Published in final edited form as:
Cancer Causes Control. 2013 February ; 24(2): 277–285. doi:10.1007/s10552-012-0095-7.

RACIAL DISPARITIES IN COLORECTAL CANCER INCIDENCE BY TYPE 2 DIABETES MELLITUS STATUS

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Abstract

Purpose—Type 2 diabetes mellitus (T2DM) prevalence has increased dramatically in the United States since the early 1970s. Though T2DM is known to be associated with colorectal cancer (CRC), information on racial differences in the relationship between T2DM and CRC is limited.

Methods—Using a retrospective cohort design we compared the association between T2DM and CRC, including subsites of the colon, in African Americans (AAs) and European Americans (EAs) in South Carolina, a region with large racial disparities in rates of both diseases. A total of 91,836 individuals who were ≥30 years old on January 1, 1990 and had ≥12 months of South Carolina Medicaid eligibility between January 1, 1990 and December 31, 1995 were included in the analyses. Cancer data from 1996 to 2007, included information on anatomic subsite.

Results—Subjects who had T2DM (n=6,006) were >50% more likely to be diagnosed with colon cancer compared to those without T2DM (n=85,681). The association between T2DM and colon cancer was higher in AAs [odds ratio (OR) = 1.72 (95% Confidence Interval:1.21,2.46); n=47,984] than among EAs (OR = 1.24; 0.73,2.11; n=43,703). Overall, individuals with T2DM were over twice as likely to be diagnosed with *in situ* or local colon cancer (OR = 2.12; 1.40,3.22; n=191) compared to those without T2DM, with a higher likelihood among AAs (OR = 2.49;1.52,4.09; n=113).

Conclusions—Results from a Medicaid population in a high-risk region of the country, showed an increased likelihood of CRC with T2DM and suggest a racial disparity that disfavors AAs and provides further impetus for efforts aimed at diabetes prevention in this group.

Keywords

cohort study design; colorectal cancer; diabetes mellitus type II; health status disparities; incidence; South Carolina

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Conflicts of Interest: The authors declare that they have no conflict of interest.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a large and growing public health concern in the US [1]. T2DM has been linked to a variety of other conditions that are important causes of disability and death [2]. Colorectal cancer (CRC), and cancers of the colon in particular, represent a serious public health concern [3,4] and have been linked to DM (type 1 or type 2) [5–15]. Though it is known that both T2DM and CRC disproportionately affect African Americans (AAs), the relationship between the two has not been extensively explored with respect to race. AAs in South Carolina, who are concentrated in rural areas (where they account for over 40% of all residents) are generally economically deprived relative to European Americans (EAs) [16,17], and rates of DM tend to be higher among the poor [18,19].

CRC is the fourth most commonly diagnosed cancer in South Carolina [20]. Although the state's CRC incidence rate is slightly lower than the U.S. national average, at 47.0 per 100,000 among men and 36.8 per 100,000 among women (vs. 51.6 and 38.7, respectively for the nation as a whole in the most recent data) [20], rates among AAs in South Carolina (47.2 per 100,000) are higher than in EAs (39.6 per 100,000) [21,20]. CRC risk may be influenced by genetic and environmental factors [22]. Non-modifiable risk factors for CRC include age and a family history of the disease [21]. Modifiable risk factors include obesity, smoking, lack of physical activity, and certain aspects of diet [23,24]. Markers of inflammation that also are well known to be related to each of these other factors are strongly associated with T2DM, which in turn has been shown to be associated with increased risk of CRC [25–27].

Consistent with an association between inflammation and cancer, a number of studies have observed an association between T2DM, a condition marked by increased inflammation, and CRC [10,6,11,5], including among AAs in the Multiethnic Cohort [28]. In the United States, the prevalence of T2DM dramatically increased from the early 1970s to 2004. Data from the National Health and Nutrition Examination Survey (NHANES) show that the prevalence of T2DM during 1999–2004 was highest in AAs (13.8%), intermediate in Mexican Americans (13.2%) and lowest in EAs (7.8%) [1]. Of equally great concern, the increases in diagnosed and undiagnosed T2DM during this period have been over 200% in AAs (206.7%) and Mexican Americans (288.2%), vs. 169% in EAs [1]. Using data from the Behavioral Risk Factor Surveillance System (BRFSS), the prevalence of DM in South Carolina in 2009 was ≈10.3% [29]. This self-reported information is likely to underestimate the prevalence of DM because about one third of individuals with DM are unaware that they have the disease [30].

Overall, it appears that T2DM is associated with the risk of total CRC, but studies are inconsistent on the association between T2DM and risk of cancer at specific subsites of the colon and rectum. Also, there is limited information on the association in different racial groups in the United States, especially comparing AAs and EAs [28,31]. Accordingly, this study was designed to assess the association between T2DM and CRC and subsites of the colon and rectum among EAs and AAs in South Carolina.

