Re: Colorectal Cancer Screening: Sifting Through the Evidence

In his editorial, Dr. Levin (1) states that “the report by Mandel et al. substantiates the important and clear finding that screening of men and women more than 50 years of age for colorectal cancer can save lives.” However, the article by Mandel et al. (2) clearly demonstrates that overall mortality was unaffected by screening. The cumulative all-cause mortality in the annually screened group was 342 per 1000 compared with 343 per 1000 in the control group. Dr. Levin confuses a reduction in colorectal cancer mortality with saving lives. This distinction is important and must be kept in mind when considering the trade-offs of screening, whether from a public health or an individual perspective.

In counseling patients about the value of colorectal cancer screening, it would be inappropriate to imply that it can save their lives. It must be noted that the very small reduction in colorectal cancer mortality in this study (4.6 fewer deaths per thousand patients over the course of 18 years for the annually screened group; 2.9 for the biennially screened group) was balanced by an equivalent increase in mortality due to other causes. It may certainly be that a reduction in colorectal cancer mortality would be a desirable end in itself to some patients, but this desirability cannot be assumed, and it is certainly not the same as saving lives.

There are several possible explanations for the increase in mortality due to causes other than colorectal cancer in the screened groups. First, colorectal cancer occurs mostly in older individuals. Competing mortality, therefore, becomes an important factor. It may be that patients who are spared a death due to colorectal cancer are merely given an opportunity to develop another deadly disease in its place. Second, many patients with advanced cancer die without evidence for an immediate cause, such as infection, bleeding, or organ failure. Such deaths are often, not inappropriately, labeled as being due to “carcinomatosis.” However, it is certainly possible that some, or many, of these patients actually died of another disease. Had these patients not been diagnosed with cancer, or had their cancer been previously treated and cured, their survival might have been identical, but their causes of death listed differently. This bias is unavoidable in any study that uses cause-specific mortality as an end point, regardless of the care taken in determining the cause of death. Third, I will dismiss as improbable the possibility that the screening of normal individuals simply scared some of them to death.

Screening for colorectal cancer may indeed prove to be beneficial to the public health. However, all screening programs for the general population are hampered by the low proportion of individuals destined to die of the disease in question, in this case, one in 81 (1.2%) (3). It is, therefore, important to maintain perspective and to avoid exaggerating the value of screening.

Carl D. Atkins

REFERENCES


NOTE

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RESPONSE

Dr. Atkins is correct in observing that there is no statistically significant difference in all-cause mortality in the screening and control groups of the Minnesota trial. However, all-cause mortality was not the end point of interest in this trial, and screening trials cannot reasonably address such an end point. The variability present in all-cause mortality is so great that it dominates even substantial differences in disease-specific mortality. Evidence of this is that the 95% confidence intervals for all-cause mortality in Table 1 of Mandel et al. (1) are far too wide to be able to detect a difference on the order of 4.6 deaths per 1000. Detecting such a difference in all-cause mortality with 90% power would require a trial with at least 500,000 participants.

There may well be screening interventions that cause death, either directly or indirectly, but this possibility has not been demonstrated for annual or biennial fecal occult blood testing. Therefore, it is appropriate to view such screening as saving lives, and it is reasonable to estimate this savings at 4.6 per 1000 screened.

Bernard Levin

REFERENCE