Incidence of Colorectal Adenocarcinoma by Anatomic Subsite

An Epidemiologic Study of Time Trends and Racial Differences in the Detroit, Michigan Area

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BACKGROUND. Colorectal adenocarcinoma may represent more than one disease process. Numerous epidemiologic studies suggest that rates of occurrence of colorectal adenocarcinoma at particular anatomic subsites (e.g., right colon, left colon, and rectum) may be associated with distinctive geographic, demographic, and risk factor profiles. This study explored time trends over a 22-year period of the incidence of adenocarcinoma of the colon and rectum at various subsites among patients of different race, gender, and stage of disease.

METHODS. Data on the incidence of colorectal adenocarcinoma were obtained from a population-based cancer registry in the Detroit, Michigan area funded by the National Cancer Institute. Age-adjusted incidence rates were analyzed by year of diagnosis. Relative survival rates were also obtained for different race and gender categories, along with disease stage at diagnosis.

RESULTS. A major rise was revealed in the incidence of adenocarcinoma in the right colon among African American men and women between the mid-1970s and the early 1980s. The rise was greatest among African American men and accounts for increases in late stage disease among them. Corresponding decreases in survival among African American men were noted.

CONCLUSIONS. These findings indicated widely differing disease patterns based on anatomic subsite and patient demography and also indicated a need for targeted efforts at early detection of adenocarcinoma of the right colon among African Americans. ***Cancer* 1997; 79:441–7.** © *1997 American Cancer Society.*

KEYWORDS: colorectal, adenocarcinoma, race, subsite, trends.

Colorectal cancer among men and women in the U. S. is the third most commonly diagnosed cancer and the second leading cause of cancer mortality. The American Cancer Society estimates that there will be 133,500 new cases of colorectal cancer in the U.S. in 1996, and 54,900 deaths due to this disease.[1] Typically defined as a malignant neoplasm involving an organ extending from the cecum to the anus, cancer of the large intestine is receiving major research attention because of more coherent hypotheses regarding genetic and environmental risk factors, and the recent publication of new screening guidelines.[2] Research on the etiology of colorectal cancer has focused on dietary factors, specifically high fat and low fiber consumption, patterns of preferences for fruits and vegetables, vitamin supplementation, level of regular physical activity, and family history.[3–8] Possible occupational risk factors include asbestos exposure and work in pattern and model making.[9,10] Risk factors vary in relation to race and ethnicity, country of birth and migration, and anatomic location in

the large intestine.[3] Increased knowledge of changing incidence trends may provide clues to further enhance understanding of the etiology of colorectal cancer.

The potential for screening for colorectal cancer is largely dependent on the anatomic location of the premalignant or early phase of the tumor. The recent evolution of fiberoptic technology allows endoscopy to assist in direct viewing of the entire surface of this organ. Coupled with the knowledge that most colorectal cancers originate as polypoid growths on the surface of the colon and rectum, endoscopy theoretically allows for visualization of adenomas and early invasive cancers. Once visualized, polyps can be removed to prevent subsequent neoplastic disease.[11–12] The revised U.S. Preventive Services Task Force guidelines suggest that the risk of colorectal cancer mortality in the general population can be reduced by annual fecal occult blood testing in conjunction with periodic flexible sigmoidoscopy in persons older than 50 years.[13–17] The need to understand patterns of tumor location within the colon and rectum is underscored by the fact that screening endoscopy (flexible sigmoidoscopy) provides visualization of only the distal 60 cm of the colorectal surface, extending approximately to the splenic flexure. The evolving experimental and epidemiologic evidence regarding causal mechanisms and the potential efficacy of screening heighten the importance of developing additional strategies for prevention of colorectal cancer.

Descriptive population-based epidemiologic studies may provide insights into dynamic demographic patterns and their relationship to the natural history of colorectal cancer. Therefore, this study was undertaken to analyze the interrelations of anatomic tumor location, race, gender, diagnostic stage, and time trend data for colon and rectal cancer in the Detroit Metropolitan area from 1973–1994.

METHODS

Data were obtained from the Metropolitan Detroit Cancer Surveillance System, which represents one of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program sites. These data are population-based, encompassing the metropolitan Detroit area of Wayne, Oakland, and Macomb counties. These counties have a combined 1990 population of 3.9 million people, of whom 23.9% are African American.

