Response

We thank Drs Wiebelt and Hakulinen for their thoughtful comments, which, after all, reflect shades of meaning rather than differences in opinion. The views expressed by them refer to biologic interpretation as well as analytic strategies.

With reference to the first of these two aspects, Drs Wiebelt and Hakulinen report that in the data from the Saarland study, women with cancer had an average of 92% of the excess risk that men had of dying from cancer. This difference by gender is surprisingly close to our reported value of 88% after adjustment for the following three major cancer sites: lung, stomach, and cervix (1). We consider these differences, 8% and 12%, respectively, big enough to be of definite biological interest.

Wiebelt and Hakulinen consider gender a surrogate "for other uncontrolled or unmeasured prognostic factors" and show that the female survival advantage in malignant melanoma disappears once histology and tumor thickness are factored into the analysis. It is, however, far from clear whether such adjustment entails improved validity due to control of confounding. Tumor thickness, as well as other prognostic factors, may be looked on rather as an intervening variable in the association between gender and survival, as recently discussed (2). In other words, if females with cancer have a better prognosis than males and this is due to differences in tumor biology and tumor-host relationship, then it would not be surprising to find a more favorable distribution among women with various prognostic factors that measure biologic features of the tumor, eg, lymph-node and distant metastases, tumor differentiation, and thickness.

The other major issue raised by Wiebelt and Hakulinen refers to the need to adjust for site or type of cancer rather than gender when temporal trends in survival are studied. However, this need depends entirely on the specific hypothesis under study. Adjustment is clearly necessary to answer the following question: "Has cancer prognosis improved after proper account for changes in distribution by site and type?" It would, however, be inappropriate if the focus is on trends in overall risk of dying in patients assigned a cancer diagnosis. The quantitative impact of this distinction is likely to differ between studies and populations, and it was seemingly minor in Sweden (1). A multivariate model with follow-up year, age at diagnosis, and sex revealed a 32% decrease in the relative risk of dying from cancer, during the first 5 years of follow-up, from the period 1960 through 1964 to 1980 through 1984. Additional adjustment for cancers of the lung, stomach, and uterine cervix changed this estimate only marginally to 29% (1).

Our discussion with Drs Wiebelt and Hakulinen illustrates, after all, the limitations of epidemiologic research in explaining observed phenomena. But also the possibilities to improve our understanding by refining the research hypothesis and, perhaps, by closer collaboration with tumor biologists.

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UK Breast Screening Program

Sir Patrick Forrest alludes to the vital importance of uptake rates in any breast screening program when he observes that “screening can be effective in reducing total mortality from breast cancer within a nation only if it is applied to a greater number of women than a self-selected 30% of the population” (1). Indeed, to maximize benefit, a high proportion of the target population must accept repeated screenings.

Furthermore, although the former Secretary of State emphasized that the United Kingdom National Health Service (NHS) Breast Screening Program not only would provide facilities for screening mammography but also would provide for all necessary backup including treatment facilities, funding for the latter has not been forthcoming. Special allocation of funds has been made only to introduce the screening program (2). As the clinical workload has increased during the first “prevalence” round of screening, increased resources for treatment have not been available. This may have great implications for the success of the national program.

To consider only one aspect of this lack of increased funding, Forrest (3) recently reported that fear of outcome is a factor in non-attendance at screening; mastectomy is seen by some women to be a deterrent for attendance, and the greater use of conservation therapy for screen-detected cancers can be viewed as a positive benefit.

However, in the Royal College of Radiologist’s Fractionation Survey (4) of Consultant Radiotherapists practicing in the United Kingdom who hold a Fellowship from the College, 43% of respondents to a questionnaire said they normally used 2.5 Gy per fraction or more for radiotherapy following lumpectomy. When asked about factors influencing the choice of fractionation schedule, 29% of respondents cited logistical constraints.

Within existing services, then, the greater number of patients to be treated with limited surgery followed by irradiation will increase pressure on machine time, further compromising
fractionation schedules, and may lead to poor cosmetic results. While not affecting survival on an individual basis, the positive benefit of conservation therapy may be lost. If this situation is reflected in lower uptake rates for screening, it would most certainly have implications in achieving a reduction in population-based mortality.

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References

Response
The implications in Dr Sizer's letter that radiotherapists in the United Kingdom may be supplying less than ideal treatment because of logistic constraints is not one on which I am qualified to comment. However, it is perhaps relevant that in the survey which he quotes, no less than 51 different dose schedules of radiotherapy (varying from 133 to 583 cGy per fraction) were used. Of the 170 participating consultant radiotherapists, only 10% considered their treatment to be less than optimal (1).

This is not to say that radiotherapy centers are not finding it difficult to meet the demands of conservation therapy for breast cancer. This problem of increasing workload is affecting most sectors of the NHS, particularly at a time of reorganization and the introduction of a new system of budgetary control. This increased workload is leading to increased waiting times for those requiring treatment for nonurgent conditions, but this situation does not imply that essential services are denied those in need.

It is relevant that a recent review by the Department of Health's Advisory Committee on Breast Screening, while consolidating the evidence on which the decision to introduce the NHS Breast Screening Program was based, recognizes the difficulties that some screening units face in meeting the costs of investigating and treating mammographic abnormalities. However, this review concludes that, provided consultant surgeon time was available, as was initially recommended (2), sufficient resources are being allocated for treating cases detected by screening (3). The situation is being closely monitored and will be further analyzed.

Although the introduction of population screening does cause an increase in the number of reported cancers suitable for treatment with breast conservation (4), the total increase in the number of cases is temporary. Reports from Sweden and the Netherlands have confirmed that while initially the number of cancer cases requiring treatment rises, this number returns to normal levels after a few years, indicating that the introduction of screening does not lead to the overtreatment of cancers that would not otherwise have become apparent (5,6). Further, it is likely that an increasing number of cases of noninvasive and small invasive cancer will be treated by wide, local excision alone, ie, without immediate radiotherapy, as indeed has been reported from Sweden and now is one option in the UK trial of the management of ductal carcinoma in situ (7-9).

As stressed by Dr Sizer, factors that reduce attendance for mammographic screening must be avoided. It is encouraging that recent surveys of the British program indicate that a 70% uptake is being maintained (3).

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References