

## To Grow or Not to Grow ? That is the Cancer Question

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The study by Braithwaite et al "Screening Outcomes in Older US Women Undergoing Multiple Mammograms in Community Practice: Does Interval, Age or Comorbidity Score Affect Tumor Characteristics or False Positive Rates?" published in the Journal of the National Cancer Institute suggests that screening women ages 66 to 89 every two years does not appear to result in finding cancers at a larger size and later stage than screening them annually.

Most do not know that The Journal of the National Cancer Institute is not the National Cancer Institute's Journal. The public has been misled for years. It was sold to Oxford University Press almost 20 years ago and does not carry the imprimatur of the NCI. One has to wonder why peer-review did not raise questions about the potential major selection biases in this study. It was not a prospective randomized trial. It was, in fact, a retrospective analysis of prospectively collected data from the Breast Cancer Surveillance Consortium linked to Medicare claims. The authors compared cancers among women who underwent annual mammography to women who, apparently, were screened every two years. The fundamental problem is that these are likely distinctly different populations. These women were not randomly assigned and the authors provide no information as to why some women were screened annually and others were screened every two years. It is likely that the women screened annually were considered to be at higher risk of developing breast cancer while women screened every two years were likely considered to be at lower risk and therefore not recommended for more frequent screening.

Some women have very heterogeneous breast tissues with numerous confusing findings on mammography while others have almost all fat in their breasts with little to be seen by mammography. The fact that there were more recalls among women screened every year could be due to the fact that this was a population of women who had the former types of breasts, and their physicians or health care providers, therefore, recommended that they be screened more frequently. This would select a population that would be expected to have more frequent recalls from screening, rather than screening annually being the reason for more recalls. They also provide no information as to whether a smaller number of women with these difficult breasts were recalled numerous times vs. at least half of the individuals being recalled at least once making the absolute, individual recall rate much lower.

It is also unclear why the authors were allowed to never provide combined data but always presented the data based on the "Charlson" score. Since they have concluded that comorbidities did not appear to have any influence on the size and stage of cancers in the groups, it is unclear why they persisted in segregating the two groups in their presentation of the data. It is possible that by looking at one year versus two year screening among the entire group the differences in size and stage may become statistically significant. They also did not provide the actual sizes. Grouped data can be misleading. Lives are saved by finding smaller cancers within stages and not simply reducing the rate of advanced cancers.

The consequences of so called "false positives" has been exaggerated. These women are not recalled because the radiologist interprets the findings as cancers that proved to not be cancer, but rather findings on a mammogram that raise the concern of the radiologist who requests additional evaluation. The vast majority of these recalls amount to a few additional

mammographic pictures or perhaps an ultrasound to resolve the issue. Only approximately 1 to 2% of screened women have a needle biopsy using local anesthesia and approximately 30 to 40% of these women will be diagnosed with breast cancer which is a high yield. If, in fact, the women in this review who were screened every year were screened at this frequency because they had a lot of mammographically visible changes in their breasts, then the selection process that put these women into annual screening would be the reason that they had more frequent recalls and biopsies.

The fundamental question is not answered or even addressed. If the groups are comparable (which is unlikely), these results suggest that breast cancers did not grow over the extra year among women in this trial who were screened every two years compared to those screened annually. Otherwise, the delay in screening of one year should have been reflected in larger cancers. Did the cancers stop growing and wait to be detected? The suggestion will be that "these are the data" even though they make little biological sense. I suspect that cancers do grow, and these results are based on biases introduced by the study design and not the fact that annual screening is not more efficacious than biennial.