result can be reproduced in the future is unclear, but as treatment improves and more importantly, as we gain the ability to discriminate risk of progression from biomarkers linked to targeted therapies, the picture can change.

So, what can we do with this information? One approach would be to discourage patients from participating in the screening regimen (15). However, in the absence of a better alternative and with inertia behind any national program, screening mammography is likely to continue. Recognizing that the cost and morbidity of this imperfect solution to breast cancer have raised the stakes when measuring the benefits of early screening has proven elusive, we have few options, and not all of them are practical. We could target screening to subpopulations according to risk, perhaps with the help of new biomarkers that improve specificity. Better diagnostic tools used to evaluate breast cancer candidates found on screening would compensate for the limitations of population-based imaging. Eventually, through better knowledge of breast cancer etiology and biology, we can address the concerns regarding overdiagnosis and overtreatment and see them minimized. As our tools improve, we can begin to fully realize the promise of breast cancer screening to arrest this dread disease at its earliest stage with the least morbidity and cost.

Nobody said it would be easy.

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Is the Breast Cancer Mortality Decrease in Sweden Due to Screening or Treatment? Not the Right Question

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Autier et al. (1) attempt, in this issue of the Journal, to study the time trends of breast cancer mortality by county in Sweden from 1960 to 2009 by dividing the 21 counties into four groups depending on the year in which organized breast cancer screening started. The authors find a continuous decrease in breast cancer mortality during the period studied but claim that this decrease was not related to the introduction of screening. Their conclusion is based on a comparison between observed mortality trends and expected trends that they modeled assuming different levels of screening effectiveness. No effect on mortality was appreciated in two groups of Swedish counties, whereas the mortality trends in two other groups of Swedish counties declined by 5% and 8% more steeply than the mortality trends observed before screening started.

The analysis of time trends of breast cancer mortality rates following the introduction of screening is definitely not the most reliable method to assess its effectiveness. There are several limitations that produce a diluting effect, such as the inclusion of deaths from cancers diagnosed before screening started or before women reached screening age, the phased build-up of screening, or the presence of opportunistic screening that took place before organized screening started. Furthermore, it is well known that ecological studies suffer from important shortcomings (2); it is extremely difficult, if not impossible, to know and properly account for the multiple, diverse, and intertwined reasons for the observed trends, especially if time trends are compared across countries or regions. It is therefore paradoxical that descriptive analyses of this
kind are used to challenge the results of randomized trials (3) or to confute the results of incidence-based mortality studies (4) that have used individual data and have been conceived for the purpose of overcoming some of these limitations.

The article by Autier et al. (1) reports a relatively long follow-up period, but it presents all of the general limitations that we have mentioned regarding studies of its kind, with dilution of the screening effect by the inclusion of all women 40 years of age or older being particularly severe. In addition, the classification of counties by the time when screening started has partially overlapping categories, and the modeling of the screening effect seems rather simplified compared with the standard in this field (5). Therefore, the authors’ conclusion that the important “downward trends [37% decrease in 38 years] in breast cancer mortality in Sweden have evolved practically as if screening had never existed” seems to be difficult to justify and implausible. It is also partially unsupported by the data; two of the four groups of counties do show a mortality decrease that, according to the stated criteria, could be linked to screening.

In the presence of stable or increasing incidence trends, better treatment is the obvious candidate of this success story. Its synergistic effect with screening has been modeled under different assumptions, taking into account that screening can reduce the rate of death from breast cancer only when followed by treatment (5). Not only is mammography screening likely to have detected breast cancers at earlier stages, allowing the adoption of less harmful and more effective treatments, but also the presence of an organized screening program may have promoted the provision of more effective care by monitoring the treatment quality of screen-detected cancers and by favoring the creation of multidisciplinary units of breast cancer specialists (6). Efforts to disentangle the effects of organized screening, early diagnosis, and treatment based on descriptive population data are therefore unlikely to be a reliable exercise, also because screening itself is intrinsically part of clinical practice (7).

In our opinion, it is time to move beyond an apparently never-ending debate (8–10) about the extent to which screening for breast cancer in the 1970s to 1990s has reduced mortality from breast cancer—as if it was isolated from the rest of health care. The current scenario is completely different from the past: asymptomatic patients with screen-detected breast cancers represent a large proportion of the breast cancer patients in developed countries. Current priorities should be to increase the accuracy of breast cancer screening and the appropriateness and availability of treatment, to improve communication, and to advance research. In the European Union, member states have been encouraged (11) to extend breast cancer screening programs to the entire target population, to monitor the quality of the screening process, and to link screening, diagnosis, and treatment in a comprehensive framework of quality-assured health care. Recognition of the merits and limitations of breast cancer screening, as well as of its clinical management, should help design more mature and evidence-based communication with the public and with individuals. In terms of research, the identification of indolent cancers that may be candidates for no or less aggressive treatment, the recognition of clues on how to safely reduce the intensity of screening in low-risk women, and the development of more accurate screening technology would be important steps forward that would be likely to have a large impact on future practice. These improvements would allow lowering the harms, in primis overdiagnosis and overtreatment, and increasing the benefits of the whole continuum of breast cancer screening, diagnosis, and care with the goal to sustain, extend, and amplify the impressive decreasing mortality trends that have been documented in Sweden.

References

Notes
Drs Segnan, Ponti, and Rosso are employed in a cancer epidemiology unit that is in charge of, among other things, cancer screening evaluation in the Italian Piedmont region.

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