During the last quarter of the 20th century, the incidence of colorectal cancer in the United States declined by 22%. Half of this decline has been attributed to changes in health behaviors, such as red meat consumption and physical activity, and the other half has been ascribed to increased screening with fecal occult blood testing, sigmoidoscopy, and colonoscopy (1). The declining incidence of colorectal cancer accelerated from 1999 to 2008 with average annual reductions of 2%–3% for both men and women (2), representing a shared accomplishment of public health and health care.

These improvements, however, have been disproportionately concentrated among more educated and affluent Americans. In 2000, rates of obesity were higher and rates of colorectal cancer screening were substantially lower among adults with less education, as reported in the National Health Interview Survey (3). As a result, even though the overall incidence of colorectal cancer has declined in recent decades, socioeconomic disparities in colorectal cancer incidence remain substantial (4). Moreover, disparities in colorectal cancer mortality by education and race have actually increased since 1993 and thus represent a growing concern (5).

In this issue of the Journal (6), Doubeni et al. assess the extent to which health behaviors and obesity have contributed to persistent socioeconomic disparities in the risk of colorectal cancer. They studied approximately 500,000 middle-aged and elderly Americans from eight states who were surveyed about their education, height, weight, diet, physical activity, and smoking in 1995 or 1996. Using census tract data, the investigators also categorized these individuals according to a neighborhood deprivation index developed for this cohort (7). The participants were followed through 2006 for new diagnoses of colorectal cancer—which occurred in 1.5% of the cohort—and the anatomic location of these cancers (proximal colon, distal colon, or rectum).

The study by Doubeni et al. (6) had three key findings. First, statistically significant inverse gradients in the overall incidence of colorectal cancer were associated with the educational attainment of the participants and the socioeconomic status of their neighborhoods. Relative to the most advantaged adults and neighborhoods, respectively, incidence rates were 42% higher among the least educated adults and 31% higher among those living in the most disadvantaged neighborhoods. Second, socioeconomic gradients were steeper for cancers of the distal colon and rectum than for proximal colon cancers. Third, health behaviors and body mass index explained 95% of the association between education and the incidence of proximal colon cancer but only 38% of the association of education with distal cancer and 24% with rectal cancer. These contrasting results for proximal and more distal cancers may reflect the impact of an important omitted variable—colorectal cancer screening by socioeconomic status.

Recent studies of colorectal cancer screening have shown it to be more effective in reducing cancer incidence and mortality in the distal colon and rectum than in the proximal colon (8–10). Because adults who are less educated and from less affluent communities are less likely to be screened (3,11), the greater effectiveness of screening for distal colorectal cancer may explain why socioeconomic gradients were much steeper for these anatomic sites than for proximal cancer. The lesser effectiveness of screening for proximal colon cancer may also explain why Doubeni et al. (6) found that diet, physical activity, smoking, and obesity accounted for a much greater proportion of the socioeconomic gradient in the incidence of proximal cancer.

Why might health behaviors and obesity be more important risk factors for proximal colon cancer? Ingestion of charred red meat containing heterocyclic amines and reduced vitamin D intake have been shown to affect the colonic microbiome (12). Higher concentrations of bile acids are found in the proximal colon, where bacteria metabolize molecules that affect proliferation of the colonic epithelium (13). Higher body mass index is associated with an increased incidence of adenomas, particularly in the proximal colon (14). Older black adults, for example, have a greater prevalence of large adenomas in the proximal colon than older white adults (15), which may be related to health behaviors and obesity. Decreased physical activity and obesity are linked with hyperinsulinemia that may promote the formation of colon cancer (16). Insulin stimulates Wnt signaling, the gatekeeper pathway for initiating colonic neoplasia (17).

Through these mechanisms, health behaviors can influence the local environment of the colon and in turn dictate the genetic and morphologic makeup of subsequent cancers. More than 70% of colorectal cancers with microsatellite instability (MSI) occur in the proximal colon (18), because this genetic tumor subtype progressively increases in frequency from the rectum to the cecum (19). Many MSI tumors arise from sessile serrated adenomas: flat, laterally spreading polyps that grow rapidly, often contain foci of cancer, and are difficult to detect at colonoscopy (20,21). MSI tumors are associated with health behaviors that may promote their development, including smoking (22) and dietary consumption of refined carbohydrates and red meat (23).

Changing these health behaviors could reduce the risk of MSI tumors. Chemoprevention through the use of aspirin or nonsteroidal anti-inflammatory drugs may be effective in preventing MSI tumors (24). More practically, screening for colonic neoplasia with flexible sigmoidoscopy (10) or colonoscopy (25) provides the highest sensitivity for detection and greater reduction in mortality relative to other
approaches including DNA stool tests and fecal immunohistochemical techniques (26). Colonoscopy is the only test that visualizes the proximal colon where most MSI tumors occur, but its effect on reducing mortality from proximal cancer is lower than predicted (8,9), perhaps in part because sessile serrated polyps are difficult to detect.

The study by Doubeni et al. (6) demonstrates the intricate interplay of socioeconomic and behavioral factors affecting the risk of colorectal cancer for individuals and communities. This study also underscores the need for more effective public health strategies to improve nutrition and physical activity in the United States and thereby curb the rising tide of obesity, particularly for those with less education and in disadvantaged communities. Using a multilevel framework (27,28), these strategies can be informed by growing insights into the biological mechanisms of colorectal cancer and coupled with clinical and policy interventions to address socioeconomic and racial disparities in health behaviors and colorectal cancer screening. Such efforts can help to ensure that the steadily declining incidence of colorectal cancer since 1975 accelerates more rapidly over the next decade (1,29).

References


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