METHODS

Study Design and Sample

We created a retrospective cohort to examine the relationship between T2DM and CRC incidence. The sample included individuals ≥30 years old as of January 1, 1990 with ≥12 months of South Carolina Medicaid eligibility between January 1, 1990 and December 31, 1995. The sample was limited to individuals with Medicaid because T2DM diagnosis from claims information is a good proxy for T2DM status and because this sample would only include individuals who were income eligible, thus reducing the influence of economic

status, a common confounder in racial comparisons. Because our focus was on T2DM, and in order to establish the temporality of the associations, subjects were excluded if they had a diagnosis of type 1 DM (which is etiologically distinct from T2DM) or CRC during this 6-year period. In our sample, 50.6% (n=109,971) of individuals with Medicaid eligibility in this time period (without type 1 DM or CRC, and ≥30 years of age) had ≥12 months of Medicaid eligibility. The study sample was then limited to individuals of EA or AA race, with known sex and marital status (which excluded an additional 18,135 individuals).

The sample from Medicaid was then linked with CRC data from the South Carolina Central Cancer Registry (SCCCR) using probabilistic matching techniques. Funded by the National Program of Cancer Registries in the CDC Division of Cancer Prevention and Control, the SCCCR exceeds the NPCR National Data Quality and Completeness standards, consistently receiving a "gold" rating for completeness and timeliness. Data were linked by first name, last name, middle name (if provided), date of birth, SSN (if provided), and Medicaid number (if provided). Individuals with a CRC diagnosis from 1996–2007, as described below, were classified as cases, while all other individuals in this sample were used as the comparison group in analyses.

CRC Classification

CRC status was obtained from the SCCCR. CRC status was available from January 1, 1996 to December 31, 2007 and was determined using the International Classification of Diseases for Oncology Third Revision (ICD-O-3) codes. Overall CRC and CRC subsites were defined using the following ICD-O-3 codes: total CRC using C18.0 – 18.9, C19.9, C20.9, and C26.0; colon cancer using C18.0 – 18.9 and C26.0; proximal colon cancer using C18.0 – C18.5; distal colon cancer using C18.6 and C18.7; and rectal cancer using C19.9 and C20.9. SEER summary staging was used to further classify CRC cases into three groups. SEER summary stage groups were defined as: 1) local or *in situ*, 2) regional spread to adjacent organs or regional nodes, and 3) spread beyond adjacent organs or regional nodes.

Type 2 diabetes mellitus (T2DM) Classification

T2DM was assigned using ICD-9 codes from Medicaid records. Individuals with ICD-9 codes 250 with a fifth digit value of 0 and 2 were classified as having T2DM. Individuals were classified as having T2DM if the ICD-9 code appeared at least one time on their record between January 1, 1990 and December 31, 1995.

Covariate classification

Age, in years, was determined as of January 1, 1990 from the Medicaid records. Data on sex and race also were obtained from Medicaid files. Marital status was obtained from Medicaid records and assigned as 1) married or 2) single, separated, divorced, and widowed. Hypertension status was obtained from Medicaid data using ICD-9 codes 401.0 to 405.99. In instances where sex and race status differed between SCCCR and Medicaid, the individuals were assigned values from the SCCCR. Before exclusion criteria were imposed, 251 (12.9%) and 40 (2%) out of 1,952 cancer cases that linked to Medicaid records had discrepancies in race and sex, respectively. The decision to use SCCCR to establish sex and race when differences existed was based on the more rigorous data abstraction and management methods of the cancer registry.

Statistical Analyses

Descriptive statistics of categorical potential risk factors by CRC status were assessed using χ^2 tests. Characteristics measured on continuous scales were assessed using 2-sample t-tests. To assess the association between T2DM and total CRC (and subsites), odds ratios

(OR) were obtained from the full cohort using logistic regression analysis. To assess the association between T2DM and SEER summary stages of CRC (and subsites), multinomial logistic regression was carried out. All models controlled for sex, race, age, marital status, hypertension, and number of months Medicaid eligibility between January 1, 1990 and December 31, 1995. All analyses were stratified by race as was decided *a priori*. All analyses were performed using SAS® version 9.2 (SAS Institute, Cary, NC).

RESULTS

Compared to CRC-free individuals, a higher proportion of CRC cases had T2DM and hypertension (Table 1). Also, CRC cases had significantly less Medicaid eligibility time. Table 2 shows ORs for CRC and subsites of the colon and rectum comparing those with T2DM vs. those without T2DM. Overall, individuals with T2DM were ≈1.5 times more likely to be diagnosed with colon cancer, and the effect was more pronounced for cancer of the proximal (right) colon and appeared to be higher in AAs both for colon cancer overall (OR=1.72 or 72% higher) and for proximal colon cancers (OR=1.77 or 77% higher), compared to no effect in EAs. Similar associations were observed for distal colon cancer, though results were not statistically significant when adjusted for covariates. Although the interaction term for race and T2DM was not significant for total CRC and subsites of the colon and rectum, stratification by race was based on an *a priori* hypothesis. Presentation of stratified findings (Table 2) allows for the examination of the specific group which may be driving the overall effect. For both overall colon and proximal colon cancer, a significantly increased likelihood of cancer among individuals with T2DM was observed in AAs but not EAs. In addition, analyses revealed that individuals with T2DM were significantly less likely to be diagnosed with rectal cancer in the pooled analyses. However, confidence intervals were wide, indicating lack of precision around these estimates. Power calculations revealed the effect size (OR) needed for 80% power are: all CRC ≥1.5, CRC stratified ≥1.7, colon cancer ≥1.6, colon cancer stratified ≥1.8, proximal colon cancer ≥1.8, proximal colon cancer stratified ≥2.0, distal colon cancer ≥2.0, distal colon cancer stratified ≥2.0, rectal cancer ≥2.0, rectal cancer stratified ≥2.0.