The study was limited to African Americans and whites with histologically confirmed first primary invasive adenocarcinomas of the colon or rectum. Diagnosis of these adenocarcinomas was made inclusive of calendar years 1973–1994. Histologic types were limited to noncarcinoid adenocarcinomas, because these constitute the vast majority of colorectal malignancies.[18] In addition to analyses by race, gender, and subsite of origin, the influence of stage of disease was also evaluated. Stage is defined according to SEER guidelines as local when the cancer is confined to the mucosa, submucosa, muscularis, or subserosa; regional when the cancer spreads to adjacent lymph nodes, adjacent organs, or the omentum; and distant when the cancer involves distant lymph nodes or other metastases.

The subsite of anatomic origin constituted a key analytic variable and was grouped as the right colon, left colon, or rectum. The right colon subsite included the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure. The descending colon and sigmoid represented the left colon subsite. The rectum subsite included the rectum and rectosigmoid junction, with the latter location defined as the peritoneal reflection, approximately 15 cm from the anal orifice.

Incidence rates were age-adjusted to the 1970 U.S. standard population, and plotted for the colon, rectum, and subsites of the colon and rectum, and by stage, gender, and race. Time trends were plotted using 3-year moving averages. Tests for linear trend in the age-adjusted rates were computed by simple linear regression.[19] In addition, 5-year relative survival rates were determined by year of diagnosis (1973–1988) for adenocarcinomas in the right colon, left colon, or rectum.

RESULTS

All cases among African Americans and whites from 1973–1994 are summarized in Table 1. The proportion of colorectal malignancies in the right colon was 30.8% among white males, compared with 41.1% among African American males. Among females, a greater proportion of right colon adenocarcinomas was observed among African American females (44.9%) compared with white females (38.1%). The percentage of adenocarcinomas in the rectum and rectosigmoid junction was 37.4% in white males, compared with 27.5% among African American males. Similar racial differences were observed for rectal adenocarcinomas among white (31.0%) and African American (24.0%) females. Almost identical proportions were described for primary adenocarcinomas in the left colon in white and African American males and females.

Annual age-adjusted incidence rates for adenocarcinomas of the colon and rectum combined between 1973 and 1994 are shown in Figure 1. Although the incidence rates appeared to increase for all four race/gender groups from 1973–1988, increases were more evident among African Americans. Testing for trends

TABLE 1
Adenocarcinoma of the Colon and Rectum by Subsite, Race, and Gender Detroit Metropolitan Area, 1973–1994 Cases

Site	White males		White females		African American males		African American females	
	n	Rates[a]	n	Rates[a]	n	Rates[a]	n	Rates[a]
Colon	8704	27.9	8652	19.7	2016	28.9	2290	24.3
Right	4282	13.8	4793	10.7	1150	16.6	1355	14.3
Cecum	1825	5.9	2107	4.6	463	6.7	573	6.1
Ascending	1069	3.5	1112	2.5	259	3.7	293	3.1
Hepatic flexure	362	1.2	388	0.9	97	1.4	122	1.3
Transverse	716	2.3	901	2.0	187	2.7	241	2.6
Splenic flexure	310	1.0	285	0.7	144	2.1	126	1.3
Left	4422	14.1	3859	9.0	866	12.4	935	10.0
Descending	802	2.6	694	1.6	208	3.0	250	2.7
Sigmoid	3620	11.5	3165	7.4	658	9.4	685	7.3
Rectosigmoid junction and rectum	5159	16.3	3870	9.1	776	10.9	717	7.7
Rectosigmoid junction	1890	6.0	1481	3.5	238	3.4	289	3.1
Rectum	3269	10.3	2389	5.6	538	7.5	428	4.6
Total colorectum	13863	44.2	12,522	28.8	2792	39.8	3007	32.0

[a] Rates are per 100,000 and are age-adjusted to the 1970 U. S. standard population.

