

CORRESPONDENCE

Diet and Cancer Prevention

Recent articles and commentaries in the Journal cast doubt on the dietary prevention of cancer (1-4). Is this pessimism really justified?

Migration studies of populations moving from low-incidence to high-incidence locales (such as Japanese to Hawaii) suggested that dietary factors existed that altered colorectal cancer risk. The rapid increase in the incidence of colorectal cancer incidence throughout the first 13 years of the Surveillance, Epidemiology, and End Results (SEER) Program¹ (1973 through 1986; a National Center for Health Statistics program for monitoring cancer incidence and outcomes in the United States beginning in 1973) added urgency to define these dietary factors. However, SEER reported that the rapidly rising incidence of colorectal cancer in the United States suddenly reversed in 1986, and since then the incidence has declined at a rate greater than 1% per year. More than a 25% drop in the incidence of distal colorectal cancer occurred in white men and women from 1986 through 1994 (Fig. 1). Prevention of colorectal cancer is clearly occurring here in the United States (5).

This reversal in trend provided a unique opportunity to determine what happened in the United States to cause this change in a time trend study of all suspected risk factors for colorectal cancer. The focus was on data representative of the whole U.S. population, beginning 15 years before the change in cancer trend, in 1971, both because there is a considerable lag time from exposure to tumor formation and diagnosis and because it was at that time that most nationally representative data became available through the National Health and Nutrition Examination Surveys. Unlike the studies cited in the "News" section of the Journal (2), the dietary factor most supportive of the decline in colorectal cancer incidence in this time trend study was fiber. Other factors clearly played a role, the most important being

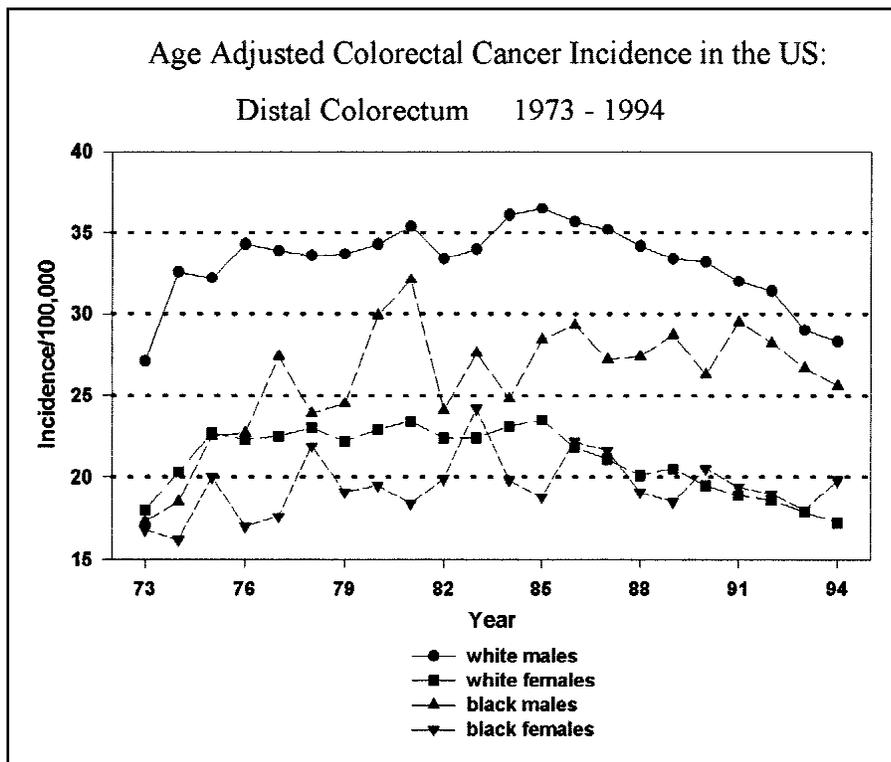


Fig. 1. Distal colorectal cancer incidence from 1973 through 1994 by race and sex (Surveillance, Epidemiology, and End Results Program). Distal cancer is defined as adenocarcinoma located from the sigmoid colon to the distal rectum, excluding the anal canal.

the increasing use of colonoscopic polypectomy (5).

In judging therapeutic efficacy, the randomized, controlled clinical trial is thought to be the method least subject to bias in evidence gathering. By analogy, this design has been used in cancer prevention studies, but perhaps with less efficacy, which may be due to recruitment of atypical subject populations or substitution of surrogate endpoints for cancer, as in the polyp prevention trials cited (2,3). However, in spite of the inability of the trials and analytic studies described in the Journal (1-4) to provide a generally accepted template for colorectal cancer prevention, prevention, as stated above, is occurring.