Table 3 shows the results from the multinomial logistic regression, which accounted for disease stage. Individuals with T2DM were significantly more likely to be diagnosed with *in situ* or local CRC, colon cancer, proximal colon cancer, and distal colon cancer. ORs were higher in AAs, while ORs among EAs were lower and not statistically significant. There were no significant associations when examining T2DM and regional CRC or CRC that spread beyond adjacent organs.

DISCUSSION

Results from this study suggest a significant increased likelihood of CRC, especially proximal colon cancer, among AA type 2 diabetics, but not EAs, in South Carolina. When comparing groupings of SEER summary stage CRC to those without CRC, type 2 diabetics had at an increased likelihood for *in situ* or localized cancer, but not CRC that spread into, or beyond, adjacent organs. Estimates for *in situ* or localized cancer were largest for AAs. Similar increased likelihood of *in situ* and local cancer was observed for all colon cancers combined, proximal colon cancer, and distal colon cancer. By contrast with results on colon cancer, T2DM was inversely associated with the likelihood of rectal cancer.

A meta-analysis carried out in 2005 assessing the association between DM and CRC found an overall increase in risk of 30% (RR = 1.3; 95% Confidence Interval = 1.2–1.4) among individuals with DM compared to non-diabetics, with no difference observed between colon and rectal cancer or subsites of the colon [9]. Since 2005, a number of epidemiologic studies

have corroborated these results, but with some variations in the association between T2DM and subsites of the colon and the rectum. Limberg *et al.* found that the Standardized Incidence Ratio (SIR) of CRC was significantly elevated among T2DM patients (SIR = 1.39), but seemed to be confined to men (SIR = 1.67) [11]. Another study published in 2006 also found a significantly increased risk of CRC among diabetics (RR = 1.39) [5].

T2DM appears to be associated with the risk of total CRC, but studies are inconsistent on the association between T2DM and risk of cancer among subsites of the colon and rectum [6,15,9,10,8,12]. Results from previous studies looking at subsites of the colon are limited. Our study revealed a significant increased likelihood of proximal colon cancer and a non significant increased likelihood of distal colon cancer among type 2 diabetics. Flood *et al.* found a significant increased risk of distal colon and rectal cancer, but not proximal colon cancer among women [6]. In a Swedish male population, T2DM was associated with a significantly increased risk of total CRC, colon cancer, and rectal cancer. However, when results examined proximal and distal cancer separately, the increased risks were not statistically significant [9].

We observed an increased likelihood of colon cancer, but a decreased likelihood of rectal cancer among type 2 diabetics. It has been known for over a quarter century that rectal and colon cancers have different etiologies [32–35]; so, it should not be too surprising to have heterogeneity in the results. Because rectal cancers are rarer than colon cancers, the confidence limits are wider and concomitant ability to draw inferences from the data tend to be more limited for rectal cancer. Similar to our results, Sturmer *et al.* found DM to be associated with a significantly increased risk of CRC (Hazard Ratio = 1.5), with a stronger association between DM and colon cancer and a weaker association between DM and rectal cancer [15]. A prospective study in Norway found a significant association between DM and colon cancer, but not rectal cancer [12]. In a Japanese study, there was a significant association between DM and colon (but not rectal) cancer among men; however, after excluding cases that occurred in the first 5 years of follow up, results were no longer significant [36]. To our knowledge, this is the first study to find an inverse association between T2DM and rectal cancer. Previous studies have found an increased risk of rectal cancer among type 2 diabetics or no association [9,6,15,10,8,12,36,14,13]. A recent study published using data from India observed a nonsignificant increased risk of colon cancer among tobacco users and a nonsignificant decreased risk for rectal cancer [37]. Although not statistically significant and examining a different exposure, other studies also have reported conflicting results between colon and rectal cancer.

Two studies have examined the association between DM and CRC in EAs and AAs [28,31]. Vinkoor *et al.* found a significantly higher likelihood of rectal cancer among diabetics compared to non-diabetics in EAs, but no association for colon cancer. Also, no association was observed among AAs for colon or rectal cancer [31]. Results using data from the Multiethnic Cohort Study [28] suggested increased risk of CRC among those with DM, with no difference in the strength of the association between EAs and AAs (≈16% increase for both), and a significant increased risk of distal colon cancer in AAs (RR=1.38;1.01,1.89). Both of these studies [28,31] relied on DM status based on self-report, which would tend to bias results toward the null [38].

