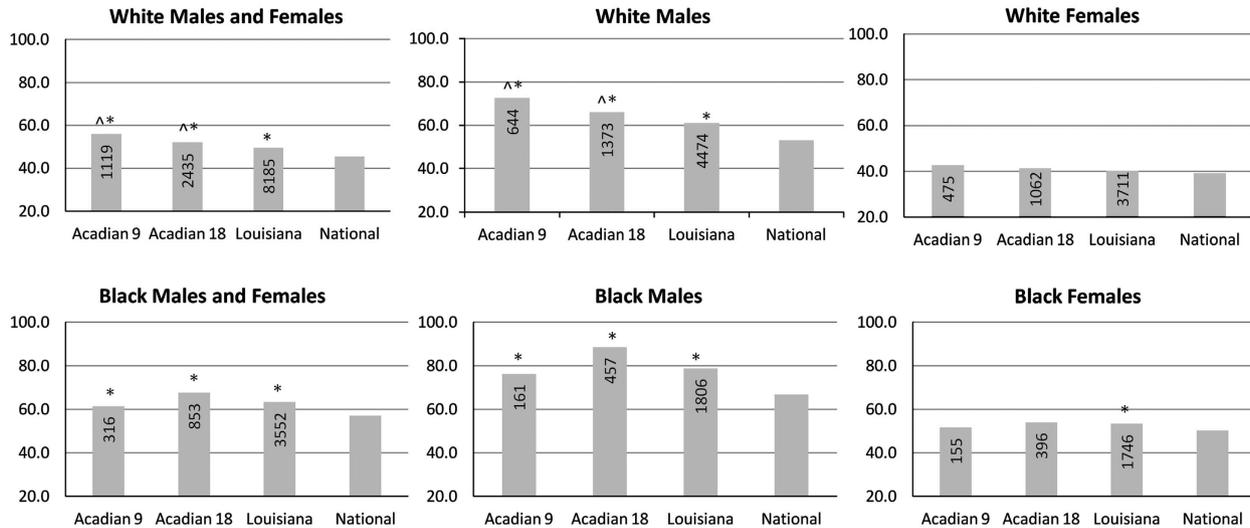
^ indicates P value <.05 for increase in rates when compared to Louisiana and U.S. SEER rates
*indicates P value <.05 for increase in rates when compared to U.S. SEER rates
Total case counts of CRC for the 5 year period are specified within each bar
Note: There were no statistically significant differences between the Acadian 9 and Acadian 18

Figure 3 Race and gender stratified colorectal cancer (CRC) incidence rates per 100,000 population in the 9 Acadian parishes and 18 Acadian parishes compared with Louisiana and US SEER rates.

white males had statistically significantly higher rates of CRC compared with not only the US population, but LA as well. The all-age white population rate of 52.2 (95% CI, 50.1–54.5) was 5.5% higher than the statewide rate of 49.5 ($P<0.0319$) and 15% higher than the national rate of 45.4 ($P<0.0001$). The all-age white male population rate of 66.0 (95% CI, 62.3–69.8) was 8% higher than the statewide rate of 61.0 ($P<0.0200$) and 24% higher than the national rate of 53.1 ($P<0.0001$).

When a similar analysis was performed on the Acadian 9 with a higher percentage of French speakers, the rates in almost every white subgroup increased when compared with the Acadian 18 while the rates in the African-American population decreased (Figure 3 and Acadian 9, Supplementary Data). The all age/combined sex white population in the Acadian 9 rose to 56.1 (95% CI, 52.7–59.7), 13% higher than LA ($P<0.0003$) and 23% higher than the US rate ($P<0.0001$). The CRC incidence rate in the all age white male population rose to 72.6 (95% CI, 66.8–78.9), 19% higher than LA ($P<0.0002$) and 37% higher than the US rate ($P<0.0001$).