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¹Editor's note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local non-profit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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RESPONSE

We thank Drs. Nelson, Persky, and Turyk for emphasizing that colorectal cancer is largely preventable. Indeed, we agree that much progress has been made in recent years to identify modifiable factors that can prevent colon cancer: increasing physical activity, avoiding obesity, using folic acid-containing multivitamin supplements, not smoking, reducing alcohol use, and reducing red meat consumption. We raised these issues in our recent article in the *Journal* (1) and have estimated that more than 70% of colon cancer cases might be preventable by modification of the diet and lifestyle risk factors (2).

Studies with migrant populations indicate that environmental factors play a role in colorectal carcinogenesis, but factors other than diet—listed above—may also contribute. Recent data suggest that some aspects of diet may not be as important as previously assumed. While consumption of red meat has frequently emerged across studies as a risk factor for colorectal cancer and folic acid seems to reduce the risk, dietary fiber (3,4) and consumption of fruit and vegetables (1,5,6) seem less influential. This lack of an association is fairly consistent among more recent prospective cohort studies, in which problems of recall and selection bias are avoided. Also, large cohort studies have accounted for numerous potentially confounding variables. Nelson et al. mention a trend of increasing fiber consumption captured by the National Health and Nutrition Examination Survey that coincides in time with a decrease in colorectal cancer incidence. However, many variables have changed over time so that time trends may not reflect causal relations. For example, in the mid-1970s, the U.S. Food and Drug Administration first allowed the recommended dietary allowance level of folic acid to be added to multiple vitamins; in contrast to fiber, a beneficial effect of folic acid has been supported in epidemiologic studies [e.g., (7)].

We agree with Nelson et al. that screening and polypectomy can play a role in colorectal cancer prevention, but it is even more important to act on other modifiable risk factors that can

prevent the large majority of cases and that will have many other health benefits as well.

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RESPONSE

Nelson et al. argue that, even though some recent observational (1) and experimental (2) epidemiologic studies have yielded null results, pessimism about diet and cancer is unwarranted because colorectal cancer incidence has been declining in the United States. Ecologic (aggregate) studies, including those of time trends (3), international correlations, and migration, do indeed suggest a causal relationship between diet and colorectal cancer risk. These studies are far from conclusive, however, because of the possibility of confounding: Many potential etiologic factors (besides diet) change over time, from country to country, and with migration.

It was at least partially in recognition of the promising ecologic data on diet and colorectal cancer risk that investigators around the world initiated individual-level observational and experimental epidemiologic studies. Some of these studies are consistent with the ecologic data on fiber/fruits and vegetables and colorectal cancer; some, including some recent ones, are not.

Animal experiments clearly show that diet modulates colorectal tumorigenesis, but it has been a challenge to move beyond the ecologic data and demonstrate comparable causal relations in humans. Because we are likely dealing with modest relative risks for most foods and nutrients, inconsistencies in the epidemiologic evidence—for fiber and fruits/vegetables *vis-a-vis* colorectal cancer, for example—are not surprising. Moreover, we need to acknowledge potential limitations of our observational and experimental epidemiology. Perhaps dietary assessment instruments do not measure the intake of key foods and nutrients with sufficient accuracy to discern important but modest alterations in cancer risk. Maybe traditionally assessed “fiber” and “fruits and vegetables” only partially capture the central functional role of nutritional exposures such as chronic insulin stimulation (4) and methyl group availability (5). Perhaps null adenoma recurrence trials followed people for too short a time or evaluated the wrong part of the neoplastic process.

The recent null studies can be seen as a source of pessimism, but they are better taken as indicators of the com-

plexity of the diet and cancer field and the difficulties inherent in identifying precisely what dietary factors, singly or in combination, modulate carcinogenesis in people. Perhaps the most constructive stance is to regard the recent studies as incentives to identify and address the limitations in our individual-level epidemiologic research.

The actual cause of the declining cancer rates in the United States has been a source of some controversy (6,7). In addition to diet, colonoscopic polypectomy has been cited as a potential determinant of the falling rate. In fact, Nelson et al., in their ecologic analysis (3), cite increased use of colonoscopic polypectomy as the one factor "most consistent with the observed pattern of [colorectal cancer incidence] change." It is particularly noteworthy—if ironic—that in the past few years colorectal cancer incidence in the United States

has ceased its decline and is actually increasing. One hopes that this recent upward "blip" reflects increased screening rather than some deleterious dietary practice.

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