

10,000 Deaths a Year Due to False and Misleading Mammogram Reports

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Analysis Overview

Each year, nearly 40 million women in the United States obtain screening mammograms for the early detection of breast cancer. For 40% of them - over 15 million women - a mammogram alone is an ineffective screening tool. This information is systematically withheld from these patients, who often rely on false and misleading mammogram results. Our analysis demonstrates that between 40,000 and 45,000 women each year receive false negative mammogram reports, meaning that their cancer is allowed to spread undetected and untreated.

False negative mammograms are not reported or tracked in the United States. However, their impact on the lives of these women and their families is tragic, as an estimated 10,000 will die as a result of the undetected cancer.

Our goal in publishing this analysis is twofold:

- 1) To educate women regarding the wide variation of mammogram effectiveness for screening purposes;*
- 2) To change the way mammogram results are reported to women so that they have truthful and accurate information on which to base their own health care decisions in accordance with existing federal statutes as well as the ethical guidelines of the American Medical Association.*

Introduction

Breast cancer is one of the leading causes of death for women in the United States. Each year, in excess of 200,000 women are diagnosed with invasive breast cancer, and approximately 40,000 women die of breast cancer^[1]. Mammograms, which are simply x-rays of the breast, have been the primary screening tool used in the United States for the early detection of breast cancer.

Mammograms have been widely used across the population of women in the United States, with a screening penetration rate of approximately 66% of women^[1]. The mammogram has helped to detect cancer in many women, for whom the disease has been effectively treated, resulting in lives saved^[3,17].

However, the mammogram is only effective in a portion of the women who are screened each year. The average effectiveness of mammograms across all populations is 75%. However, this statistic alone is not meaningful, given the wide variation of mammogram effectiveness among women. For the 40% of women screened who have high breast tissue density (BTD) (see box below), the mammogram alone is an ineffective screening tool, identifying an average of 27% (for film mammograms) and an average of 59% (for digital mammograms) of cancers. Over half of women below the age of 50 and a third of women over the age of 50 have high BTD^[2].

Despite a federal statute requiring that the results of mammograms be provided to each patient directly in language easily understood by a layperson^[7], women with BTD are not informed that the mammogram is an ineffective screening tool for them. If no cancer is detected, the patient simply receives a report stating that her results are normal^[8,9].

We can predict with a high degree of certainty that thousands of women each year will receive false negative mammogram reports. Our estimates, which are detailed in this document, place the number of false negative reports conservatively in the range of 40,000 to 45,000 each year.

Each false negative is a woman with undetected cancer.

A false negative report means that the patient does have breast cancer, but that the cancer was not detected by the screening mammogram. Many patients who receive false negative mammogram reports have high breast tissue density, but are not informed that the mammogram alone is not an effective screening tool for them. Instead, the patient receives a report stating that her results are normal. As a result, she does not seek out readily available adjuvant screening which would provide a significantly higher degree of certainty regarding the existence of cancer.

Unfortunately, the fact that mammograms alone are not effective at detecting breast cancer in millions of women means that breast cancer screening programs have fallen woefully short of their potential impact on mortality reduction.

Our analysis indicates that up to 10,000 women die each year due to their reliance on false negative mammogram results.

We believe that providing women truthful and accurate information on their mammogram results and encouraging an individualized approach to screening would save the lives of thousands of women each year. Providing accurate information could have a meaningful impact on mortality, reducing the number of deaths by up to 25%.

This analysis is divided into three sections as follows:

1) Upper Threshold of Preventable Deaths

- a. In this section, we develop parameters within which the number of deaths is likely to fall.

2) Estimate of False Negatives

- a. Because information on false negative mammogram results is not available, the first approach estimates the number of false negatives based on demographic information, prevalence of screening, and the outcomes of peer reviewed scientific studies from the United States and other countries.
- b. The second approach utilizes the data from the Breast Cancer Surveillance Consortium, the source for the USPSTF Task Force 2009 Recommendation on Breast Cancer Screening.
- c. The third approach provides a validation of the first estimate utilizing recent data gathered in Connecticut to measure the impact of legislation requiring information on BTM and adjuvant screening be provided to patients.