We compared the incidence rates of CRC in the white population of the Acadian region to other states, in addition to LA, with the highest rates of CRC in the United States (Figure 4). With this comparison, the overall white population and the white male subgroup had one of the highest rates of CRC in the country when compared with white populations ranked by state. In the Acadian 9 specifically, white males had the single highest rate of CRC in the United States. The CRC incidence rate of 72.6 in the Acadian 9 was 11% higher than the white male population of Kentucky, the state with the highest rate of CRC in white males in the United States ($P<0.0175$).

With regard to early-onset CRC, the overall age-adjusted incidence rate in those under age 50 in the Acadian 18 was 29% higher than the US rate of 6.5 ($P<0.0001$; Figure 2). In the Acadian 9, the incidence rate in those under age 50 was 31% higher than the US rate ($P<0.0046$). Incidence in both the Acadian 9 and Acadian 18 were numerically higher than LA rates; however, this was not statistically significant. In multiple young, white sub-groups of the Acadian 9 and Acadian 18, CRC incidence was significantly higher than US rates (Table 1 and Supplementary Data online). Incidence also appeared to be numerically higher in these subgroups compared with LA particularly in the Acadian 9, but statistical significance was not met. As can be seen in Table 1, however, there appeared to be a descending gradient trend in CRC rates from the Acadian 9 to the Acadian 18, LA and United States in the majority of subgroups.

Age-specific incidence rates by race and gender for breast, uterine, lung, pancreatic cancer, and all malignancies combined in the Acadian 18 and Acadian 9 were studied (data only shown for all malignancies combined, Figure 5). Although a number of white subgroups in the different malignancy categories had statistically significantly higher rates than the corresponding subgroup nationally, in contrast to CRC, no white subgroups in any of the categories had a statistically significantly higher incidence rate than the corresponding subgroup in the statewide population. The only other subgroups in our study with significantly higher cancer rates than statewide rates were all age/combined sex and all age/female African Americans of both the Acadian 9 and Acadian 18 who had higher rates of lung cancer.