In our study, the associations between T2DM and CRC, colon cancer, and proximal colon cancer was higher among AAs. Estimates among EAs were smaller and not statistically significant; and the interaction by race was not statistically significant. In the multinomial logistic regression results, we found T2DM to increase the likelihood of *in situ* and localized colon cancer, proximal colon cancer, and distal colon cancer, but no increased likelihood was observed with increasing cancer stage. If studies differ in severity of CRCs (e.g., with

differences in patterns of screening), results in the strength of the association between T2DM and CRC also may differ. Potential reasons for the differences in the results between studies looking at the association between T2DM and CRC could be due to: differences by racial group, severity of cancer, reliance on self-reported diabetes status (vs. medical records), inability to statistically evaluate subsites of the colon and rectum, or some combination of these. Another explanation for differences between studies may be the severity of the cancer. Also, conflicting results may be attributed to the inability to assess the association between T2DM and subsites of the colon and rectum. In 2009, Li *et al.* proposed that CRC should be sub-divided into 3 distinct sections, proximal colon cancer, distal colon cancer, and rectal cancer [39]. The authors state that this distinction is important given the heterogeneity that exists in physiology, exposure to carcinogens, genetic mechanisms, and prognosis [39].

Strengths and Weaknesses

The current study has a number of unique attributes that set it apart from the few other studies that have addressed CRC in diabetics. Our sample population is restricted to Medicaid beneficiaries which somewhat limits the generalizability of the findings. Our goal was to examine these relationships in a population at high risk of both T2DM and CRC. Also, restricting this to Medicaid beneficiaries would: 1) blunt the influence of economic status, a common confounder in racial comparisons; 2) expand the research by including people who are grossly underrepresented in existing cohorts; and 3) would eliminate reliance on our collecting income-related data, which are notoriously difficult to collect with accuracy (instead relying on Medicaid income eligibility). However, we also recognize that Medicaid-eligible individuals may differ in important ways from those covered by private or other health insurance. Another limitation in using Medicaid claims data is the inconsistency in coverage eligibility. Individuals may go in and out of Medicaid eligibility throughout their lifetime or may be eligible for only a short period of time. This may lead to missing T2DM diagnoses if individuals were diagnosed when they were not covered by Medicaid. To reduce the potential for this misclassification of T2DM exposure, the study population was limited to individuals covered for at least 12 months between January 1, 1990 and December 31, 1995. Related to this, is the potential that many of the cases of T2DM identified in this study may have a more severe disease. Individuals with more severe diabetes would visit health care institutions more frequently and, as a result, have a higher likelihood of being classified with T2DM using the methods implemented in this study. This may bias results away from the null if the risk of CRC is greater with increased T2DM severity. Thus, it also may be possible that there was an ascertainment bias in terms of CRC stage at diagnosis, which results from individuals with T2DM being more likely to be followed; thus, more likely to be screened and detected earlier (i.e., more likely to be screened or to catch early symptomology) in the natural history of their CRC.

T2DM status was determined between January 1, 1990 and December 31, 1995, but not during the period in which CRC status was captured. It is possible that individuals were diagnosed after December 31, 1995. In this sample the prevalence of T2DM, as estimated by claims data, was 6.5%, somewhat lower than what would be expected in a population of this age. It is possible that, due to the limitation mentioned above, a number of individuals with T2DM were misclassified as T2DM free. If there is an increased risk of CRC among type 2 diabetics, then results would be biased towards the null. Due to the nature of these publicly available data, important information on potential confounders, such as CRC screening, certain aspects of diet, obesity, smoking, and lack of physical activity, was unavailable. Controlling for these factors could potentially explain some of the observed association between T2DM and CRC, since T2DM is positively associated with obesity, physical inactivity, and certain aspects of diet [40]. As a counterpoint to this limitation, it is important

to note that T2DM is a strongly pro-inflammatory condition [41,42], and can be measured with much greater accuracy than diet. It also is important to note that we and others have used this methodology with great success [43–45] – notwithstanding that it provides us with data on a high-risk population that is normally neglected in medical research. Power calculations identifying the effect size needed to have 80% power revealed adequate power for the association observed for overall colon cancer and rectal cancer, but also revealed insufficient power among the stratified analyses, and overall proximal and distal colon cancer. One other limitation to mention is the number of records with inconsistent race/ethnicity coding between the Medicaid and SCCCR data. Among CRC cases that linked to Medicaid records, before exclusion criteria were imposed, 12.9% had discrepancies in race. It is important to note that while in Medicaid claims data, for which the primary purpose is reimbursement, race is an extremely low priority, the cancer registry (SCCCR) has stringent QA/QC measures to ensure accurate data collection on race (and all other required data fields). In addition to the strengths noted above, using Medicaid claims data allowed for a large sample size, which in turn enabled assessment of the association between T2DM and subsites of the colon and rectum. Also, demographics in South Carolina (i.e., about 30% AA) allowed for assessing differences in these associations by race in a population whose eligibility was determined by income, a potentially important confounder in most studies on this subject. Using Medicaid claims data provides an opportunity to assess relationships in hard-to-reach, underserved populations, who tend to have the most extreme health disparities. We were also able to obtain DM status from medical records, not self-reports as in other studies on this subject [28,31]. Results from this study can be replicated in any state or territory with Medicaid and cancer registry data. Publications based on public-access data will increase familiarity with their use. This could allow for the very efficient use of these publicly available datasets as a way to create prospective follow-up studies. As most existing cohorts focus mainly on more affluent, well-educated individuals [24,46] who tend to be at lower risk of CRC, this also would help to address racial and socioeconomic status-related disparities.