Number of False Negative Mammograms

False negative mammogram results are not tracked in the United States except at the facility level. Information is not aggregated or made available to the public, despite the fact that false negatives often result in death.

Therefore, the impact of false negatives on the overall success of the breast cancer screening program in the United States has remained opaque, and those organizations responsible for communicating results to women have not only failed to make this information available, but have also avoided accountability for the impact on mortality.

3) Impact of False Negatives on Mortality

- a. Once we have made a reasonable estimate of the number of false negative mammogram results that are likely to occur, we develop a reasonable range of mortality utilizing a study tracking long term survival rates based on size of tumor at diagnosis.

SECTION I Upper Threshold of Preventable Deaths

Our first step was to develop a hypothesis regarding the range of casualties which result from withholding critical health information from women in the patient mammogram report. Anecdotally, we know that the number of deaths is greater than 0. Despite routine annual mammograms, many women only discovered that they had breast cancer when the tumor was palpable, the cancer had metastasized, and the prognosis for survival was severely impacted. We know that many of these women have died as a result of the cancer.

The upper band of our estimate was approached as follows:

The total number of annual breast cancer deaths in the US is approximately 40,000^[1]. The percentage of eligible women who obtain mammograms is 66.5%^[1]. First, we divided the total number of deaths proportionately between the screened and non-screened

“Interval Cancers” are False Negative Mammogram Results

What is an interval cancer?

“Interval cancer” is a term used within the medical industry to describe a cancer which is detected “between” mammograms. The interval often varies by country (*e.g.*, 1 year in the United States, 18 months in Sweden, etc.).

In U.S. practice, the interval that is considered for individual patients for internal MQSA audit requirements is the period between a patient’s last mammogram and her next; however, there are other factors which also account for differences in classifying a cancer as “interval.”

Often, this cancer is detected because it has grown to the point at which it is now palpable, or “clinical.” By the time the cancer is palpable, it has usually advanced at least one or more stages. The implication is that the cancer was present but not detected when the previous mammogram was taken, generally due to the existence of high BTDR.

While the “interval cancer” is detected after the most recent mammogram, it is likely to have been present for a longer period of time and progressed beyond early, more treatable stages.

population. Of the 40,000 annual deaths, 66.5%, or 26,600, is the potential number of deaths associated with breast cancer in the screened population.

However, mammogram screening does have an impact on mortality. Studies indicate that the reduction in mortality from mammogram screening is approximately 30% [3, 17], although some estimates are much lower [24]. Reducing the deaths associated with the screened population by the more conservative 30% leaves 18, 670 deaths within the screened population that could potentially be associated with false negative mammogram reports.