White males and females
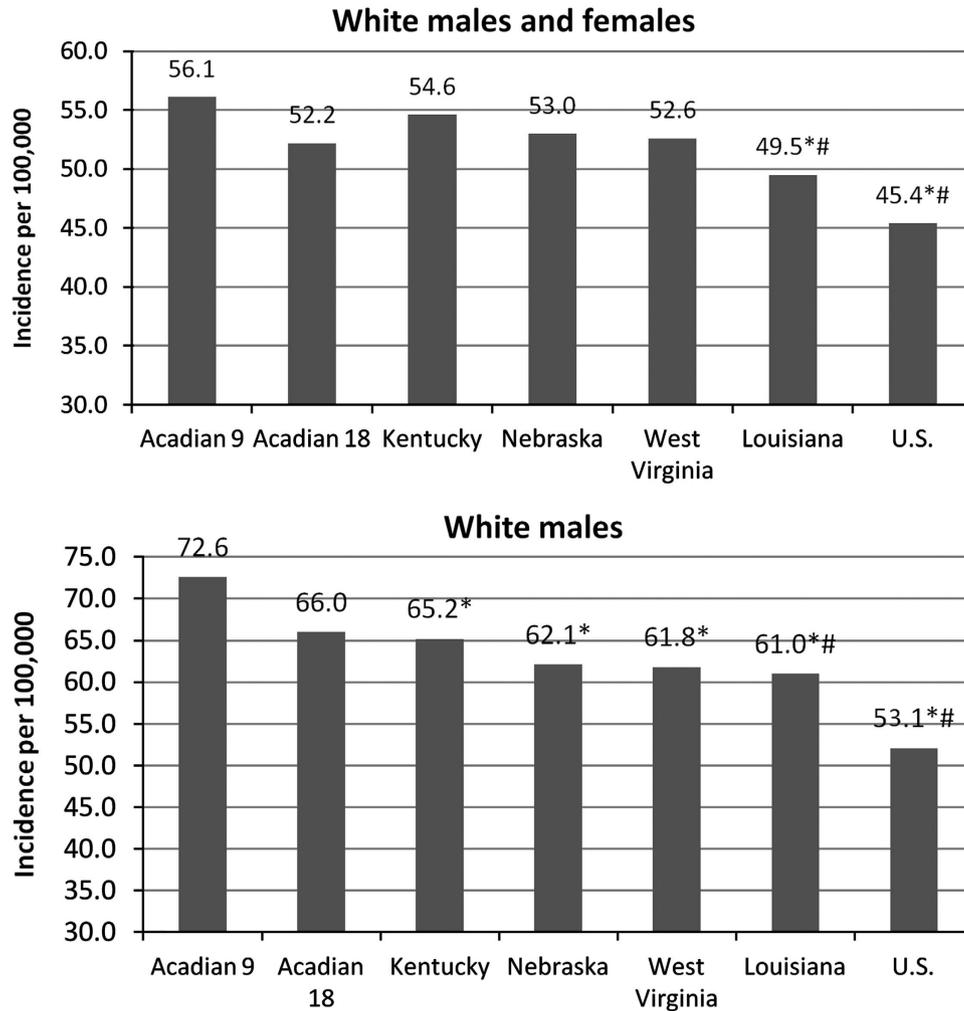
White males

* indicates rate less than Acadian 9 rate with p value <.05
\# indicates rate less than Acadian 18 rate with p value <.05

Figure 4 Colorectal cancer (CRC) incidence rates per 100,000 population in the overall white population and white male population of the 9 and 18 Acadian parishes compared with the highest ranking states.

Table 1 Colorectal cancer incidence rate per 100,000 in young, white subgroups in the Acadian 9 compared with Acadian 18, LA, and US SEER

Patient demographic	Acadian 9	Acadian 18	Louisiana	US SEER
Ages 40–49				
White male and female	31.3 (24.6–39.2)	26.0 (22.0–30.4) $P<0.2139$	25.2 (23.1–27.6) $P<0.1011$	21.5 (21.0–21.9) $P<0.0025$
White male	34.4 (24.8–46.7)	27.4 (21.7–34.1) $P<0.2722$	26.7 (23.6–30.2) $P<0.1579$	22.9 (22.3–23.5) $P<0.0167$
White female	28.1 (19.4–39.4)	24.6 (19.2–30.9) $P<0.5814$	23.8 (20.8–27.1) $P<0.4121$	19.9 (19.4–20.5) $P<0.0683$
Age<50				
White male and female	8.6 (6.9–10.5)	7.5 (6.5–8.6) $P<0.2977$	7.4 (6.8–8.0) $P<0.1869$	6.2 (6.1–6.3) $P<0.0038$
White male	9.9 (7.4–13.0)	7.5 (6.1–9.2) $P<0.1292$	7.8 (7.0–8.7) $P<0.1314$	6.6 (6.4–6.7) $P<0.0062$
White female	7.3 (5.2–9.9)	7.4 (6.0–9.0) $P<1.0000$	6.9 (6.2–7.7) $P<0.8090$	5.9 (5.7–6.0) $P<0.2101$

