

Effect of Three Decades of Screening Mammography on the Incidence of Breast Cancer

Interview of Archie Bleyer, MD

by Kirk Hamilton, PA-C of VitaSearch.com

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Can you please share with us your educational background and current position?

I am Clinical Research Professor, Knight Cancer Institute at the Oregon Health and Science University, Professor of Pediatrics at the University of Texas Medical School at Houston, Chair of the Institutional Review Board for the St. Charles Health System in Central Oregon. I have been Chair of the Children's Cancer Group (CCG), Mosbacher Chair and Professor of Pediatrics at the University of Texas M.D. Anderson Cancer Center, and Director of the M.D. Anderson Community Oncology Program. I received a B.S. degree in Life Sciences from Massachusetts Institute of Technology and M.D. degree from the University of Rochester School of Medicine and Dentistry. At the University of Washington, I was Professor of Pediatrics, Adjunct Professor of Medicine and Radiation Oncology, and American Cancer Society Professor of Clinical Oncology. I was also a Full Member of the Fred Hutchinson Cancer Research Center.

As Chair of the Children's Cancer Group, the world's largest pediatric cancer research organization, I directed the group to include research on older adolescent and young adult (AYA) oncology. Breast cancer in young women become one of my research targets.

What got you interested in studying the role of screening mammography and its effect on reducing the incidence of advanced breast cancer and death from breast cancer?

While an American Cancer Society Professor (ACS) of Clinical Oncology at the University of Washington in Seattle during 1984-1990, I accepted a primary extramural responsibility of assisting the Washington Division of the ACS in promoting screening mammography. We successfully petitioned the State and several private insurers to offer low-cost mammograms to indigent women, and we started the now-popular, nationally conducted Race for the Cure to raise breast cancer awareness including importance of screening mammography, which the ACS adopted nationally and is held annually today as one of its most successful fund raisers. As a member of the ACS National Board I also become involved with mammography screening as a national priority. I was convinced that screening was broadly beneficial for all women including those in their 40s. During the 1990s however, I became involved with neuroblastoma screening in infants, which in advanced form was highly lethal and refractory to medical therapies available at the time. As Chair of the Children's Cancer Group I supported trials of neuroblastoma screening in Minnesota and Ontario, Canada, In Texas where I headed the Pediatrics program at MD Anderson Cancer Center, I was co-investigator of a \$1 million grant to implement neuroblastoma screening in Texas. Within a few years neuroblastoma screening was found to be ineffective and unnecessarily subjected infants to staging tests (scans, CTs, biopsies, etc.) and treatment (surgery and sometimes chemotherapy and/or radiotherapy). It's was then that I learned about over diagnosis and began to worry about what I had advocated in Washington in the 1980s.

We did this research together because we were interested in learning how well mammography was working in terms of basic screening principles. For a screening test to help patients it must not only cause more early stage cancers to be found, it must also cause fewer late stage cancers to be found (demonstrating its ability to advance their time of diagnosis to an earlier time and earlier stage). Unless late-stage cancer is reduced, any observed improvement in cancer deaths must be due to something else and for breast cancer that would primarily be better treatment.

What has screening mammography done with regards to the incidence of picking up early breast cancer?

Screening mammography more than doubled the rate at which women in the U.S. were identified to have as early-stage cancer. This benefit of screening is evidenced in incidence trends by an increase in early-stage cancer during the late 1980s and early 1990s [did you mean 1990s] that was followed by a slight decrease in the incidence of late-stage cancer. Screening mammography has had, however, a much greater effect on the detection of findings that in retrospect have no evidence that they would have become true cancer and progressed to late-stage if nothing was done. The latter phenomenon is over diagnosis in which the finding(s) would have never become known during the rest of the patient's life if screening had not been done. Yet these situations have been treated as cancer and for breast cancer, that has meant mastectomy or lumpectomy with radiation therapy, five or more years of hormone therapy, and in some patients chemotherapy and/or molecularly targeted therapy (e.g. herceptin therapy administered intravenously).