Figure 1: Estimated Upper Limit of False Negative Mammogram Deaths

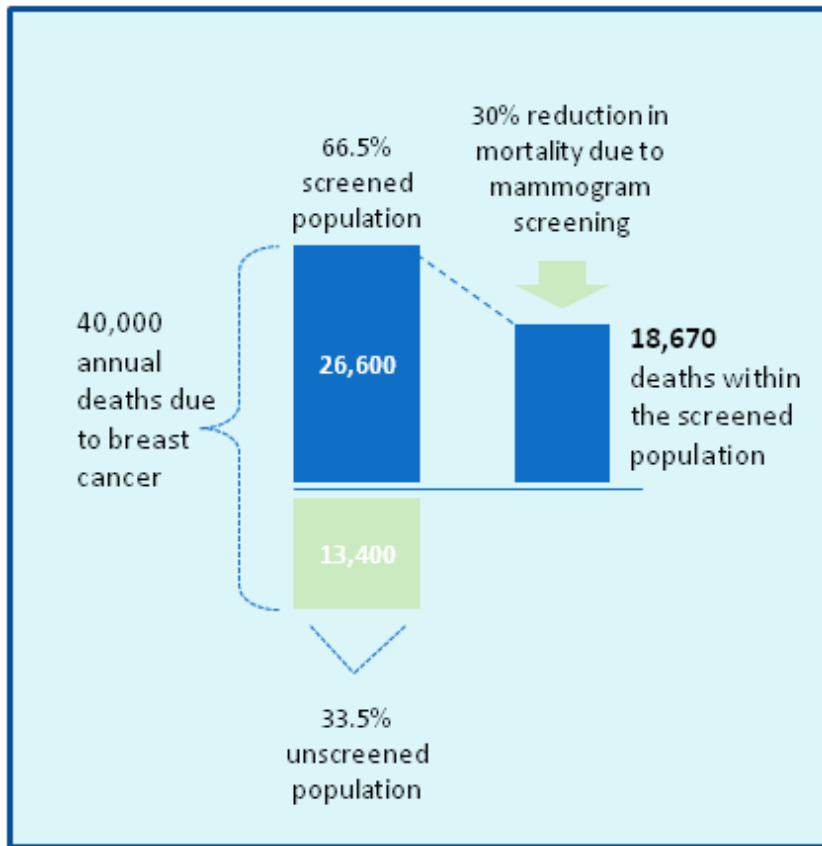


Figure 1 illustrates how this estimate of the number of deaths within the screened population was obtained.

We can assume that a portion of these 18, 670 deaths are due to other factors such as a missed diagnosis (which is also related to the “masking effect” associated with mammography), unique characteristics of the disease which may accelerate its progress, availability or affordability of treatment, or other reasons. However, our calculations support the notion that a large portion of these deaths are directly attributable to delayed diagnosis of the disease because of the ineffectiveness of the mammogram in detecting cancer in patients with high BTDR.

Below, we utilize existing information to ascertain the approximate number of false mammogram results provided to women who have been screened for breast cancer, and to extrapolate the impact of delayed diagnosis on mortality.

SECTION II

Estimate of False Negatives

First Approach

Our initial analysis relied on several pieces of information which are widely available including:

- US demographic information
- Estimated number of women who obtain regular mammograms in the US
- Number of women diagnosed with breast cancer in the US
- Number of women who die from breast cancer in the US

False negative results are not tracked in the United States and information on the impact on mortality is not available to the public. To estimate the number of false negative mammograms we extrapolated from available data as well as from peer reviewed studies conducted both within the United States and in other countries.

There are several different ways of approaching this estimate. We have attempted to be conservative yet realistic in our assumptions. Because of the lack of adequate reporting within the United States, our analysis must rely on reasonable assumptions. We welcome feedback and comments on our methodology and alternate approaches to estimation.

New cases of invasive breast cancer diagnosed in 2010 ^[1]	Breast cancer deaths in 2010 ^[1]	Number of women who receive breast cancer screening through mammography, estimated	Percentage of eligible women who receive mammogram screening ^[1]
230,000	40,000	38,000,000	66.5%

For the purposes of this estimate, we will assume that a proportionate number of cancers occur in the screened and unscreened populations.

Dense Breast Tissue and Undetected Cancer

The fact that high BTM obscures cancers on a mammogram has been well documented for years. Studies have supported that breast tissue density may vary over a women's lifetime, and often decreases with menopausal status. Overall, the percentage of women who are screened with high BTM is approximately 40% [2].

Studies have demonstrated that high density is also

associated with a higher degree of risk for breast cancer [14, 15]. 71% of all breast cancers appear in women with high BTM [18]. A 2007 study conducted by Boyd et al further indicates that approximately 43% of cancers in women with high BTM are not detected by a mammogram [19].

BREAST TISSUE DENSITY

For clinical purposes, the American College of Radiology measures breast tissue density on a mammogram along a four point BI-RADS™ (4th ed.) scale [16] for breast density:

1	2	3	4
Predominantly Fatty Tissue	Scattered Fibroglandular Densities	Heterogeneously Dense	Extremely Dense
<i>Having no areas of tissue that obscure cancer.</i>	<i>Having at least one area of tissue that can obscure cancer.</i>	<i>Tissue may obscure cancer in 50-75% of the breast.</i>	<i>Tissue may obscure cancer in >75% of the breast.</i>

For women with dense breast tissue (BI-RADS categories 3 and 4) both the dense breast tissue and cancer appears white on a mammogram, making cancer much more difficult to detect.