Note: 95% Confidence intervals are noted in parentheses. *P*-values reflect comparison of the Acadian 18, LA, or US SEER with the Acadian 9. Statistically significant (*P*<0.05) *P* values are highlighted in bold.
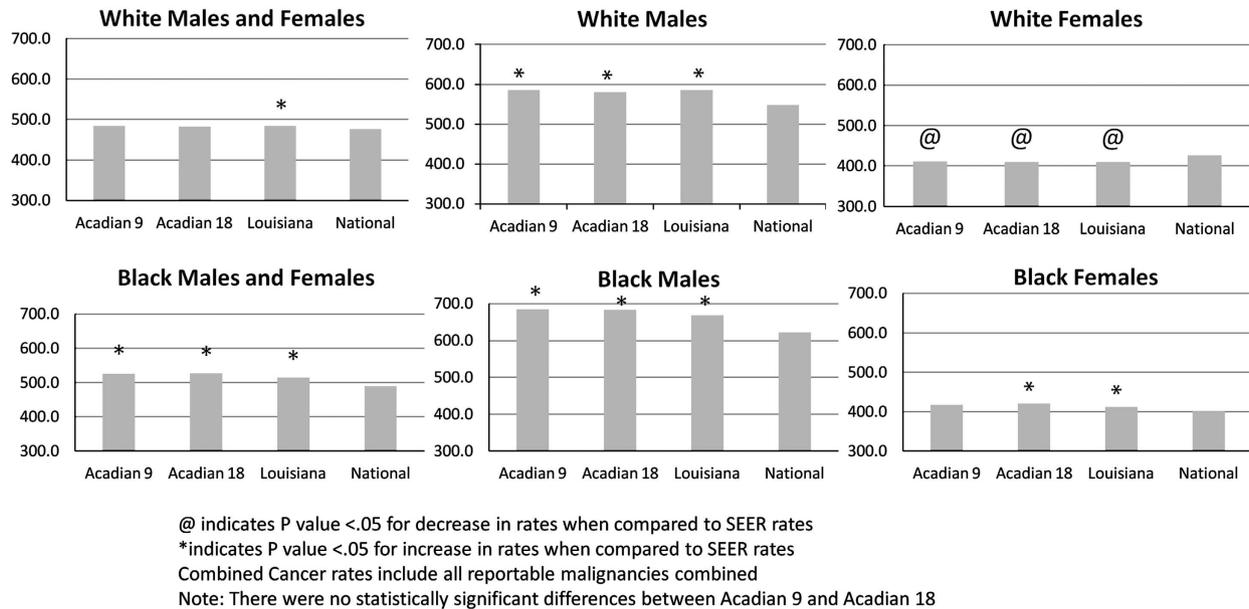
@ indicates P value <.05 for decrease in rates when compared to SEER rates
*indicates P value <.05 for increase in rates when compared to SEER rates
Combined Cancer rates include all reportable malignancies combined
Note: There were no statistically significant differences between Acadian 9 and Acadian 18

Figure 5 Race and gender stratified combined cancer incidence rates per 100,000 population in the 9 Acadian parishes and 18 Acadian parishes compared with Louisiana and US SEER rates.

DISCUSSION

Our analysis revealed disproportionately high rates of CRC in the white population in the Acadian region compared with both statewide and US rates. In the 9 Acadian parish subgroup, with the highest proportion of French speakers, we have demonstrated that white males have the highest rate of CRC in the United States when compared with other white male populations nationally. There also appears to be a trend of increased CRC incidence in young, white patients in the Acadian parishes, particularly in the Acadian 9, in relation to LA and the United States. Although our initial inclination to study the Acadian population was due to the fact that founder effects for multiple diseases had previously been demonstrated in the region, it is important to address the potential not only for underlying genetic risk, but environmental factors as well to explain the high CRC incidence.

With regard to genetic predisposition, as Cajuns are a known founder population, it is possible that there could be a founder effect for hereditary CRC in the population. If this were the case, as Cajuns make up a large proportion of the Acadian parishes' population, this could potentially explain the high regional rates of CRC. Familial CRC has been felt to underlie high incidence rates of CRC in other populations.[9] With regard to non-colonic malignancies, a breast cancer study conducted in the Bahamas, demonstrates the degree to which a founder effect can change a population's hereditary cancer burden for a malignancy that is generally sporadic in nature.[26] In this study, breast cancer patients in the population unselected for age or family history were found to have a very high BRCA mutation rate of 23%. Supporting the possibility of hereditary CRC in the Acadian region is that the white population has statistically significantly higher CRC rates compared with the state as a whole, which may share similar environmental exposures with the Acadian parishes. In addition, rates of CRC increased in parallel with the proportion of French speakers, a marker for parishes with higher numbers of those with Cajun ancestry. Furthermore, in the Acadian 9, CRC rates increased in the white population as rates in African Americans declined suggesting the absence, or decreased effect, of a shared environmental risk factor. A study utilizing mean genome-wide individual ancestry estimates demonstrated that people of self-reported Cajun ethnicity in LA are of mainly European as opposed to African ancestry. Hence, if there is a founder effect in the Cajun population, this may explain why CRC rates are disproportionately high compared with the state of LA in whites as opposed to African Americans.[27]