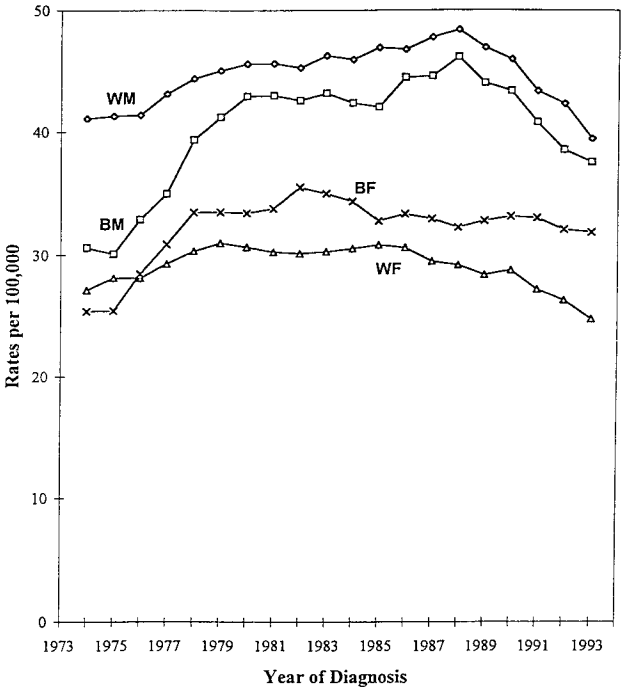

FIGURE 1. Combined annual age-adjusted rates for adenocarcinomas of the colon and rectum between 1973 and 1994.

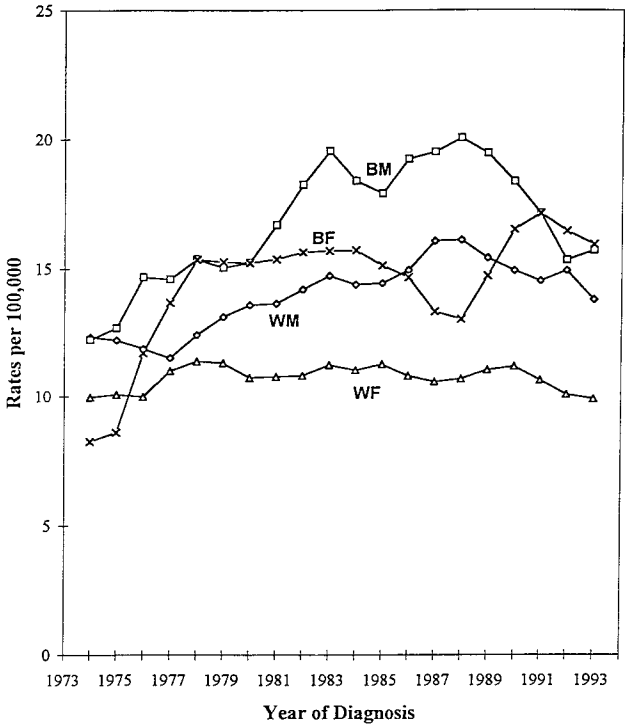

FIGURE 2. Time trends for right colon adenocarcinoma incidence rates.

showed statistically significant increases for white males ($P< 0.001$), African American males ($P< 0.001$), white females ($P= 0.048$), and African American females ($P= 0.012$). These trends showed a reversal (a decrease in incidence rates) from 1989–1994 for white males ($P= 0.008$), African American males ($P= 0.009$), and white females ($P= 0.010$), whereas rates for African American females have remained stable in recent years ($P= 0.444$). Figure 2 shows time trends for right colon adenocarcinoma incidence rates. Although right

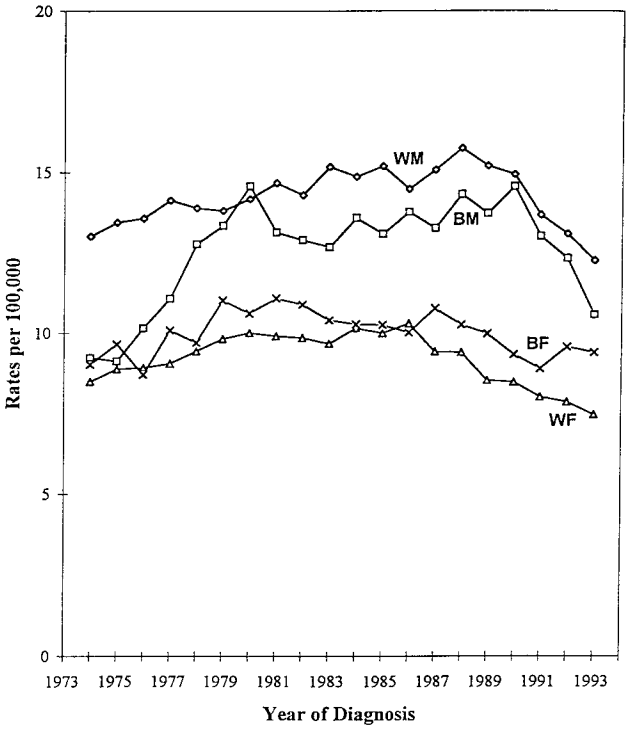

FIGURE 3. Time trends for left colon adenocarcinoma incidence rates.

