

Breast Cancer Screening Series:

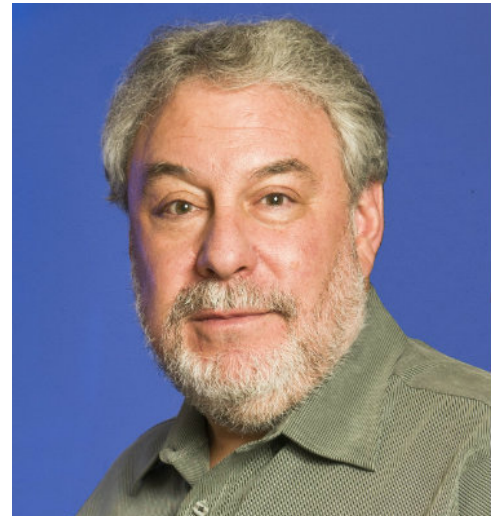
Dr. Martin Yaffe

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A Rational Approach To Breast Cancer Screening

by Martin J. Yaffe, PhD, C.M, Senior Scientist and Tory Family Chair in Cancer Research, Sunnybrook Research Institute, Professor, Depts. Medical Biophysics and Medical Imaging, University of Toronto, Director, Smarter Imaging Program, Ontario Institute for Cancer Research

Several times per year an article appears in the popular media, usually referring to a “new study” demonstrating that breast cancer screening is ineffective. And as has happened now, with the publication by Jorgensen *et al.*[\[1\]](#) and the resulting media coverage, I am asked to comment on the “debate regarding the value of screening”. In fact, there really is no debate about the science, if one restricts oneself to studies that have been carefully conducted using appropriate methodology and analysis. The debate is really about values (those of women, health providers and government) in preventive medicine. Screening is expensive. Is the cost justified by the saving of lives and are the negative aspects of screening – abnormal recalls and negative biopsies – acceptable?



Screening works: Many studies have been conducted to test the efficacy or the effectiveness of screening. However, the conclusion that breast screening with mammography is both efficacious and effective is based not on any single study, which is susceptible to statistical uncertainties and methodological error, but on the objective overview of multiple randomized trials and observational studies by several different panels of expert scientists. For example, in its report, “The Benefits and Harms of Breast Cancer Screening”,[\[2\]](#) The Independent UK Panel on Breast Cancer Screening, chaired by Professor Sir Michael Marmot, concluded that “the best evidence for the relative benefit of screening on mortality reduction comes from 11 randomised controlled trials (RCTs) of breast screening. Meta-analysis of these trials with 13 years of follow-up estimated a 20% reduction in breast cancer mortality in women invited for screening. The relative reduction in mortality will be higher for women actually attending screening ...” They also stated “the Panel’s estimate of benefit is in the range of one breast cancer death prevented for approximately 250 women invited”. More recently the WHO IARC Working Group on the Evaluation of Cancer-Preventive Interventions reported on the efficacy and effectiveness of breast cancer screening.[\[3\]](#) The

Working Group, which included 25 international experts in breast cancer epidemiology, concluded that there was sufficient evidence, both for the invitation and the actual participation of women aged 50-74 years to organized screening by mammography in reducing mortality from cancer of the breast and limited evidence (the conclusion as to “sufficient evidence” in this age range was short by one vote) for women in the age range 40-49. Finally, after its synthesis of evidence^[4] the American Cancer Society recommended^[5] “that women with an average risk of breast cancer:

- should undergo regular screening mammography starting at age 45 years (strong recommendation).
- Women aged 45 to 54 years should be screened annually (qualified recommendation).
- Women 55 years and older should transition to biennial screening or have the opportunity to continue screening annually (qualified recommendation).
- Women should have the opportunity to begin annual screening between the ages of 40 and 44 years (qualified recommendation).
- Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or longer (qualified recommendation).”

A study based on outcomes from modern organized screening programs with current therapies in Canada found that women aged 40-74 who participated in screening were 40% less likely to die of breast cancer than those who did not.^[6] Furthermore, screen-detected breast cancers are often found at an earlier stage or at a smaller size within a stage than those detected clinically allowing greater flexibility in treatment options, possibly reducing the need for chemotherapy or mastectomy. Therefore screening may provide reductions in morbidity as well as in mortality.

Screening mammography has limitations: The sensitivity of mammography screening is typically between 80% and 90% and decreases to as low as 65% in women who have dense breasts.^[7] For women at high risk for breast cancer, contrast-enhanced breast MRI, which reports on tumour angiogenesis, is a more sensitive screening tool. The specificity of screening mammography can be as low as 86% on initial screening examinations, but increases to 93% or higher on recurring screens^[8], when previous images are available for comparison.