In terms of early-onset CRC, which historically has been associated with LS, we demonstrated that patients under 50 in the Acadian region had a statistically significantly higher rate of CRC than under age 50 US rates. Compared with statewide rates, incidence was numerically higher but this was not statistically significant. With regard to young, white subgroups specifically, although direct subgroup comparisons between the Acadian region and LA did not reveal statistically significant differences, there appeared to be a descending incidence trend between the Acadian parishes, LA, and the United States, particularly for the Acadian 9. Hence, it is possible that direct subgroup comparisons may be limited by smaller case numbers. However, it is also important to highlight, that LS patients may develop CRC at a later age than originally thought. A recent study demonstrated that the average age of development of CRC in LS was age 61, as opposed to patients being in their 40s.[8] This was a large, high-quality study that looked not only at probands with CRC, but mutation carrying family members as well. Reflecting the possibility of a later age of onset of CRC is the fact that the NCCN (National Comprehensive Cancer Network) guidelines were amended in 2013 and now suggest that it may be appropriate for all CRC patients, regardless of age, to undergo molecular tumor analysis screening for LS screening.[28]

Although rates of CRC in all age white females and young white females were not statistically higher than LA rates, several subgroups were significantly higher than US rates. Similar to above, smaller case numbers in the Acadian region may be limiting the ability to demonstrate significant differences when comparing Acadian subgroups to LA. Alternatively, studies have demonstrated that male mutation carriers express a malignant phenotype more frequently than female counterparts in those with LS.[29]

Breast cancer is similar to CRC in that a substantial percentage of cases are the result of a heritable mutation. Although theoretically possible that there is a genetic founder effect for BRCA1 or BRCA2 in the Acadian region, no such effect has been demonstrated. Rates of breast cancer in both the Acadian parishes and LA were low in white women in comparison to US SEER rates. It is possible that there may be underlying protective factors in the population. Multiparity and pregnancy prior to age 20 are both protective for the development of breast cancer.[30] In this light, LA had the 11th highest birth rate in the United States in 2007 and the fourth highest percentage of live births to mothers under 20 years of age in 2006.[31,32]

Fitting with a pattern seen in southern states, uterine cancer rates were disproportionately low in the Acadian parishes and LA in relation to the United States. A recent study, however, has demonstrated that LA has the third highest hysterectomy prevalence in the United States.[33] As hysterectomy will prevent the development of endometrial cancer, the authors calculated that the corrected uterine cancer rate in white women in LA is 110.5% higher (36.0/100,000 vs. 17.1/100,000) than previously reported. This, in conjunction with the fact that corrected Acadian region rates are not available, makes interpretation of uterine cancer incidence difficult. Further study will be needed, particularly as endometrial cancer is the most common extra-colonic malignancy associated with LS.

It is also important to address environmental risk factors for CRC, including obesity and smoking, as other factors may underlie the high regional CRC rate. According to the CDC, in 2010 31.0% of LA's population was obese, the sixth highest rate in the country.[34] However, when ranked by parish, only one of the Acadian parishes (Terrebonne) was among the top seven parishes in LA with a rate over 35%.[35] Lafayette parish, the most populous in the Acadian region, had the second lowest obesity rate (29%) in LA.[36] In 2004, just prior to the data collection period for this study, the statewide rate of obesity was even lower with a rate of 25.8% and an Acadian region prevalence range of 24.6 in Lafayette parish to 31.9 in St Mary parish.[37,38] According to the CDC, LA had a smoking prevalence rate of 22.1 in 2009 which was the eighth highest in the United States.[39] However, a LA-based study conducted several years earlier in 2006, at the beginning of our data collection period, determined that the smoking prevalence in the Acadian region was 22.8%, which was the third lowest in LA when compared with eight other state regions.[40] Hence, although the rates of obesity and smoking are high in LA, the overall rates in the Acadian parishes are lower than other regions of the state. This leads us to believe that other factors may be present to help explain the disproportionately high rates of CRC.