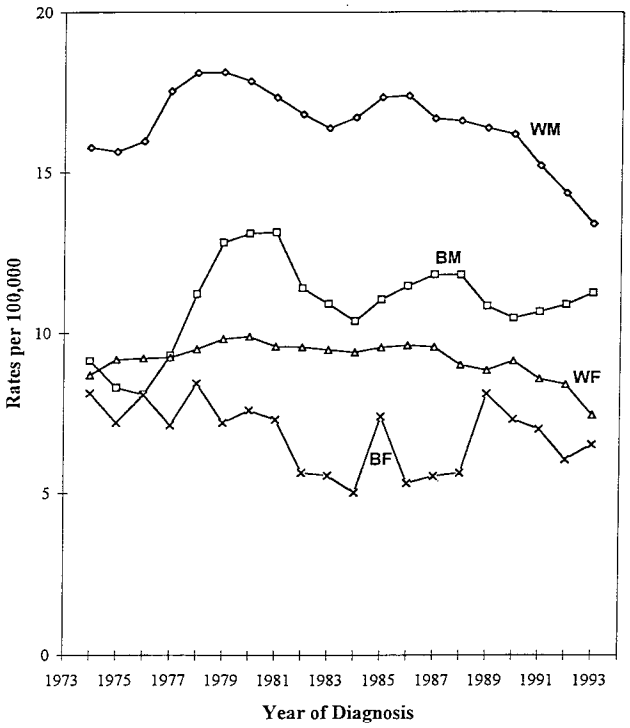

FIGURE 4. Incidence rates for rectal adenocarcinoma among white men compared with African American men and women of both races.

colon adenocarcinoma rates remained relatively stable among both white males and females, these rates increased notably in African American men from 1975 through 1983 and in African American women from 1975 through 1978. Rates for African American women surpassed those for white women in 1976 and remained consistently higher through 1994. Although right colon adenocarcinoma rates were equal for both white and African American men in the early 1970s, the rates in African American men exceeded those in white men during the period 1976–1994. Figure 3 shows time trends for left colon adenocarcinoma incidence rates. These rates remained essentially unchanged among white men and women and African American women through the mid-1980s. Conversely, rates among African American men increased steadily from 1973 through 1980. Rates of left colon adenocarcinoma showed steady declines for African American and white men and women beginning in the mid to late 1980s. Incidence rates of rectal adenocarcinoma reflected a persistent excess among white men compared with African American men and women of both races with no obvious shift in the trends by race and gender (Fig. 4).

The most striking temporal patterns appeared when racial trends for right colon adenocarcinoma were considered by stage at diagnosis (Fig. 5). Rates for distant stage disease for the right colon among African American men began to rise sharply in 1980, and were approximately double those of white men from 1981 through 1988. However, since 1988, distant stage right colon adenocarcinoma among African American men has been decreasing. A less dramatic, more gradual increase was observed among African American women, with this increase peaking in 1980 and reaching a plateau thereafter. Distant stage, right colon adenocarcinoma for white men and women appeared to be stable from 1973–1994.

With the consideration that a significant increase in the incidence of distant stage disease in the right colon might be associated with decreasing survival, 5-year relative survival rates were computed for African American males and compared with that for white males diagnosed from 1973–1989 (Table 2). Males were selected for this analyses because of the observed increase in right colon, late stage disease noted among African American males (Fig. 5). Relative survival at 5 years for male patients with right colon adenocarcinoma was approximately equal among both African Americans and whites diagnosed in 1973–1977 (49–50%) and rose to 61.3% for white males diagnosed in 1984–1989 (P= 0.005), although dropping to 38.5% for African American (P= 0.140). In contrast to that observed for right colon adenocarcinoma among African