Conclusions

Our results provide additional evidence of an increased likelihood of CRC, specifically colon cancer, among individuals with T2DM. Also, these results suggest that this association may be stronger among AAs. This is important because AAs are twice as likely to be diagnosed with T2DM compared to EAs [1]. Also, AAs in South Carolina are generally economically deprived relative to EAs [16,17] and account for a large proportion of rural residents [47,48,17,49]. One explanation for the difference in the association between EAs and AAs may be differences in the control of blood glucose levels between the two racial groups. Previous studies that examined the rates of self monitoring of blood glucose among diabetics have found lower rates of checking among AAs compared to EAs [50]. If glucose among type 2 diabetics is controlled, this may limit the damage that increases the risk of CRC. However, if not controlled, damaging effects of T2DM may increase the risk of CRC.

Future studies are needed to confirm our findings of differential associations between T2DM and CRC by race. Etiologic reasons for different associations by race and subsite need to be identified. If confirmed, interventions aimed at diabetes prevention or control may also have a beneficial effect on CRC, particularly among AAs.

Acknowledgments

Funding was provided by the National Cancer Institute, Center for Research and Cancer Health Disparities (Community Networks Program) to the South Carolina Cancer Disparities Community Network (SCCDCN) [1U54 CA153461 Hebert, JR (PI)]; The South Carolina Central Cancer Registry (SCCCR), funded by the CDC National Program of Cancer Registries [U55CCU421931]. Dr. Hébert was supported by an Established Investigator Award

in Cancer Prevention and Control from the Cancer Training Branch of the National Cancer Institute (K05 CA136975). The Cancer Prevention and Control Program of the University of South Carolina provided support to Drs. Cavicchia, Adams, Steck and Hébert.

Effort of Others: We would like to acknowledge the support of the staffs of the South Carolina Central Cancer Registry, especially Deborah Hurley and Jonathan Savoy, for access to cancer-related data and the South Carolina Budget and Control Board's Office of Research Statistics, especially Heather Kirby, for access to Medicaid data including information on diabetes.

Abbreviations Used

AAs	African Americans
CRC	colorectal cancer
EAs	European Americans
OR	odds rat
SCCCR	South Carolina Central Cancer Registry
SIR	Standardized Incidence Ratio
T2DM	Type 2 diabetes mellitus

Literature Cited

1. Zhang Q, Wang Y, Huang ES. Changes in racial/ethnic disparities in the prevalence of Type 2 diabetes by obesity level among US adults. Ethnicity & Health. 2009; 14(5):439–457. [PubMed: 19360513]
2. Diabetes Statistics. [Accessed 29 December 2011] American Diabetes Association. 2011. http://www.diabetes.org/diabetes-basics/diabetes-statistics/.2011
3. US Cancer Statistics Working Group. United States Cancer Statistics: 1999–2007 Incidence and Mortality Web-based Report. U.S. Department of Health and Human Services Centers for Disease Control and Prevention and National Cancer Institute; 2011. www.cdc.gov/cancer/npcr/uscs
4. Howlader, N.; Noone, AM.; Krapcho, M.; Neyman, N.; Aminou, R.; Waldron, W.; Altekruse, SF.; C.L.K; Ruhl, J.; Tatalovich, Z.; Cho, H.; Mariotto, A.; Eisner, MP.; Lewis, DR.; Chen, HS.; Feue, EJ.; Cronin, KA.; Edwards, BK., editors. SEER Cancer Statistics Review. 2011. p. 1975-2008.
5. Ahmed RL, Schmitz KH, Anderson KE, Rosamond WD, Folsom AR. The metabolic syndrome and risk of incident colorectal cancer. Cancer. 2006; 107(1):28–36. [PubMed: 16721800]
6. Flood A, Strayer L, Schairer C, Schatzkin A. Diabetes and risk of incident colorectal cancer in a prospective cohort of women. Cancer Causes & Control. 2010; 21(8):1277–1284. [PubMed: 20383575]
7. Jee SH, Ohrr H, Sull JW, Yun JE, Ji M, Samet JM. Fasting serum glucose level and cancer risk in Korean men and women. JAMA. 2005; 293(2):194–202. [PubMed: 15644546]
8. La Vecchia C, Negri E, Decarli A, Franceschi S. Diabetes mellitus and colorectal cancer risk. Cancer Epidemiology, Biomarkers & Prevention. 1997; 6(12):1007–1010.
9. Larsson SC, Orsini N, Wolk A. Diabetes mellitus and risk of colorectal cancer: a meta-analysis. Journal of the National Cancer Institute. 2005; 97(22):1679–1687. [PubMed: 16288121]
10. Larsson SC, Giovannucci E, Wolk A. Diabetes and colorectal cancer incidence in the cohort of Swedish men. Diabetes Care. 2005; 28(7):1805–1807. [PubMed: 15983343]
11. Limburg PJ, Vierkant RA, Fredericksen ZS, Leibson CL, Rizza RA, Gupta AK, Ahlquist DA, Melton LJ 3rd, Sellers TA, Cerhan JR. Clinically confirmed type 2 diabetes mellitus and colorectal cancer risk: a population-based, retrospective cohort study. American Journal of Gastroenterology. 2006; 101(8):1872–1879. [PubMed: 16790032]
12. Nilsen TI, Vatten LJ. Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. British Journal of Cancer. 2001; 84(3):417–422. [PubMed: 11161410]