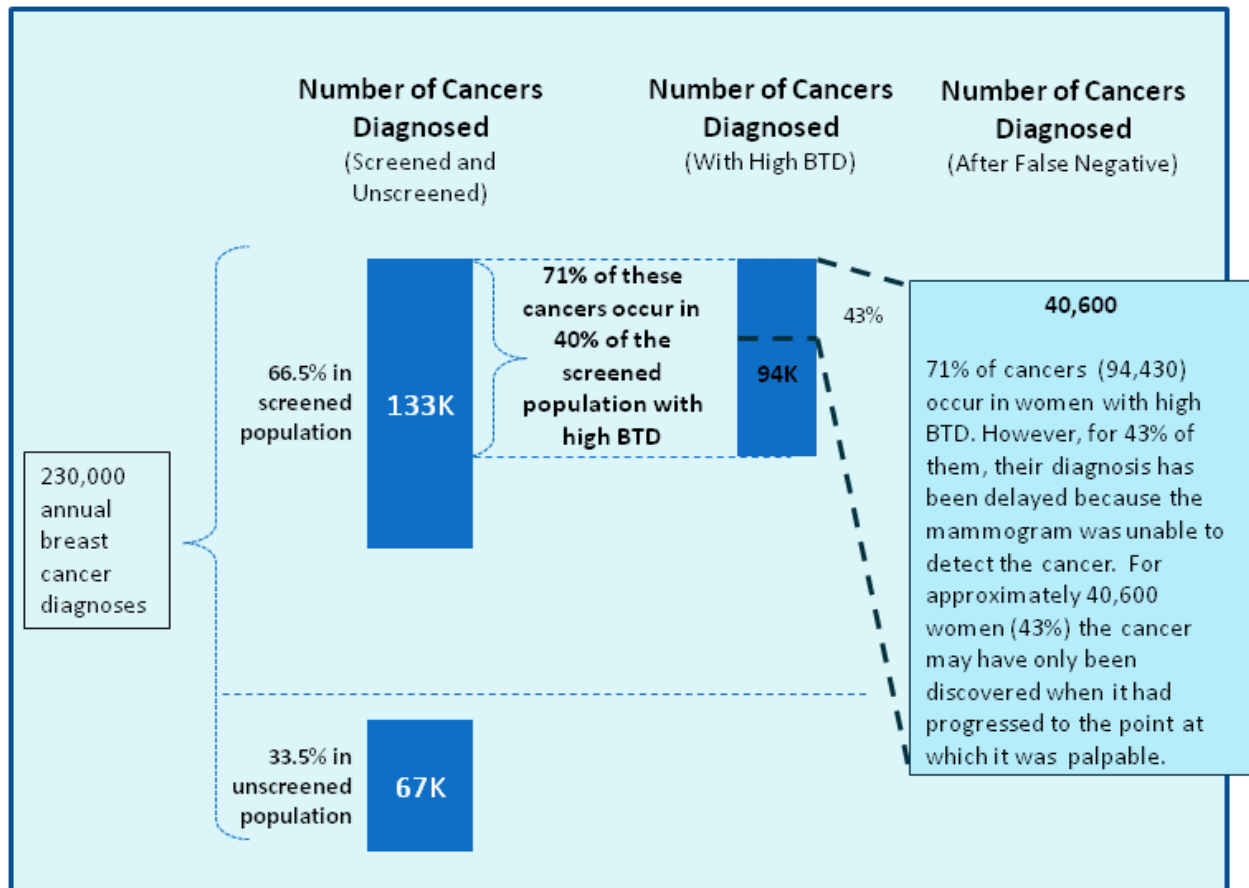
	Screened Population (With BTM)	Cancers in Screened Women (With BTM) (Figure 2)	Undetected Cancers in women (With BTM) (Figure 2)	Mammogram Impact on Mortality (Figure 1)
Percentage	40%	71%	43% [19]	30% Reduction
Formula or Assumptions	38,000,000 (number of women screened) * 40% = 15.2M	= 71% * 133,000 (cancers detected annually)	We assume that 43% of cancers which are diagnosed in women with BTM have been obscured on previous mammograms, increasing sojourn time.	=40000 (deaths per year) * 66.5% (% of population screened by mammogram); =26,500; reduced by 30% =
Total	15.2M	94,000	40,600	18,670

In Figure 2, the total number of cancers diagnosed are assumed to occur proportionally among women who are screened and those who are not screened. 66.5%, or 133,000, cancers diagnosed in 2010 ($230,000 \times 66.5\%$) are assumed to occur in women who have obtained screening mammograms.