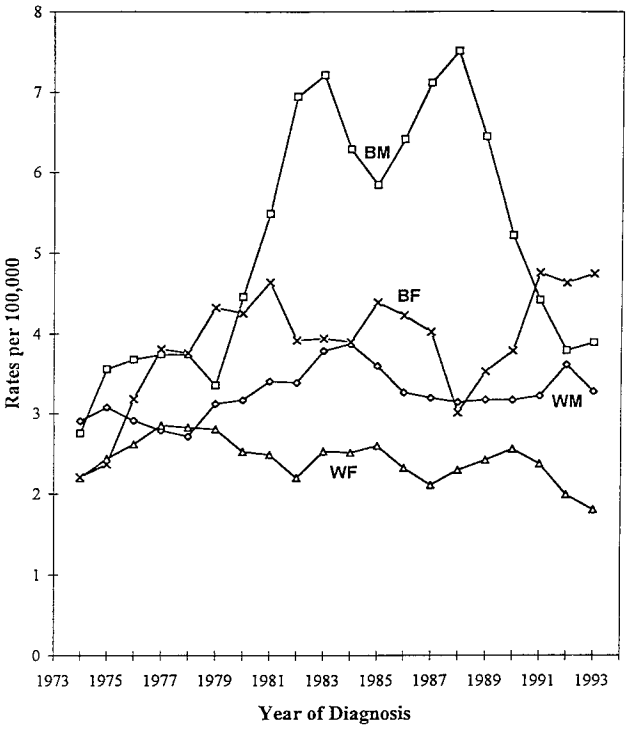

FIGURE 5. Racial trends for right colon adenocarcinoma considered by stage at diagnosis.

American men, the trend for 5-year relative survival percentages improved from 39.8% in 1973–1977 to 58.4% in 1984–1989 for African American men with left colon and rectal adenocarcinoma, although the rates were generally improving, particularly after diagnosis in 1978–1983 ($P= 0.002$), as they were for white males from 1973–1977 (49.3%) to 1984–1989 (64.4%) ($P< 0.001$).

DISCUSSION

Results from this study revealed that there are differences in colorectal adenocarcinoma incidence rates among whites and African Americans. These results are not obvious in U.S. national data, which suggest generally equal and stable rates among African Americans and whites.[20] In the Detroit SEER data, an increase in colorectal adenocarcinoma incidence was observed among African Americans and was primarily accounted for by increasing rates of right colon adenocarcinoma. Research findings indicate an increase in colorectal adenocarcinoma among African Americans, which is accounted for by increases in right colon adenocarcinoma that was previously undocumented. Although the rapid increase observed in rates of right colon adenocarcinoma among African Americans beginning in the mid-1970s and extending to the mid-1980s has subsequently shown a decrease among African American men and level rates among African American women, incidence rates among African Americans continued to exceed those among white men and women.

There are perplexing racial differences in the comparisons of tumors located in the proximal and distal segments of the colon and in the rectum that have been noted in other epidemiologic studies. In the U.S., Devesa et al. studied 120,000 colon cancer cases from 1976 through 1987 using data from the SEER program, and reported higher rates in African Americans compared with whites for cancer of the transverse colon, splenic flexure, and descending colon.[21] They advised further study using colorectal cancer subsite. Johnson et al. showed a greater proportion of proximal tumors among African Americans relative to whites.[22] Similar epidemiologic findings were later published by Thomas et al.[23] and reinforced by the findings of Offerhaus et al. in an "epidemiologic necropsy" study, which described the distribution of adenomatous polyps concentrated in the proximal colon among African Americans.[24] Elixhauser et al. reviewed the clinical records of 188,109 patients from the Hospital Discharge Survey and showed excessive rates per 1000 hospital discharges of colorectal cancer subsites among whites compared with African Americans. African Americans showed higher rates of "unspecified" subsite locations.[25]

What rationale is there for considering the hypothesis that proximal and distal subsites of colorectal adenocarcinoma may reflect distinctive pathogenic mechanisms? Subsites of the colon and rectum originate from the midgut and hind gut, respectively.[26] Fecal transit time throughout the large intestine tends to be slower in the proximal than in the distal colon, allowing for differential contact time for the fecal stream with colonic and rectal mucosa.[27] Animal fat consumption and body size are suggested risk factors for tumor development in the proximal colon.[28,29] A literature review by Bufill summarized genetic and other biologic characteristics that may explain differing susceptibilities to neoplastic transformation between the proximal and distal colon.[30] McMichael and Potter reviewed the biologic significance of bile acid metabolism and cholecystectomy in relation to the pathogenesis of carcinomas in the proximal colon.[31] Offerhaus studied genetic alterations by tumor location and found evidence to suggest that diploid cancers are found more frequently in the right colon, and 17p deletions are more common with left-sided malignancies.[32]