13. Ren X, Zhang X, Gu W, Chen K, Le Y, Lai M, Zhu Y. Type 2 diabetes mellitus associated with increased risk for colorectal cancer: evidence from an international ecological study and population-based risk analysis in China. Public Health. 2009; 123(8):540–544. [PubMed: 19664792]
14. Seow A, Yuan J-M, Koh W-P, Lee H-P, Yu MC. Diabetes mellitus and risk of colorectal cancer in the Singapore Chinese Health Study. J National Cancer Inst. 2006; 98(2):135–138.
15. Sturmer T, Buring JE, Lee IM, Gaziano JM, Glynn RJ. Metabolic abnormalities and risk for colorectal cancer in the physicians' health study. Cancer Epidemiology, Biomarkers & Prevention. 2006; 15(12):2391–2397.
16. Jia H, Lubetkin EI. The statewide burden of obesity, smoking, low income and chronic diseases in the United States. J Public Health. 2009; 31(4):496–505.
17. McKeehan N, Trettin L, May J. Improving access to health information in rural South Carolina. J Health Care Poor Underserved. 2008; 19(2):484–492. doi:S1548686908200148 [pii] 101353/hpu.0.0010. [PubMed: 18469419]
18. Bolen JC, Rhodes L, Powell-Griner EE, Bland SD, Holtzman D. State-specific prevalence of selected health behaviors, by race and ethnicity--Behavioral Risk Factor Surveillance System, 1997. MMWR CDC Surveill Summ. 2000; 49(2):1–60.
19. Landrine H, Corral I. Separate and unequal: residential segregation and black health disparities. Ethnic Dis. 2009; 19(2):179–184. [Review] [78 refs].
20. US Cancer Statistics Working Group. United States Cancer Statistics: 1999–2006 Incidence and Mortality Web-based Report. 2010. US DHHS/CDC/NIH-NCI. www.cdc.gov/cancer/npcr/uscs
21. Daguise VG, Burch JB, Horner MJD, Mosley C, Hofseth LJ, Wargovich MJ, Lloyd SC, Hebert JR. Colorectal cancer disparities in South Carolina: Descriptive epidemiology, screening, special programs, and future direction. J South Carolina Med Assoc. 2006; 102:212–220.
22. Lin OS. Acquired risk factors for colorectal cancer. Methods Mol Biol. 2009; 472:361–372. [PubMed: 19107442]
23. Harriss DJ, Atkinson G, George K, Cable NT, Reilly T, Haboubi N, Zwahlen M, Egger M, Renehan AG. Lifestyle factors and colorectal cancer risk (1): systematic review and meta-analysis of associations with body mass index. Colorectal Dis. 2009; 11(6):547–563. [PubMed: 19207714]
24. Moghaddam AA, Woodward M, Huxley R. Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. Cancer Epidemiol Biomark Prev. 2007; 16(12):2533–2547.
25. Erlinger TP, Platz EA, Rifai N, Helzlsouer KJ. C-reactive protein and the risk of incident colorectal cancer. JAMA. 2004; 291(5):585–590. see comment. [PubMed: 14762037]
26. Gunter MJ, Stolzenberg-Solomon R, Cross AJ, Leitzmann MF, Weinstein S, Wood RJ, Virtamo J, Taylor PR, Albanes D, Sinha R. A prospective study of serum C-reactive protein and colorectal cancer risk in men. Cancer Research. 2006; 66(4):2483–2487. [PubMed: 16489056]
27. Otani T, Iwasaki M, Sasazuki S, Inoue M, Tsugane S, Japan Public Health Center-Based Prospective Study G. Plasma C-reactive protein and risk of colorectal cancer in a nested case-control study: Japan Public Health Center-based prospective study. Cancer Epidemiology, Biomarkers & Prevention. 2006; 15(4):690–695.
28. He J, Stram DO, Kolonel LN, Henderson BE, Le Marchand L, Haiman CA. The association of diabetes with colorectal cancer risk: the Multiethnic Cohort. British Journal of Cancer. 2010; 103(1):120–126. [PubMed: 20531412]
29. Diabetes Public Health Resource. [Accessed 31 December 2011 2011] Public Health Service, Centers for Disease Control and Prevention. 2011. http://www.cdc.gov/diabetes/statistics/index.htm.
30. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998; 21(4):518–524. [PubMed: 9571335]
31. Vinikoor LC, Long MD, Keku TO, Martin CF, Galanko JA, Sandler RS. The association between diabetes, insulin use, and colorectal cancer among Whites and African Americans. Cancer Epidemiology, Biomarkers & Prevention. 2009; 18(4):1239–1242.

