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Consortium Modelers Interpret U.S. Trends in Breast Cancer Mortality

Do screening mammography and adjuvant therapy really reduce breast cancer mortality outside of clinical trials? While the benefits of therapy are more clear, a unique consortium of seven biostatistical teams has added important evidence to address the still controversial question regarding mammography. The problem of separating out the impact of mammography and advances in therapy, which occurred at about the same time during the 1980s and 1990s, was addressed by the consortium in their study reported in the October 27 *New England Journal of Medicine*.

This approach used population data to describe the dissemination and usage patterns of mammography and adjuvant therapy that occurred over time in the United States. The usage patterns were then coupled with seven independent modelers' synthesis of all available information on the benefits of these advances. The authors make the case that each factor accounted for half of the historic 24 percent decrease in mortality that was actually observed between 1990 and 2000.

Until now, the debate over mammography included many who questioned the evidence that screening does in fact reduce cancer deaths, one of them being lead author Dr. Donald Berry, head of biostatistics at the University of Texas M.D. Anderson Cancer Center. "The controlled trials on which the mortality assertion was based were uneven and not without flaws," he says.

Nonetheless, citing more recent papers, screening advocates have said that mammography can reduce mortality by up to 69 percent. But, says Dr. Berry, "Fervor doesn't substitute for evidence. Here we brought the pieces of evidence together in a novel way and separated the effects of screening and treatment. I would say the question is now at least 95 percent settled, in favor of mammography reducing breast cancer mortality."

"The ability to come at important questions like this in a unique way was part of the motivation when NCI formed the Cancer Intervention and Surveillance Modeling Network (CISNET) in 2000," says project director Dr. Eric J. Feuer, chief of NCI's Statistical Research and Applications Branch, who is also one of the study's 10 authors.

The CISNET approach includes bringing together distinct teams - including some of the leading biostatistical investigators in the cancer community - with an interest and expertise in a particular cancer site, framing a common problem, and letting each team develop its own independent model of how to solve it. The network also includes grantee teams that specialize in lung, prostate, and colorectal cancers.

"All models agreed that both screening and treatment reduced breast cancer mortality, and that the observed reduction in the actual population - 24 percent during the 1990s - could not be attributed to either one acting alone," says Dr. Kathy Cronin, a mathematical statistician who helped develop the common assumptions all teams used. Just under half of the combined effect came from screening. "There will never be a final piece of evidence on such a complex and tangled question, but this result provides additional evidence for mammography's role in the undeniable progress seen during the

1990s," she adds. "The study also helped refine the population mortality impact of important treatment advances in the use of multiagent chemotherapy and tamoxifen."

The proportion of the total reduction in the death rates from breast cancer attributed to screening varied in the seven models from 28 to 65 percent (with a median of 46 percent), with adjuvant therapy contributing the rest. The variability across models in the absolute contribution of screening was larger than it was for treatment, reflecting the greater uncertainty associated with estimating the benefit of screening.

"Comparative modeling yields a powerful outcome," explains Dr. Feuer, "because you actually produce a meta-result that no single group could achieve. This is a testament not only to the intellectual rigor used to build each of the models, but to the scientists' willingness to collaborate and cooperate."

Links to the journal and more study details can be found at <http://cisnet.cancer.gov/>.

By Addison Greenwood