Overdetection/Overdiagnosis: Some cancers, if not detected through screening would not appear before the woman had died of some other cause. This is referred to as overdetection. If such cancers are also overdiagnosed, i.e., they are assessed by the pathologist at biopsy as having the potential for lethality, then they are likely to be overtreated and this phenomenon is considered as a harm associated with screening. The harm arises both from morbidity resulting from treatment and the fact that a woman lives part of her life with an unnecessary diagnosis of breast cancer. The frequency with which this is estimated to occur varies wildly, from a few percent of cancer cases to over 50%.^{[9][10]} While certainly some cancers will not reveal themselves during a woman’s lifetime, no study has been carried out that will accurately estimate the amount of overdetection. Current estimates all suffer from the need to make often large assumptions. For example, Welch reported on overdetection twice, in the New England Journal using the SEER database.^{9[11]} First he guessed that the year-to-year increase in incidence was 0.5% and two years later assumed that there was no temporal increase. The latter assumption seems unfounded as in most countries independent of whether screening takes place or not, there has been a consistent annual increase in

incidence, in many cases at a rate of 2% or higher.^{[12][13]} The higher the rate of increase the lower will be the estimated rate of overdiagnosis.^[14]

Overdiagnosis is a bit of a red herring. To find and treat the cancers with potential to kill it is also necessary to detect some cancers that won't. The challenge is not to lose the opportunity to save some lives, but to identify at pathologic diagnosis, those cancers that will be indolent so that overtreatment can be avoided.

Truth and accuracy in science: As scientists, clinicians and citizens we should be concerned about the standards and objectivity of the mainstream media in their reporting on medicine and health. For example, both The New York Times and The Globe and Mail tend to give markedly more space and headlines to reports suggesting that screening is less effective than previously thought or is associated with harms and less to those studies and reviews that have concluded that screening saves lives and that its harms are overstated. Reporters virtually never delve deeply enough into the history of the research to discover that the publication with negative findings on which they are reporting is an outlier among many other well-conducted studies that had positive results or may have undergone serious scientific criticism with respect to methodology as was the case with the work of Jorgensen *et al.*,¹ where others who have more carefully studied the same Danish populations have found mortality reductions of 25% or more without increase in mastectomy procedures^[15] and have estimated the rate of "overdiagnosis" (actually overdiagnosis) among screening participants to be to be between 1% and 5% of cancers detected.^{10, [16],[17]} The weaknesses of the Jorgensen publication include the fact that data on individual women were not available, for example the number of women who actually participated in screening and assumptions were made on homogeneity in characteristics between the populations in the screened and unscreened regions of the country.

The media reporters, who are usually not scientists and who face short deadlines, do not have the time or resources to delve more deeply into the research literature to discover major shortcomings of a publication. They rely on the journal peer review for vetting of the research. But, unfortunately, articles containing serious methodological flaws and/or poorly-founded assumptions can and do get through peer review.

A rational approach: Women and the health care providers who advise them need accurate, unbiased information to make what should be a personal choice regarding screening. Such a choice requires though that access to high-quality screening be available at age 40 when incidence begins to increase.⁵ Articles like that by Jorgensen *et al.*, and the media coverage, both which ignore solid research with more positive results only cause them to be misinformed. Rather than contributing to this problem^[18], our health agencies should work toward accurate, more effective, agenda-free knowledge translation.

Most lay people are somewhat innumerate, particularly around statistics. Rather than providing relative risks (such as I used here) where the numbers may seem frighteningly large or absolute statistics where they appear deceptively

small, perhaps the key is to indicate the same information in a familiar population (*eg* Canada or a province) what the numbers of breast cancers, abnormal recalls from screening, negative biopsies and deaths averted through screening would be. For example, screening could avert about 1800 breast cancer deaths in Canada each year, but a woman would have a 1 in 5 chance of having an unnecessary (*i.e.* negative) needle biopsy in her lifetime.

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The opinions expressed in this article are the author’s own and do not reflect the view of Cancer Knowledge Network or Multimed Inc.

Martin Yaffe, PhD — Dr. Yaffe received a doctorate in Medical Biophysics from the University of Toronto and is a Professor in the Departments of Medical Biophysics and Medical Imaging at the University of Toronto and a Senior Scientist at the Sunnybrook Research Institute where he holds the Tory Family Chair in Cancer Research in the Imaging Research program. He is Director of the Smarter Imaging Research Program of the Ontario Institute for Cancer Research. With his group of 23 scientists, engineers and students, he conducts research in improving medical imaging as applied to detection, diagnosis and management of breast cancer. He led the Physics Consulting Group for The Ontario Breast Screening Program from its inception in 1990 until 2015. His research on digital mammography helped move this new modality into clinical evaluation and widespread use internationally. His group continues to develop techniques for assessing image quality and conducting quality control for mammography and breast tomosynthesis. He is part of the leadership team of TMIST, a clinical trial evaluating the potential impact of tomosynthesis for breast cancer screening. He chaired the International Atomic Energy Agency (IAEA) Committee to develop harmonized quality control standards for digital mammography and several other international committees focussing on image quality standards in breast cancer detection. Dr. Yaffe has authored over 260 scientific papers. He is a co-author of the book: Digital Mammography with Dr. Etta Pisano. His current work is directed towards optimization and evaluation of breast tomosynthesis, assessment of image quality, breast density and breast cancer risk, and development of

quantitative imaging biomarkers in pathology to inform choices for precision therapy. In July 2015 he was awarded membership in The Order of Canada.