The article by Chu et al. (1) inadequately describes the changing trends in incidence and mortality due to colon cancer and the possible implications. Recently reported data (2) document the substantial decline in colon cancer mortality in the southern European countries of Portugal, Greece, Italy, and Spain from 1975 to 1988, similar to the trends in the United States (with a greater decrease in mortality in women than men). The decline is similar in younger and older age groups. Thus, any factor that effectively reduced mortality is not limited to the United States. Increased use of early detection methods as a result of Ronald Reagan’s colon cancer in 1985 is very unlikely to have affected a similar decline in colon cancer mortality in these European countries between 1975-1988.

Hemoccult screening used in the Minnesota trial (3) resulted in a 13-year reduction in colon cancer mortality of 33%, but only in the group that received intensive follow-up with annual evaluations and a high incidence of colonoscop y. In individuals followed bi-annually, which is a good estimate of overall behavior in the community, there was no evidence of a reduction in mortality as compared with the control group. It is extremely unlikely that a very large segment of the U.S. population for the past 15 to 20 years has been having annual hemoccult testing and careful follow-up with colonoscopy, as would be required to model the Minnesota experience. In the Kaiser case-control hemoccult study (4), for example, approximately 20% of control subjects had a fecal occult blood test within 1 year. Even if testing reduced mortality by 25%, the overall benefit would be only about 5% on colon cancer mortality. In the Kaiser case-control sigmoidoscopy study (5), 25% of control subjects versus 8.8% of the patients with fatal colon cancers had a rigid sigmoidoscopy within 10 years of diagnosis. Even if this 16% difference in rigid sigmoidoscopy screening was associated with a 75% reduction in mortality, it would have resulted in a 12% reduction in colon cancer mortality over 10 years as compared with the 30% reported decline in colon cancer death rates. It is unlikely that screening programs that were in place in the 1970s in other countries account for the decline in mortality. This does not mean that screening, especially flexible sigmoidoscopy and colonoscopy, are not effective, but rather that the overall use of these procedures since the 1970s, when the decline in colorectal cancer mortality began, is an unlikely explanation for the observed decline.

It is also extremely unlikely that cigarette smoking contributes to either the increase or decrease in colon cancer. We, for example, have followed 360,000 Multiple Risk Factor Intervention Trial-screened individuals over approximately a 15-year follow-up. We identified 989 colon cancer deaths among nonsmokers and 462 deaths among cigarette smokers from the screening population (Neaton J: personal communication). There was no relationship between cigarette smoking and colon cancer in this analysis.

There has been a substantial increase in incidence and mortality due to colon cancer in Japan and China and in migrants from low-risk areas to the United States (2,6). This change has occurred very rapidly, which suggests that an environmental agent or agents that cause a rapid increase in the incidence of disease could also be associated with a rapid decrease when the risk factor, i.e., the environmental agent, is modified. Clearly, the most likely candidates are dietary constituents. There is recent evidence in the United States of a substantial decline in saturated fat and cholesterol intake and a very marked subsequent decline in blood cholesterol. It is possible that changes in other dietary factors such as fiber or an unknown micronutrient could also be contributory.

The changes in blood cholesterol level have been greater in women than in men, especially among older women, suggesting a possibility that dietary change with regard to saturated fat and cholesterol may explain the greater decline in colorectal cancer mortality among women. There has been little evidence, except in recent years, for any changes in calcium intake or physical activity. Obesity, especially among women, is increasing (7), so it is unlikely that these factors are related to the decline in colon cancer. Increased use or availability of prostaglandin inhibitors might have contributed to the decline in U.S. incidence and mortality, but it would not explain the international data.

The most rational explanation for the decline in colon cancer is a multifactorial one. First, the decline in mortality is almost certainly in part related to improved treatment of colon cancer and especially mortality associated with complications of surgical therapy. Second, there have been changes in the diet of the U.S. population, which have probably contributed to a decrease in the incidence of colon cancer and perhaps to a reduction in the rate of progression of colon cancer, i.e., a decrease in more advanced disease. Third, there has probably been a modest effect of screening for colon cancer, which probably has had little long-term effect but may have an effect in the future.

The proper interpretation of the trends in colon cancer has major implications for cancer prevention. The opportunity to test important dietary hypotheses is critical. At the same time, one should carefully evaluate the trend data within the United States and across communities and especially the international variations, in order to determine the specific dietary or other factors that are involved.