To further explore an environmental role for the development of malignancy, rates of non-colonic malignancies, particularly those sharing environmental risk factors with CRC were examined. If rates of non-colonic cancers, including pancreatic and lung cancer, were also disproportionately higher than statewide rates, this may suggest a shared regional environmental predisposition for malignancy. As our analysis did not show disproportionately higher rates of these malignancies in the white population compared with LA, a non-environmental predisposition for the development of CRC in the region is plausible. Alternatively, there may be an as of yet unidentified environmental risk factor specific for CRC that is concentrated in the French speaking parishes, particularly in the white population. Dietary factors would be important to address. Dietary studies in CRC have mainly focused on red meat consumption. Some studies have demonstrated an increased risk of developing CRC in those who have increased rates of red meat consumption.[41] However, in other studies an association has been less clear.[42,43] It is uncertain if red meat consumption in the Cajun population is any higher than other areas of the United States. However, there are certain culinary practices and food ingredients that are frequently utilized in Cajun cooking and it may be possible that there is an unidentified dietary risk factor present in the population. However this is speculative and it is important to note that fresh fruits and vegetables are an important staple of the Cajun diet, which may actually play a modest protective role for the development of CRC.[44,45]

It is important to address the issue of health-care access as it is possible that a lack of availability to preventive screening colonoscopy could be responsible for the high rates of CRC. However, given that there appears to be a trend of early-onset CRC in patients under age 50, before screening colonoscopy is typically offered, argues against this. In addition, when one examines health-care insurance rates in 2007, the median year of our study, in all individuals under age 65 (before Medicare eligibility) in the Acadian Parish region, the insured rates were similar to statewide rates. The LA insured rate was 77.2% compared with insured rates of 77.5% in the Acadian 9 and 76.9% in the Acadian 18.[46]

In summary, we have identified a very high rate of CRC in the white population of the French speaking Acadian parishes of LA. This appears to be the first descriptive study in the United States identifying a higher rate of CRC (or any cancer) in a large, regional founder population. In the white population, there does not appear to be a disproportionately higher rate of non-colonic malignancies. In addition, there does not seem to be higher rates of smoking and obesity in the region compared with LA and health-care insurance rates are similar to statewide rates. Furthermore, rates of CRC in whites increased in parishes with a higher proportion of French speakers, a marker for those with Cajun ancestry, and there appeared to be a trend of increased cases of early-onset CRC in the region, particularly in the white population of the Acadian 9. Given the summation of these observations and the fact that founder effects for other Mendelian inherited diseases have been demonstrated in the Cajun population of this region, it is possible that the increased rates of CRC may be explained, at least in part, by a high rate of hereditary CRC.

Alternatively, or in conjunction, there may be environmental risk factors that are concentrated in the Acadian parishes that have yet to be identified that may underlie the high CRC incidence. If such a risk factor is present, it appears to be disproportionately affecting the white, as opposed to African American, population of the Acadian 9. Regardless of etiology, a region with very high rates of CRC has been uncovered for which clinical resources, including adequate access to screening colonoscopy, need to be focused in order to help prevent the development of malignancy.

Future studies, including tumor microsatellite instability and immunohistochemistry analysis, and ultimately germline genetic testing, will be needed to explore the possibility of hereditary CRC. As CRC in this population has never been studied, the potential could exist to identify novel susceptibility genes. If such genes are identified, this may be important for hereditary CRC testing in the general United States and global population because many worldwide regions have a significant portion of the population of French descent. Further studies to assess environmental risk factors will also be important. For example, dietary patterns that are concentrated in the Acadian parishes would be important to explore as it is possible that novel dietary risk factors may be uncovered. We would also like to study other US regions with a high density of the population that historically descends from the Acadian region of Canada, as there may be important parallels between these populations and the Acadian parishes of LA. For example, Aroostook County, Maine has the highest regional percentage of French speakers (22.4%) in the United States outside of LA. Similar to the Acadian parishes of LA, there is an established Acadian population descended from Northeast Canada (including Nova Scotia) and very high rates of CRC in whites and white males that are disproportionately higher than the state as a whole (26.9% higher than the state of Maine in whites and 30.5% higher in white males).[22,47,48] Although we did not demonstrate rates of CRC in the African-American population in the Acadian region to be statistically significantly higher than statewide rates, the CRC rates were extremely high, particularly in the Acadian 18, and warrant further study.

