

The facts about breast cancer screening and the Canadian National Breast Screening Study (CNBSS)

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I have been an active breast cancer researcher for the past 36 years with much of my work focusing on breast cancer detection. My work is done at Sunnybrook Health Sciences Centre Research Institute, The Ontario Institute for Cancer Research and The University of Toronto where I am Professor in the Departments of Medical Biophysics and Medical Imaging.

Here are some facts:

Breast Cancer

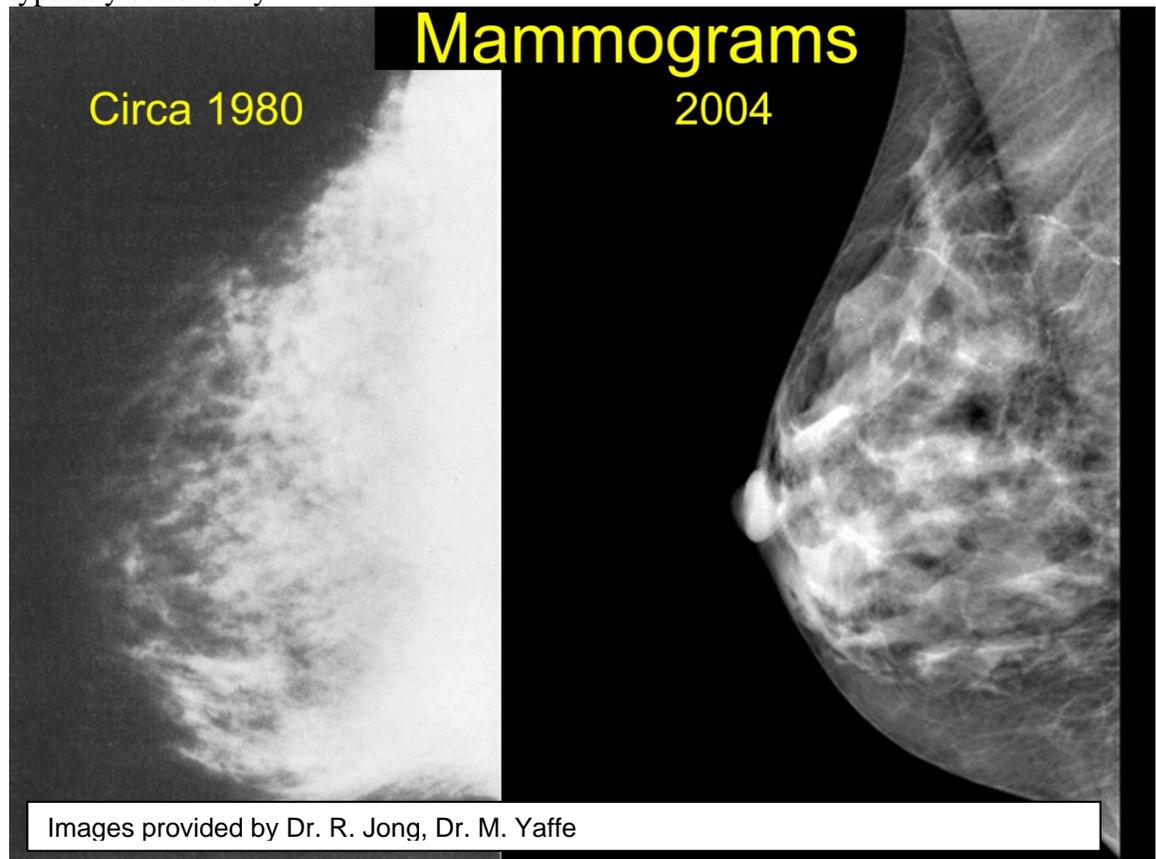
- The risk of breast cancer begins to increase in women starting at about age 40
- The main risk factors are being a woman and increasing age
- There are certain groups at much higher risk (women who carry one of the breast cancer gene mutations called BRCA1 or BRCA2 or who have a strong family history of breast or ovarian cancer.
- Deaths from breast cancer are caused when the disease spreads (metastasizes) to other critical organs (brain, bone, liver) in the body.

Screening

- Many studies have been done and have clearly shown that earlier detection of breast cancer through routine screening saves lives
- 10 more recent studies using more modern technology showed a reduction of deaths between 25% and 50% in women ages 40-74.
- When cancers are found earlier, not only does this increase the chances of survival, but the woman is less likely to have to undergo the harsher types of therapy
 - For example, she may be able to have a lumpectomy rather than a mastectomy
 - Or being able to avoid chemotherapy
- In Canada, each year, this means that about 1000 women don't die from breast cancer because they get screened

What is wrong with the CNBSS or the reports on its findings?