Overall, approximately 35.6% of colorectal adenocarcinomas among residents of the Detroit metropoli-

TABLE 2
Five-Year Relative Survival for Right Colon and Left Colon/Rectum Subsites: Males by Race, 1973–1989

Year of diagnosis	Right colon		Left colon and rectum	
	African Americans	Whites	African Americans	Whites
1973–1977	48.6%	50.0%	39.8%	49.3%
1978–1983	48.6%	57.0%	40.9%	56.9%
1984–1989	38.5%	61.3%	58.4%	64.4%

tan area are located in the right colon. Beginning in the early to mid-1970s, right-sided colon adenocarcinoma rates among African American men and women accelerated and exceeded the rates in whites, and were most evident among African American men with distant stage disease. These findings have major public health implications, especially because the rates of late stage disease for proximal colon adenocarcinomas greatly increased among African Americans beginning approximately in 1980 and were associated with decreased survival. Similarly, a decrease in distant stage right colon adenocarcinoma since 1988 among African American men warrants explanation.

Advances in screening and early detection technologies may account for at least some of the changes in temporal trends for right-sided colon adenocarcinoma incidence in whites and African Americans. However, this is unlikely to be the major explanation because flexible endoscopic screening usually focuses on the distal segment of the large intestine. Flexible sigmoidoscopy is currently recommended as a screening procedure for men and women at normal risk beginning at age 50, but typically does not extend beyond 60 cm with maximal reach to the splenic flexure, potentially encompassing 40–65% of colorectal adenocarcinomas. Although stool occult blood testing is currently recommended as a method of screening, it has limited sensitivity in detecting adenomas and early invasive cancers.[33] Based on surveys conducted by the U.S. Centers for Disease Control and Prevention, utilization of screening methods for colorectal adenocarcinoma by whites exceeded the frequency reported during an interval of 5 years by African Americans.[34]

Coding changes in the SEER program must also be considered when such marked changes in incidence rates are observed. A careful review of historic procedures in the SEER program revealed no coding changes in registry data that would account for the findings identified in this study. In addition, any coding changes would likely affect incidence rates among all four race and gender subgroups. In the current study data, significant rate changes were observed only in African Americans.

Race specific changes in environmental exposures must also be considered. However, the introduction of a putative causal factor would be difficult to identify historically and may be associated with an induction-latency period of 10 to 30 years.[35] Therefore, a significant alteration in environmental exposure or lifestyle practices among African Americans that accounted for the increase in right colon adenocarcinoma incidence during the 1970s and 1980s would have been introduced and sustained in the 1940s, 1950s, or 1960s. The search in population-based studies for such exposures or practices as occupational/environmental exposure, dietary fat, sedentary lifestyle, or use of tobacco and alcohol would provide the basis for future epidemiologic studies.

As with many cancer registry-based studies, the current study has certain limitations. For example, data are limited to those that can be ascertained through existing hospital or pathology records. Therefore, information on risk factors, comorbidity, or other personal data are not available. Also, it is not possible to identify the method of diagnosis or to capture changing patterns of diagnosis or early detection over time. This may be a significant limitation, because differing patterns of colorectal adenocarcinoma detection may, at least in part, explain racial and gender differences in the incidence of this malignancy.

A principal strength is that this is a population-based study, utilizing SEER data, with case ascertainment approaching 100%. An additional strength is the fact that the cancer registry utilized for the current study has been in existence since 1973, with an accumulation of 22 years of colorectal cancer cases documented through 1994. Also, the Detroit SEER program has within its geographic boundaries a high proportion (approximately 24%) of African Americans.

Future directions for research must be considered in light of the findings of the current study. Epidemiologic studies of colorectal adenocarcinoma should focus on anatomic subsites of colorectal disease. Specifically, studies emphasizing differences among races, by subsite of disease, pathology by stage at diagnosis, and other prognostic biomarkers may facilitate the identification of pathogenic mechanisms intrinsic to proximal compared with distal site neoplasia. These

studies should include biologic markers of exposure and susceptibility that are linked to environmental agents. The importance of needed epidemiologic, genetic, and molecular studies that attempt to compare and contrast causal mechanisms for right-sided and left-sided colon adenocarcinoma is underscored by the observation that the incidence of right-sided colorectal adenocarcinoma has risen significantly, particularly among African American men and women.

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