32. Brownson RC, Reif JS, Chang JC, Davis JR. Cancer risks among Missouri farmers. Cancer. 1989; 64(11):2381–2386. [PubMed: 2804930]
33. Troyer H. Review of cancer among 4 religious sects: evidence that life-styles are distinctive sets of risk factors. Soc Sci Med. 1988; 26(10):1007–1017. [PubMed: 3393918]
34. Kohl HW, LaPorte RE, Blair SN. Physical activity and cancer. An epidemiological perspective. Sports Med. 1988; 6(4):222–237. [PubMed: 3067310]
35. Mettlin C. Dietary factors for cancer of specific sites. Surg Clin North Am. 1986; 66(5):917–929. [PubMed: 3532378]
36. Inoue M, Iwasaki M, Otani T, Sasazuki S, Noda M, Tsugane S. Diabetes mellitus and the risk of cancer: results from a large-scale population-based cohort study in Japan. Arch Intern Med. 2006; 166(17):1871–1877. [PubMed: 17000944]
37. Pednekar MS, Gupta PC, Yeole BB, Hebert JR. Association of tobacco habits, including bidi smoking, with overall and site-specific cancer incidence: results from the Mumbai cohort study. Cancer Causes Control. 2011; 22(6):859–868. [PubMed: 21431915]
38. Ma Y, Balasubramanian R, Pagoto SL, Schneider KL, Culver AL, Olendzki B, Tinker L, Liu S, Safford M, Sepavich DM, Rosal MC, Ockene JK, Carnethon M, Zorn M, Hebert JR. Elevated depressive symptoms, antidepressant use, and diabetes in a large multiethnic national sample of postmenopausal women. Diabetes Care. 2011; 34(11):2390–2392. doi:10.2337/dc11-1223. [PubMed: 21911776]
39. Li FY, Lai MD. Colorectal cancer, one entity or three. J Zhejiang Univ Sci B. 2009; 10(3):219–229. [PubMed: 19283877]
40. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010; 33(Suppl 1):S62–69. [PubMed: 20042775]
41. Shehzad A, Ha T, Subhan F, Lee YS. New mechanisms and the anti-inflammatory role of curcumin in obesity and obesity-related metabolic diseases. Eur J Nutr. 2011; 50(3):151–161. [PubMed: 21442412]
42. Percik R, Stumvoll M. Obesity and cancer. Exp Clin Endocrinol Diabetes. 2009; 117(10):563–566. [PubMed: 19924603]
43. Adams SA, Smith E, Hebert JR, Hardin J, Mayer-Davis E. Racial disparities in the association between breast cancer and diabetes in a Medicaid population In Preparation. 2006
44. Gross CP, Filardo G, Mayne ST, Krumholz HM. The impact of socioeconomic status and race on trial participation for older women with breast cancer. Cancer. 2005; 103(3):483–491. doi: 10.1002/cncr.20792. [PubMed: 15597407]
45. Weiss BD, Palmer R. Relationship between health care costs and very low literacy skills in a medically needy and indigent Medicaid population. J Am Board Fam Pract. 2004; 17(1):44–47. [PubMed: 15014052]
46. van den Brandt PA, Spiegelman D, Yaun SS, Adami HO, Beeson L, Folsom AR, Fraser G, Goldbohm RA, Graham S, Kushi L, Marshall JR, Miller AB, Rohan T, Smith-Warner SA, Speizer FE, Willett WC, Wolk A, Hunter DJ. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. Am J Epidemiol. 2000; 152(6):514–527. [PubMed: 10997541]
47. Alberg AJ, Horner MJD, Daguise VG, Carpenter MJ, Mosley CM, Vincent B, Silvestri G, Reed CE, Hebert JR. Lung and bronchus cancer disparities in South Carolina: Epidemiology and strategies for prevention. J South Carolina Med Assoc. 2006; 102:183–191.
48. Hebert JR, Elder K, Ureda JR. Meeting the challenges of cancer prevention and control in South Carolina: Focus on seven cancer sites, engaging partners. J South Carolina Med Assoc. 2006; 102:177–182.
49. South Carolina Office of Research and Statistics. South Carolina Rural Health Report. SC Budget and Control Board; Columbia, SC: 2005.
50. Kirk JK, Graves DE, Bell RA, Hildebrandt CA, Narayan KM. Racial and ethnic disparities in self-monitoring of blood glucose among US adults: a qualitative review. Ethn Dis. 2007; 17(1):135–142. [PubMed: 17274223]

Table 1

Descriptive Statistics by Colorectal Cancer (CRC) status; South Carolina, 1996–2007

	CRC Status		
n (%)	**CRC-free (n=91,159)**	**CRC Case (n=677)**	**P-value[a]**
Sex			0.08
Female	64,087 (70.3)	455 (67.2)	
Male	27,072 (29.7)	222 (32.8)	
Race			0.20
European American	43,476 (47.7)	306 (45.3)	
African American	47,683 (52.3)	371 (54.7)	
Marital Status			0.12
Married	16,115 (17.7)	135 (19.9)	
Not Married	75,044 (82.3)	542 (80.1)	
Type 2 diabetes mellitus			0.02
Yes	5,950 (6.5)	59 (8.7)	
No	85,209 (93.5)	618 (91.3)	
Hypertension			<0.001
Yes	17,025 (18.7)	171 (25.3)	
No	74,134 (81.3)	506 (74.7)	
Mean (Standard Error)			
Age	59.1 (0.06)	58.7 (0.55)	0.39
Medicaid eligibility in months	32.3 (0.05)	30.8 (0.65)	0.02

[a]Categorical variables were assessed using χ^2 tests and continuous variables were assessed using 2-sample t-tests.

