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Colorectal Cancer on the Decline

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less likely to have a response to the drug or survive to hospital discharge. We agree that earlier use of antiarrhythmic drugs provides a greater potential for clinical benefit that may be lost if the drugs are administered late. For example, in prespecified subgroup analyses in our trial, we observed no effect (neither benefit nor harm) from active drug among 839 patients with unwitnessed out-of-hospital cardiac arrest; these patients typically have a more prolonged duration between arrest and treatment than do patients with witnessed out-of-hospital arrest. Conversely, among 1934 patients with out-of-hospital cardiac arrest that was witnessed by a bystander, the rate of survival to hospital discharge was significantly increased by an absolute margin of 5 percentage points with active drug as compared with placebo ($P \leq 0.04$). Furthermore, among 154 patients in whom out-of-hospital cardiac arrest was witnessed by EMS and cardiopulmonary resuscitation, shock, and the study drug were administered soon after the arrest, the absolute increase in survival to hospital discharge with amiodarone as compared with placebo was 21.9 percentage points ($P<0.01$). These findings suggest a pronounced drug effect in patients who are in an earlier, more responsive stage of cardiac arrest. The overall results of the trial are arguably best interpreted in the context of this group of patients.[4]

Much remains to be learned about the effectiveness of pharmacologic therapies in patients with out-of-hospital cardiac arrest. We think that our trial has advanced the knowledge and understanding of these therapies and has provided reasons to be optimistic about their use in shock-refractory cardiac arrest.

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Since publication of their article, the authors report no further potential conflict of interest.

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Colorectal Cancer on the Decline

TO THE EDITOR: In their Perspective article, Welch and Robertson (April 28 issue)[1] provide evidence from the Surveillance, Epidemiology, and End Results Program that the population 50 years of age or older has had a steady decline in colorectal-cancer incidence that is unlikely to be explained merely by screening. Surprisingly, according to the same data source, during the period when incidence rates were declining in this population, they have steadily increased in the population younger than 50 years of age.[2] The incidence of colorectal cancer among younger people is also increasing in at least one other country.[3] Obesity or other lifestyle factors might be an explanation for the age-specific dissimilarity in time trends, especially if these factors have a greater effect on younger people than on older people.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Welch and Robertson suggest that screening cannot explain the entire decline in colorectal-cancer incidence and mortality (i.e., overall decreases of 40% and 50%, respectively, among adults in the United States) in the period from 1975 to 2012 and that other factors (e.g., risk factors such as diet, lifestyle, and drugs) must be involved. Surprisingly, the authors did not cite the respective proportions of the decline that were attributable to screening as opposed to those other factors, as analyzed in the "Annual Report to the Nation on the Status of Cancer, 1975–2006," which features colorectal-cancer trends and the effect of risk factors, screening, and treatment.[1] Using the well-validated Microsimulation Screening Analysis (MISCAN)–Colon model,[2] the authors of that report concluded that 53% of the overall observed decline in colorectal-cancer–related mortality could be explained by screening, as compared with 35% that could be explained by changes in risk factors and 12% by treatment.[1] The same MISCAN-Colon model allowed analysts to suggest that differences in screening accounted for 42% and 19% of the observed disparities in colorectal-cancer incidence and mortality, respectively, between blacks and whites in the United States.[3]

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Although we are aware of the data cited by Lowenfels et al., we believe they must be kept in proper context. The incidence of colorectal cancer is rising in the population younger than 50 years of age, but the absolute increase is small: approximately 2 cases per 100,000 persons. The corresponding decrease in the population 50 years of age or older, by contrast, is approximately 100 cases per 100,000 persons.[1] Despite these opposing trends, the incidence of colon cancer remains 15 times as high in the older group as in the younger group. Given the low absolute risk and stable mortality among young people, as well as the fact that their disease may have distinct biologic factors[2] that make it less amenable to early detection, we believe it would be a mistake to extend screening on the basis of these trends.

We are also aware of the microsimulation modeling cited by Matuchansky. We worry, as others do,[3] that although the output of statistical models have the appeal of quantitative precision, their precision may be more apparent than real. Modeling is only as good as its data inputs and often rests on unverifiable assumptions regarding factors such as the rates at which polyps transition to cancer and at which cancers transition from early to later stages.

The suggestion that 53% of the decline is due to screening overstates the precision of the estimate. We believe that it also overstates the magnitude of the likely effect of screening. As the figure in our article shows, since 1975, colorectal-cancer–related mortality has fallen from approximately 100 cases per 100,000 persons to 45 cases per 100,000, and 80% of that decline occurred before 2005 — the first year that 50% of the population was screened. How can more than half the decline in mortality be attributed to screening when more than half the decline occurred before even half the population was exposed to screening?

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Since publication of their article, the authors report no further potential conflict of interest.

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