By the very nature of detecting breast cancer earlier are you not artificially increasing the "cure" rate or the 5 year survival rate without necessarily improving the overall mortality rate from breast cancer?

Yes, by (unintentionally) including patients in survival analyses who do not actually have cancer the survival rate is obviously, automatically, and artificially, inflated. No Little wonder that the 5-year relative survival rate (relative to the general female population compare age for age) of patients with the early form of cancer known as ductal carcinoma in situ ("DCIS") in the U.S., according to federal data, is 100%. It's been 100% for consecutive years since 1988 when screening mammography became routine.

Of 61,608 females diagnosed with DCIS during 1990-2004, the 10-year relative breast cancer death rate was 0.0%. Nothing is perfect in medicine. Yet there have been no deaths due to cancer within 10-years after diagnosis of DCIS, most of which was detected via screening mammography. For those diagnosed with DCIS during 1990-1994 the 20-year relative breast cancer death rate was also 0.0%, as it is for those the 15-year rate among those diagnosed in 1995-1999. Nothing is perfect in medicine. To explain this extraordinary result, Surely the population must have contained a substantial proportion of patients who did not have cancer and thereby inflated the survival rate to near perfect (that could have progressed to death within 10 years).

For localized disease, the corresponding rate is only 5.0% in 239,406 women diagnosed during 1990-2004. It appears that screening mammography has made the results of early-stage "breast cancer" appear exceptionally good.

Can you tell us about your study and the basic results?

Screening mammography has doubled the number of women in the U.S. with what has been identified as early-stage cancer and it did to nearly 25 years ago. This was an optimistic result since the first objective of cancer screening is to detect cancer earlier when it is more curable.

Unfortunately, despite a quarter century of a lot more early cases, it has had little impact on the rate at which women present with late-stage cancer.

This combination of findings suggests a tremendous amount of overdiagnosis: women who were told they have early-stage cancer – most of whom underwent surgery, radiation, hormone therapy, molecularly-targeted therapy and in some cases chemotherapy – for a “cancer” that was never destined to progress to late-stage. In the last three decades we conservatively estimate that over a million women have been overdiagnosed. Despite all this screening, there has been no change in the rate at which women present with metastatic breast cancer. This suggests that mammography has little impact on the breast cancer death rate. It is gratifying that the breast cancer death rate is falling in the United States. Our research suggests, however, that this largely reflects better treatment – not screening.

What were or are the side effects to screening mammography? What are the costs to increase in screening mammography?

The potential harms of mammography include 1) discomfort of the procedure that in some women is pain and may persist for days, 2) anxiety and distress, 3) other procedures such as repeat mammograms, MRI and ultrasound studies and biopsies if cancer is suspected, 4) receiving a diagnosis and treatment for cancer that never would have surfaced on its own within a woman’s natural life time (overdiagnosis and overtreatment), and 5) financial cost of the mammograms themselves, of other procedures, and of the biopsies, surgery, radiotherapy, chemotherapy and molecular therapy that were not necessary. In the U.S. an estimated \$4 billion per year are spent on screening mammograms.

From the aforementioned \$4 billion per year of screening mammogram cost how much do you estimate to be necessary? 10%, 25%, 50%....what percentage of that \$4 billion is a necessary expenditure in your opinion?

Although a very important question, I don’t have an answer that I am comfortable/ If 69% of women with breast cancer are being diagnosed with true cancer — our best guest estimate of the overdiagnosis rate was 31% — one might be tempted to answer 69%. Unfortunately, the data we analyzed does not separate those who were screened and those who were not. The denominator was all women with breast cancer. The proportion may much less than 69%, but how much would be a guesstimate.

What are the side effects and costs of treating breast cancer earlier, even though you state that the mortality from breast cancer hasn’t improved all that much?

We don’t say that breast cancer mortality hasn’t improved all that much. On the contrary the reduction has been substantial and gratifying. The good news from our conclusion is that therapy is mostly responsible for the improvement and not screening. Our analysis gives more credit to treatment advances (than we have been attributing in general) since little of the advance can be attributed to screening.