- Unlike the way it was presented by the media, it is not a “new study”. The actual mammography was done only between 1980 and 1985. No other intervention took place since then.
- Mammograms from that time used technology that was primitive by today’s standards, so a study based on those mammograms does not reflect what can be accomplished with the clearer, sharper digital mammograms used today (please see Figure).
- But, many of the mammograms taken in the CNBSS did not meet quality standards even for that time. I was a consultant to that study in the 1980s and complained frequently to the investigators about quality issues. Outside expert radiologists also considered the image quality to be sub-par.
- Therapies have also advanced since the time of that study, so again the therapy received by women who were in the CNBSS is not like what is typically done today.



- The CNBSS was supposed to be a “randomized study”. This means that the women who participated were randomly assigned into one of two “arms” of the trial, either to get screening or to be in the control group. The randomization is supposed to be blind. But there is evidence that the randomization was compromised because women received a physical

examination of the breast by a trained nurse before their names were entered into the randomization list. Here is what we think happened: If a woman had a large palpable cancer, the nurse who examined her (and had the best intentions of helping her patient) could decide that this woman urgently needed a mammogram and could just skip a line in the randomization list to be sure that the woman was entered into the screening arm of the study. Therefore, the screening arm of the trial would have more women with advanced cancers and these women would be more likely to die from breast cancer. Even a few women like this who were mis-randomized, could distort the findings of the study.

- To reduce mortality it is necessary to reduce the rate of advanced cancers, by finding the cancers earlier. Due to poor quality and the faulty randomization, the CNBSS was not able to do that.
- There were other problems too. At one site, the study surgeon refused to treat a cancer unless it was palpable! Clearly he did not understand the concept of earlier detection.
- So, unlike the other trials which showed a substantial mortality reduction in breast cancer deaths, the CNBSS, due to poor image quality and flawed randomization, did not show such a benefit. And the authors, have published updates showing that this flawed study had not miraculously “fixed itself” over the last 25 years.
- Finally, the authors presented an estimate of overdiagnosis (more correctly, overdetection) of breast cancer that they attributed to screening. Unfortunately, in doing so they neglected to make key corrections for lead time from screening and for temporal trends in underlying breast cancer incidence that are required to avoid a substantial overestimate.

Why do the authors insist on aggressively publicizing the results of their flawed trial despite the errors and the positive results from many other trials?

One can only speculate. Possibly it is because they are so invested in their project that they cannot acknowledge the overwhelming evidence from many other trials that mammography screening reduces breast cancer deaths. For similar reasons they appear to be deaf to the many flaws that have been identified in the conduct of their study, which are almost certainly responsible for its failure. But whatever the reasons are, this does not represent responsible scientific behavior.

What is my best advice, based on the evidence?

- That women consider starting screening (annually if possible) at age 40. That around 50 or menopause, they shift to a 2-year interval. That they continue to be screened until age 74 or older as long as they are otherwise in good health.

- If they are deemed to be at high risk, that they investigate if there is a high-risk screening program available (There is one in Ontario) and if they are eligible to participate in it.

Are there limitations or harms of screening?

Of course. No test is perfect.

- Screening usually detects about 80% or more of cancers. For women with dense breasts this value can be lower, but digital mammography has helped improve accuracy. So screening can miss 20% of cancers (perhaps 30% in very dense breasts). Research is underway to increase detection of such missed cancers.
- The screening test may not be able to show with certainty that there is no cancer. In other words there may be a small level of suspicion raised by the mammogram and the normal procedure is to ask the woman to return for additional images, usually just to make sure that there is no cancer. This happens most often the first time a woman is screened (about 15% of the time) and is less likely (about 7%) when she has had previous screening examinations that can be used for comparison. Being called back can be stressful, but it is important to realize that, in the vast majority of cases (95%) there will be no cancer. New technology may allow the rates that women have to be called back to be reduced.
- There is also the possibility that a cancer that is detected, wouldn't ever have surfaced on its own without screening and, therefore, couldn't potentially cause death. This is called "overdetection". But the problem is there is no way of knowing in advance which cancers will be aggressive and which will not, so all cancers are treated even though some didn't need to be treated. This is called "overtreatment" and occurs even if the woman discovers a cancer herself without screening. But ignoring cancers like this is like playing Russian Roulette. Further research may allow us to "fingerprint" cancers once they are detected to determine how (or if) they should best be treated.