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We concluded that etiologic factors were likely to provide explanations for the divergence of male and female colorectal cancer trends that occurred around 1950 in the United States and speculated that cigarette smoking patterns might explain the divergent trends. The Multiple Risk Factor Intervention Trial results will contribute to the ongoing evaluation of the possible association between smoking and colorectal cancer. In this regard, a 26-year follow-up study of U.S. veterans indicates a significant association between cigarette smoking and colorectal cancer. Differences in the length of follow-up and type of control subjects appear to explain much of the inconsistency of previous studies examining this association (2). If cigarette smoking does not increase colorectal cancer risk, then other etiologic agents must be sought with sex differences in exposure large enough to produce the divergent colorectal cancer trends from 1950 through 1984. Trends in dietary fat intake from 1940 through 1985 by sex do not support a role for fat in either the increasing colorectal cancer incidence rates in males or the divergent trends by sex. Fat intake in grams per day or as a percentage of total energy intake decreased in both males and females from 1950 through 1985, with slightly greater decreases in males (3). This was true also for saturated fat intake as a percentage of energy intake (3). Comparison of cholesterol intake and mean serum cholesterol levels from the second National Health and Nutrition Examination Survey (NHANES), 1976-1980, with those from the first NHANES, 1971-1974, also show slightly greater decreases in males than in females (4,5), again inconsistent with the divergent colorectal cancer trends.

The cited International Agency for Research on Cancer (IARC) results (i.e., age-period-cohort models fit to 5-year cancer rates) do indicate abrupt mortality decreases in both sexes in some southern European countries (6). The mechanism for these mortality decreases in southern Europe warrants further investigation, but it would appear that the mechanism differs from that operating in the United States. The decreases in mortality in Portugal, Spain, Greece, and Italy preceded those in the United States by 5 to 10 years and were not accompanied by corresponding marked decreases in colorectal cancer incidence (although only limited incidence data from Italy and Spain were available) (6). Moreover, it would appear to be incorrect to characterize these decreases as extending from 1975 to 1988, as in most instances the mortality curves indicate only a transient drop in the 1980-1984 rate compared with the 1975-1979 rate. Examination of the IARC analyses indicates that colorectal cancer mortality tended to rise in these countries in the last calendar period representing the period from 1985 to 1988. Indeed, the colorectal cancer death rates for subsequent years (Table 1) suggest rates increased in all of these countries for both males and females in the late 1980s (7).

The downturn in U.S. rates after 1985 was manifest primarily as a change in the calendar period risk trend for both males and females (1), and such changes usually reflect mechanisms such as coding revisions or medical improvements, which affect all ages simultaneously (and approximately equally). Recent surveys provide no evidence of an abrupt change in dietary fat intake in the 1980s (5). Furthermore, on the basis of published trends of fat intake (3,5), one would expect declines in colorectal cancer to begin before 1985 if the mechanism affected the rate of progression of cancer.

We do not find the estimates by Kuller and Schoen of the potential impact of early detection methods on colorectal cancer mortality (i.e., a maximum 5% reduction per year for fecal occult blood testing and a 12% reduc-

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**Table 1.** Colorectal cancer death rates per 100 000 (8)

<table>
<thead>
<tr>
<th>Country</th>
<th>Sex</th>
<th>1984 rate*</th>
<th>1990 rate</th>
<th>Change, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greece</td>
<td>Male</td>
<td>9.1</td>
<td>12.5</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>9.8</td>
<td>12.1</td>
<td>37</td>
</tr>
<tr>
<td>Italy</td>
<td>Male</td>
<td>22.6</td>
<td>25.8</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>20.1</td>
<td>23.2</td>
<td>15</td>
</tr>
<tr>
<td>Portugal</td>
<td>Male</td>
<td>18.2</td>
<td>25.3</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>16.3</td>
<td>21.2</td>
<td>30</td>
</tr>
<tr>
<td>Spain</td>
<td>Male</td>
<td>18.3</td>
<td>22.0</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>17.3</td>
<td>19.0</td>
<td>14</td>
</tr>
</tbody>
</table>

*The rates for Spain are for 1987.*

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**References**


**Note**

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**Response**

Our goals were the following: 1) to investigate the divergence of U.S. male and female colorectal cancer incidence and mortality rate trends from 1950 through 1984 and 2) to examine the marked, simultaneous improvement in mortality and incidence rate trends for both males and females in the United States since 1985 (1). Kuller and Schoen appear to believe that we should not find the estimates by Kuller and Schoen of the potential impact of early detection methods on colorectal cancer mortality (i.e., a maximum 5% reduction per year for fecal occult blood testing and a 12% reduc-