There are limitations to our study that need to be addressed. When discussing these, it is important to address the size of the Cajun population in the Acadian region. Given that the LA Cajun population has been estimated at 500,000–700,000 and that the total white population of the Acadian parishes is approximately 820,000, it is suggested that the majority of whites in the Acadian region have some degree of Cajun ancestry and highlights our discussion above regarding the potential of CRC risk being translated to the Cajun population. This is supported by 1990 ancestry data for Vermilion parish described in the introduction, in which the majority of the population was of French Canadian or French ancestry. With this being said, however, there is likely a significant degree of heterogeneity and the study is limited by the fact that it is ecologic with data at the population level with no case-specific information on ancestry, body mass index, and so on. Hence, it is possible that many of the persons actually diagnosed with CRC in the region are not of Cajun ancestry. Furthermore, using French speaking parishes as a marker for the Cajun population may have limitations as not all Cajuns speak French and there may be French speakers in the region that are not of Cajun descent. Additional limitations of this study include smaller numbers of CRC cases in certain subgroups with a resulting reduction in statistical power. For example, this may limit the ability to detect statistically significant differences in incidence rates in the African-American population and in the analysis of under age 50 subgroups.

CONFLICT OF INTEREST

Study Highlights

WHAT IS CURRENT KNOWLEDGE

✓ Hereditary colorectal cancer syndromes are relatively common and have a high penetrance for development of malignancy.

✓ Genetic founder effects for hereditary cancer syndromes can lead to increased incidence rates of malignancy in a population.

✓ The Cajun population in southern Louisiana is an established founder population for several genetic diseases, however colorectal cancer has never been studied in this population.

✓ Founder populations are important to study as it may be possible to uncover mutations, potentially novel, that are important not only for the population being studied, but for other distant populations that may share similar remote ancestry.

WHAT IS NEW HERE

✓ Colorectal cancer incidence rates in the Acadian parishes of Louisiana, home of the Cajun population, are among the highest in the country.

✓ White males in a 9-parish subgroup of the Acadian region with a high proportion of French speakers have the single highest rate of colorectal cancer in the United States compared with other white male populations nationally.

✓ This is the first study demonstrating a high rate of malignancy in a large, regional founder population in the United States.

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Supplementary Information accompanies this paper on the Clinical and Translational Gastroenterology website (http://www.nature.com/ctg)

Supplemetal Data
Incidence of CRC in Acadian 18, LA and U.S. SEER 2005-2009

Average Annual Rates per 100,000, by Sub-Groups of Ages

Acadian 18 Parishes

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	^	^	^		^	^	^
30-39	7.9	^	9.4		^	^	^
40-49	26.0 ↑	27.4	24.6		39.3 ↑	50.1 ↑	30.2
20-49	12.3 ↑	12.2	12.3 ↑		17.2 ↑	19.7 ↑	15.2
0-49	7.5 ↑	7.5	7.4 ↑		10.4 ↑	11.9 ↑	9.2
All ages	**52.2 ↑#**	**66.0 ↑#**	41.4		67.7 ↑	88.6 ↑	54.0