Of the women screened, 40%, or 15.2 million, have breast tissue density (BTD) of BI-RADS 3 or 4, classifying them as high BTD. Since 71% of cancers occur in women with high BTD, we assume that approximately 71%, or 94,000, of the cancers have been diagnosed in women with high BTD ($133,000 \times 71\%$).

Since more than half of women under the age of 50 have BTD, mammogram screening alone is not as effective in this population^[28]. We also know that mammogram screening misses a significant number of cancers across the entire population. For women with high BTD, the number of missed cancers is higher. Boyd et al documented that 43% of cancers in women with high BTD were not detected by a mammogram^[19]. Thus, we assume that of the 94,000 cancers which were diagnosed in this population, 40,600 of them were diagnosed at a later stage ($94,000 \times 43\%$) due to false mammogram results.

Figure 2: 40,600 False Negatives Among Screened Population



In the second approach below, we estimate the number of false negative cancers utilizing data from the Breast Cancer Surveillance Consortium to check the reasonableness of the 40,600 false negative estimate.

Second Approach

The Breast Cancer Surveillance Consortium (BCSC) is a research resource for studies designed to assess the delivery and quality of breast cancer screening and related patient outcomes in the United States. The BCSC is a network of seven mammography registries with linkages to pathology and tumor registries in New Hampshire, Vermont, North Carolina, Colorado, New Mexico, San Francisco, and Seattle/Puget Sound.

As of July 2011, the Consortium’s database contained information on over 9.5 million mammograms (of which 7.2 million were screening mammographic examinations), 114,000 breast cancer cases (95,000 invasive and 19,000 ductal carcinoma *in situ*), and over 2.3 million women. The United States Preventive Services Task Force utilized data from the BCSC to support their 2009 recommendation on breast cancer screening, with the rate of false mammogram reports per 1,000 screened as follows:

Age at Screening	40-49	50-59	60-69	70-79	80-89
False negatives/1,000 screened	1.0	1.1	1.4	1.5	1.4

Using this data, a highly conservative estimate of the number of false negative reports among the 38,000,000 women who are screened regularly would range from 38,000 (38M/1000 * 1.0) to 41,800 (38M/1,000 *1.1).

This range supports our initial estimate of 40,600 false negatives. However, as another validation of our estimate, we also utilized the outcomes of studies recently conducted in Connecticut in Approach 3 below.

Third Approach

The masking and causal risk factors of BTM have been well-documented for years. The development of Full Field Digital Mammography (FFDM) and its aggressive deployment within

the US breast screening market at an approximate cost of \$4 billion was a response to the ineffectiveness of traditional film mammograms for women with high BTM [29,30]. FFDM does improve the detection of breast cancer in those 40% of women with dense breast tissue. However, whatever increase in effectiveness that was achieved for these women still falls woefully short of a reasonable degree of certainty. While film mammograms detect an average of 27% of cancers in women with dense breast tissue, FFDM only raised the effectiveness among this population to an average of 59%, meaning that almost half of cancers remain undetected [20, 21].

Despite this low level of certainty, women receive mammogram reports stating that their results are “normal” when no cancer is detected [8,9]. The vast majority of these women are unaware of their breast density, which is provided to their physicians, but not to the patient directly in the federally mandated patient mammogram report. For the 40% of women with high BTM, most are unaware that a mammogram alone is an ineffective screening tool, despite the fact that there are readily available technologies which can raise the level of certainty to above 90%.

A key finding of breast cancer research has been that the mechanism to reduce mortality is through the detection and treatment of the cancer at an early stage, when the tumor is small in size and responds more favorably to treatment. Mammography screening is generally cited to detect between 2.5- 4.7 per 1,000 screening mammograms [27, 31].