What do you personally think the recommendations for screening mammography be?

I personally am in accord with the U.S. Preventive Services Task Force guidelines that are now three years old and recommend 13 scans between age 50 and 75 at two year intervals, in contradistinction to prior guidelines that recommended 40 to 50 scans (depending on the woman’s natural lifespan) at annual intervals beginning at age of 40.

Are there better screens for breast cancer (i.e. MRI, thermography, etc.)? Or is really the problem the treatment is not as effective as it should be? We are diagnosing more and earlier yet the mortality rate is not much better?

Whether ultrasound scans, 3-dimensional mammograms, positron emission tomography (PET scanning), thermography, or any other technique may be better remains to be determined. Unfortunately, the resolutions of these external imaging techniques are currently too insensitive to expect them to be applicable at any time in the near future. MRI may have the best resolution but is likely fraught with detecting even more abnormalities in the direction of overdiagnosis.

How can the public or health professionals use this information?

What does this mean for women 40 years of age and older? It means women really do have a choice about breast cancer screening. The benefit of mammography in lowering the death rate is considerably smaller than has been previously recognized, and the harm of overdiagnosis is considerably larger. While no one can dismiss the possibility that screening may help some women, there's no doubt that it leads many, many more to be treated for a diagnosis of breast cancer unnecessarily. It wasn't wrong 30 years ago to start down the road of screening for breast cancer with Xray technology, but in light of emerging evidence it is wrong to continue down it. We need a new approach to protect women from overdiagnosis.

Do you have any thoughts on your approach to preventing breast cancer, not just earlier detection (diet, lifestyle, chemo-prevention, etc.)

Exercise, nutrition and obesity prevention or reduction certainly reduce breast cancer risk and have not been fully exploited in the American population. Chemoprevention with tamoxifen or raloxifene are effective in women at higher risk of breast cancer.

I believe I understand your two main messages 1) that screening mammography has not reduced the incidence of late stage breast cancer, metastatic breast cancer, nor has it been the real reason the breast cancer death rates have gone down. 2) Breast cancer treatment, not early mammographic screening, is the main reason for a reduction in breast cancer death rates. Is that correct? And if I further hear you correctly it seems like any type of early breast cancer screening (MRI, thermography, etc.) won't pay off? Is the problem the definition of what cancer really is if early-stage cancer is really not a cancer or a lethal cancer? Please clarify?

It's not that better diagnostic imaging and biopathologic evaluation cannot reduce the overdiagnosis rate. Ultimately we will have a better process with less harms than those of current screening mammography.

Markers detectable through the analysis of a sample of the breast tumor (biopsy) will probably be the most likely productive approach. Tissue that biopathologists and laboratory scientists can not only examine with more sophisticated molecular and cellular techniques but also culture and grow in vitro or in in vivo animal models will most likely provide answers to how to reduce overdiagnosis in the future. Genomics, proteinomics, or metabolinomics will likely help lead to the avoidance of overdiagnosis in the future.

The person's host genome (own DNA) could also help predict who is likely to have a screening detected abnormality that will do which of the outcomes described in D4. The person's DNA can be more readily obtained, as from saliva (a spit sample) or blood sample than a biopsy of the person breast abnormality. Ultimately it may well avoid the need for a biopsy and direct analysis of the screening-detected tissue abnormality.

Do you have any further comments on this very interesting subject?

Can our society please stop using screening mammography as a measure of how well our healthcare system is performing? Screening mammography is neither a public health imperative nor a valid measure of the quality of care. And yet physicians, their office staff, and breast cancer advocacy organizations are harassing women to be screened.

Breast cancer is arguably the most important cancer for a nonsmoking woman to care about. Diagnostic mammography — when a woman with a breast lump gets a mammogram to learn if it's something to worry about — is an important tool. No one argues about this. Preemptive mammography screening, on the other hand, is, at best, is a very mixed bag — it most likely causes more health problems than it solves.