



A Reality Check for Overdiagnosis Estimates Associated With Breast Cancer Screening
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Comments by Daniel B. Kopans, M.D., FACR, FSBI:

Etzioni et al used the estimate by Bleyer and Welch to determine what the average leadtime would have to have been in the SEER program to result in an overdiagnosis of 31%. They show that radiologists would have had to be finding small invasive cancers many more years earlier than they would have become clinically evident (lead time) in order for Bleyer and Welch to be correct and there are no data to support this. Bleyer and Welch will argue that there are cancers that have an infinite leadtime that cause the problem (they would never become clinically evident) but Etzioni et al would argue that none of the trials have ever shown such long leadtimes and we would have to assume that Americans are finding cancers that no one else has ever seen.

My explanation is below:

Bleyer and Welch claimed that 31% of cancers were overdiagnosed in 2008. Etzioni et al looked at the actual distribution of cancers in 2008 (DCIS, localized invasive, and late stage). They accepted that all DCIS was overdiagnosed (for purposes of argument) and that all advanced cancers were real. If 22% of cancers were DCIS in 2008 and 49% were invasive but localized then 31% total overdiagnosed cancers minus 22% of which were DCIS leaves 9% of the overdiagnosed cancers were localized invasive. Since 49% of all the cancers in 2008 were localized invasive, then 9% divided by the 49% means that 18% of localized cancers had to be overdiagnosed to have an overall 31% rate. [They were unraveling the fact that Bleyer and Welch combined DCIS with small invasive cancers and called them "early stage" which is less important than looking at the overdiagnosis of only invasive cancers. When I did my analysis I simply looked at invasive cancers (Kopans DB. Arguments against Mammography Screening Continue to be Based on Faulty Science. The Oncologist 2014;19:107–112)]. They then calculated what the average leadtime would have to be to have 18% of localized invasive cancers be overdiagnosed.

The authors state in the paper that "for 18% of localized cancers to be overdiagnosed, the mean lead time must be approximately 108 months. This would mean that the average lead time for detecting local invasive cancers would have to be 9 years to produce an overdiagnosis rate of 18% for just these cancers in 2008. (This would be necessary to have an overall overdiagnosis rate of 31%).

Nine years far exceeds any leadtime estimates for invasive cancers from any other trials. They show the percent of overdiagnosis (first column) under various leadtime estimates in Table 2.

I think their conclusion is that, given that we know from multiple other sources that mammograms find cancers at most 2-3 years before they become clinically evident (a leadtime of up to 3 years), that in order to have a 31% overdiagnosis rate (even if we accept that all DCIS is overdiagnosed) the leadtime needed to have the SEER results for localized invasive cancers contain 31% overdiagnosis, would have to be far longer than any other data support and therefore the estimate is incorrect.

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Comments by László Tabár, M.D., FACR (Hon):

The authors did a good job in punching a hole in Bleyer and Welch's erroneous argument. Here is some clarification:

There are two issues one must take into account when calculating "overdiagnosis":

- 1) One needs to adjust for lead time
- 2) One has to adjust for the naturally increased incidence of breast cancer during the time they look at.

A well run screening program finds cancers that would have come up to the surface next yearthe year after that.....and if screening is really good, it finds cancers that would have surfaced 3 years later. Thus the screener has detected a lot of cancers, many more than would otherwise have been found during that year. This is the main point and strength of our screening activity...but of course the foes of screening dislike it and try to use it against us.

The maximum lead time is called the sojourn time (i.e. the mean growth rate of breast cancers). It is a simple word: sojourn=journey...growth rate, i.e. how long time does it take for the baby cancer (from its beginning in the breast) to become a grown-up, palpable/advanced cancer.

We all know through our mistakes, but also from sophisticated research using the Markov model, that it does not take too long for a missed cancer to become palpable. Sam Shapiro had calculated the lead time in the 70s to be one-and-a-half years! We have calculated the MST (mean sojourn time) according to age and histologic type and found a considerable difference in the length of MST according to age- it is much shorter in younger women than in older women. This has resulted in our suggestion for different screening intervals: 12 months to a maximum of 18 months for women aged 40-54 years, and 18 months to a maximum of 24 months for women 55 and older. In our study, most of the cancers had a MST of one-and-a-half to 2.2 years!

The authors of the article referred to a lead time of 40 months (the lead time is always shorter than the sojourn time) and the meaning of the article was to point out that Bleyer and Welch

operated with an unrealistically long lead time. That is the strength of the article: they have uncovered the gross inaccuracies of the Bleyer/Welch article.

As an aside, Anthony Miller also erred (he chose the wrong denominator to calculate overdiagnosis and he only used screen detected cancers instead of all cancers in his calculations) in the recently published article on the 25 year follow up of the Canadian National Breast Screening Study.

Even the current article overestimates overdiagnosis. The authors used SEER data and not data derived from studies where all women underwent mammography. They also did not take into account that the natural incidence of breast cancer has risen constantly increasing over the past 30 years. These errors also result in an estimate of overdiagnosis which is too high.

It is important that people start to realize how anti-screening articles based on pseudoscience like the one written by Bleyer and Welch have resulted in a major movement to deny women appropriate access to screening mammography.

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