Connecticut Legislation

Due to the systemic refusal of responsible organizations and the medical community at large to properly inform women of their BTM or to provide truthful mammogram results, patients and advocates have resorted to additional legislation. Patient advocates within several states have introduced legislation mandating that patients receive accurate and truthful mammogram reports which include information on BTM. In Connecticut, legislation was passed in 2009 mandating that women with BI-RADS density of 3-4 be notified that the screening mammogram might not be effective in detecting cancer and recommending that such patients consult with their referring physicians about whether supplemental imaging in the form of ultrasound should be utilized [11].

The information on which our first two estimates were based has been widely available for years. Recent studies conducted in Connecticut as a result of this legislation again confirm the foundation for this analysis and our conclusions.

The Connecticut Study

Dr. Jean Weigert, who had opposed the legislation, assessed the clinical outcomes the first year following implementation of the legislative mandate at 6 practices with 12 sites in central Connecticut. Included in the study were 78,778 screening mammograms and 8,651 screening ultrasound exams. With the adjuvant ultrasound screening, an *additional* 3.2 cancers per 1,000 women were discovered in the population of women who were BI-RADS density 3-4 and had negative findings on screening mammography [12].

For the large majority of the ultrasound-detected cancers, lesion size was 1cm or less, and they were found to be invasive carcinoma on pathologic examination. Had these women not obtained the adjuvant ultrasound imaging, the tumor sojourn time would have increased and the cancer would have progressed beyond the stage at which it was surgically treatable.

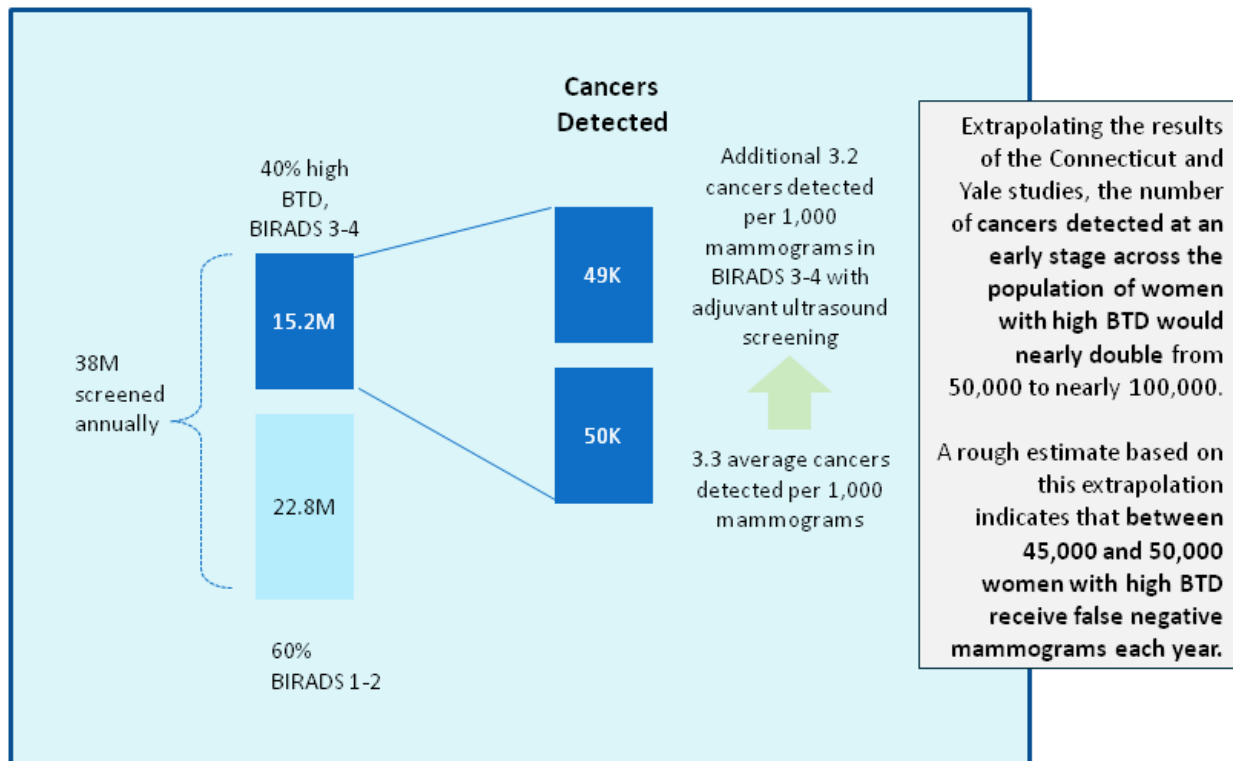
Cancers Detected per 1000 Screened	Additional Cancers per 1000 in CT Study	Additional Cancers per 1000 in Yale Study
2.5 – 4.7 (3.3 average)	+ 3.2	+3.2