Table 2

Odds of Having a Diagnosis of a Cancer of the Colon (including Anatomic Subsites) and Rectum in Subjects with T2DM compared to those without T2DM; Overall and by Race — South Carolina, 1996–2007

Outcome Race	Cases n	T2DM cases n (%)	OR (95% Confidence Interval)[a] Unadjusted	Adjusted[b]
CRC	677	59 (8.3)	**1.37 (1.05,1.79)**	1.20 (0.90,1.58)
European American	306	17 (5.6)	1.11 (0.68,1.82)	0.90 (0.54,1.49)
African American	371	42 (11.3)	**1.49 (1.08,2.06)**	1.37 (0.98,1.93)
Colon cancer	528	56 (10.6)	**1.70 (1.29,2.24)**	**1.56 (1.16,2.09)**
European American	227	16 (7.1)	1.43 (0.86,2.39)	1.24 (0.73,2.11)
African American	301	40 (13.3)	**1.79 (1.28,2.50)**	**1.72 (1.21,2.46)**
Proximal Colon cancer	265	30 (11.3)	**1.83 (1.25,2.68)**	**1.61 (1.07,2.41)**
European American	103	10[c]	1.38 (0.64,2.97)	1.23 (0.55,2.75)
African American	162	23 (14.2)	**1.93 (1.24,3.01)**	**1.77 (1.10,2.83)**
Distal Colon cancer	187	19 (10.2)	**1.62 (1.01,2.61)**	1.48 (0.90,2.44)
European American	86	10[c]	1.42 (0.62,3.25)	1.13 (0.47,2.68)
African American	101	13 (12.9)	1.72 (0.96,3.09)	1.70 (0.92,3.16)
Rectal cancer	149	<5[c]	**0.29 (0.09,0.92)**	**0.22 (0.07,0.70)**
European American	79	<5[c]	0.24 (0.03,1.74)	0.16 (0.02,1.19)
African American	70	<5[c]	0.34 (0.08,1.40)	0.27 (0.07,1.13)

Note: P-value for race/T2DM interaction in the full model for CRC=0.33, Colon cancer=0.49, Proximal Colon cancer=0.49, Distal Colon cancer=0.70, and Rectal cancer=0.75. The sample size of CRC-free individuals was 91,159 with 6.5% (n=5,950) having T2DM. Among EA, the sample size of CRC-free individuals was 43,476 with 5.0% (n=2,185) having T2DM. Among AA, the sample size of CRC-free individuals was 47,683 with 7.9% (n=3,765) having T2DM.

[a] Models were fit with CRC as the dependent variable.

[b] Adjusted for sex, race (unstratified models only), age, marital status, hypertension, and number of months Medicaid eligible between January 1, 1990 and December 31, 1995.

[c] Counts were suppressed at the request of the SCCCR due to small numbers.

Table 3

Odds of Having a Diagnosis of Stage-Specific Cancer of Colon and Rectum in Subjects with T2DM compared to those without T2DM; Overall, by Anatomic Subsite, and by Race — South Carolina, 1996–2007

	OR (95% Confidence Interval)[a]		
Outcome Race	***In situ*/Local (n=260) Vs. CRC-Free**	**Adjacent Organs/Regional Spread (n=225) Vs. CRC-Free**	**Spread beyond Adjacent Organs/ Regional (n=121) Vs. CRC-Free**
CRC	**1.63 (1.10,2.41)**	1.07 (0.65,1.77)	0.72 (0.31,1.68)
European American	0.99 (0.45,2.18)	0.94 (0.43,2.08)	0.31 (0.04,2.32)
African American	**1.99 (1.25,3.14)**	1.16 (0.61,2.24)	0.97 (0.38,2.48)
Colon cancer	**2.12 (1.40,3.22)**	1.36 (0.80,2.30)	1.04 (0.44,2.46)
European American	1.39 (0.61,3.14)	1.16 (0.49,2.76)	0.55 (0.07,4.22)
African American	**2.49 (1.52,4.09)**	1.49 (0.77,2.90)	1.27 (0.49,3.30)
Proximal Colon cancer	**1.90 (1.06,3.43)**	1.50 (0.75,2.98)	1.47 (0.56,3.85)
European American	0.37 (0.05,2.82)	2.48 (0.92,6.68)	1.06 (0.13,8.46)
African American	**2.74 (1.44,5.21)**	1.04 (0.40,2.71)	1.64 (0.55,4.90)
Distal Colon cancer	**2.21 (1.14,4.28)**	1.10 (0.46,2.63)	__ [b]
European American	2.19 (0.72,6.66)	0.32 (0.04,2.38)	__ [b]
African American	2.14 (0.94,4.86)	2.15 (0.78,5.91)	__ [b]

Note: P-value for race/T2DM interaction in the full model for CRC=0.49, Colon cancer=0.71, Proximal Colon cancer=0.21, and Distal Colon cancer=0.63. The sample size of CRC-free individuals was 91,159. Among EA, the sample size of CRC-free individuals was 43,476. Among AA, the sample size of CRC-free individuals was 47,683.

[a] Models fit with CRC Stage as the dependent variable and adjusted for sex, race (unstratified models only), marital status, hypertension status, age, number of months Medicaid eligible between January 1, 1990 and December 31, 1995

[b] Empty cells are a result of low numbers in distal colon cancers spread beyond adjacent organs and was excluded from the analysis