Louisiana

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	1.4	^	^		^	^	^
30-39	8.2 ↑	8.9	7.5		9.7 ↑	9.8	9.6
40-49	25.2 ↑	26.7	23.8 ↑		34.1 ↑	39.9 ↑	29.3
20-49	12.2 ↑	12.9 ↑	11.4 ↑		15.8 ↑	17.6 ↑	14.3
0-49	7.4 ↑	7.8 ↑	6.9 ↑		9.6 ↑	10.7 ↑	8.7
All ages	49.5 ↑	61.0 ↑	40.3		63.5 ↑	78.9 ↑	53.4 ↑

SEER

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	1.5	1.5	1.5		1.3	1.3	1.3
30-39	6.5	6.7	6.3		6.9	6.7	7.1
40-49	21.5	22.9	19.9		28.4	30.1	26.9
20-49	10.3	10.9	9.6		12.8	13.3	12.3
0-49	6.2	6.6	5.9		7.8	8.1	7.5
All ages	45.4	53.1	39.2		57.0	66.9	50.3

^ Rates are not calculated for cells smaller than 16 for the 5-year period

Cases are assigned to the parish of residence, not the parish where diagnosis/treatment occurred.

Acadian 18 Parishes: Acadia, Allen, Assumption, Avoyelles, Calcasieu, Cameron, Evangeline, Iberia,
   Jefferson Davis, Lafayette, Lafourche, Pointe Coupee, St. James, St. Landry, St. Martin, St. Mary,
   Terrebonne, and Vermilion parishes

Invasive cases only

↑ or ↓ Acadian 18 rate differs significantly from SEER rate (p ≤ 0.05).

↑# or ↓# Acadian 18 rate differs significantly from both the SEER rate and the Louisiana rate (p ≤ 0.05)

Please note that there were no statistically signficant differences between subgroups of the Acadian 9 and Acadian 18

Supplemental Data
Incidence Rates of CRC in Acadian 9, LA and U.S. SEER 2005-2009

Average Annual Rates per 100,000, by Sub-Groups of Ages

Acadian 9 Parishes

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	^	^	0.0		0.0	0.0	0.0
30-39	8.4	^	^		^	^	^
40-49	31.3↑	34.4↑	28.1		29.4	^	^
20-49	14.1	16.1	12.1		13.7	^	13.7
0-49	8.6↑	9.9↑	7.3		8.2	^	8.3
All ages	**56.1 ↑ #**	**72.6 ↑#**	42.7		61.5↑	76.3 ↑	51.7

Louisiana

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	1.4	^	^		^	^	^
30-39	8.2 ↑	8.9	7.5		9.7 ↑	9.8	9.6
40-49	25.2 ↑	26.7	23.8 ↑		34.1 ↑	39.9 ↑	29.3
20-49	12.2 ↑	12.9 ↑	11.4 ↑		15.8 ↑	17.6 ↑	14.3
0-49	7.4 ↑	7.8 ↑	6.9 ↑		9.6 ↑	10.7 ↑	8.7
All ages	49.5 ↑	61.0↑	40.3		63.5 ↑	78.9 ↑	53.4 ↑

SEER

	White				Black		
	M & F	Male	Female		M & F	Male	Female
20-29	1.5	1.5	1.5		1.3	1.3	1.3
30-39	6.5	6.7	6.3		6.9	6.7	7.1
40-49	21.5	22.9	19.9		28.4	30.1	26.9
20-49	10.3	10.9	9.6		12.8	13.3	12.3
0-49	6.2	6.6	5.9		7.8	8.1	7.5
All ages	45.4	53.1	39.2		57.0	66.9	50.3

^ Rates are not calculated for cells smaller than 16 for the 5-year period

Cases are assigned to the parish of residence, not the parish where diagnosis/treatment
   occurred.

Acadian 9 Parishes: Acadia, Assumption, Avoyelles, Evangeline, Jefferson Davis, Lafourche
   St. Landry, St. Martin, Vermilion

Invasive cases only

↓ or ↑Acadian 9 rate differs significantly from SEER rate (p $\leq$ 0.05).

↑# Acadian 9 rate is significantly higher than the SEER and the Louisiana rates (p < 0.05)

Please note that there were no statistically signficant differences between subgroups of the Acadian 9 and Acadian 18