The Yale Study

In a second study conducted during the period from October 1, 2009 - September 30, 2010, Yale performed Whole Breast Ultrasound (WBUS) on 937 women who were classified as heterogeneously or extremely dense (18% of those who were eligible), had normal screening mammograms, and who elected to return for the ultrasound screening. Patients electing the additional screening returned for the study approximately 60 days following the mammogram. Yale also utilized technologists to perform WBUS, and accrued an additional 3.2 cancers per 1,000 patients screened. All of the ultrasound detected cancers were less than 1cm and all were found in post-menopausal women^[13].

The results of the two studies conducted in Connecticut indicate that for every 1,000 mammograms in the population of women with high BTM, 3.2 cancers are missed. Given a screening population of 38M women, 40% of whom (15.2M) have high BTM, we can extrapolate across the population to determine the magnitude of women who are receiving false negative mammogram results annually. **The implication is that 45,000-50,000 women each year receive false negative mammogram reports.**

Figure 3: Adjuvant Ultrasound Screening Doubles the Cancer Detection Rate in Women with High BTB



Based on the three approaches above, we may conservatively estimate the number of false negative mammograms each year at 40,600.

The report that is routinely provided to women indicates that results are “normal” when no cancer is detected, even though we know that nearly half of all cancers are missed by mammography in this population of women with high BTB. Information regarding their own BTB and the extremely low level of certainty is routinely and systematically withheld from these women. Although adjuvant imaging technologies are readily available which can dramatically increase the degree of certainty to over 90%, these patients are unaware of this option. Many die as a result.

The next step in our analysis is to determine the impact of this reliance on false negative mammograms on mortality.

SECTION III

Impact of Delayed Detection and Disease Progression on Mortality

To estimate the number of deaths associated with false negative mammogram reports, we developed 3 scenarios (conservative, moderate, aggressive) and used the survival rates observed in the Swedish Two County Trial. This trial, which originated in 1977, involved 77,092 women invited to participate in screening mammography and 56,000 women who were not invited. The women in the study have been continuously followed since the inception of the trial, and the data collected has produced dozens of scientific papers. The trial established that the reductions in mortality are attributed directly to detection and treatment of tumors at smaller sizes and with less lymph node involvement^[4, 5].

From the Two County Trial, Tabar and Dean characterized breast cancer and its progression as follows:

- 1) Breast cancer originates locally and is not systemic from the outset.
- 2) There is a predictable progression of breast cancer, which can be halted by detection and treatment at an early stage; treatment in the earliest stages has the most significant positive impact on outcome.
- 3) Breast cancer is primarily a surgically treated disease when it is detected as *in situ* or 1-14 mm invasive tumor.

The benefit that accrues from routine breast cancer screening is the earlier detection of the cancer, when it is localized and treatable primarily through surgical means. Evidence supports that the later the diagnosis, the more likely that the tumor has spread and become systemic. The greater the sojourn time (delay in detecting the tumor), the greater the medium and long term mortality. In a recent study of breast cancer detection, Mathis, et al.^[23], found that the average size of cancers detected was

What is Sojourn Time?

Sojourn time describes the length of time that a cancer remains undetected. During that time, most breast cancer follows a relatively predictable growth pattern, increasing in size and spreading to other areas of the body. This increase in size and the spread to other parts of the body (metastases) are inversely correlated to survival rate.

A cancer detected at less than 1 cm can be successfully treated surgically with low impact on mortality. A cancer that is allowed to increase in size and become systemic will eventually be fatal.

Because mammograms are not as effective for women with dense breast tissue, the sojourn time for breast cancer often increases before detection, as does the associated mortality rate.

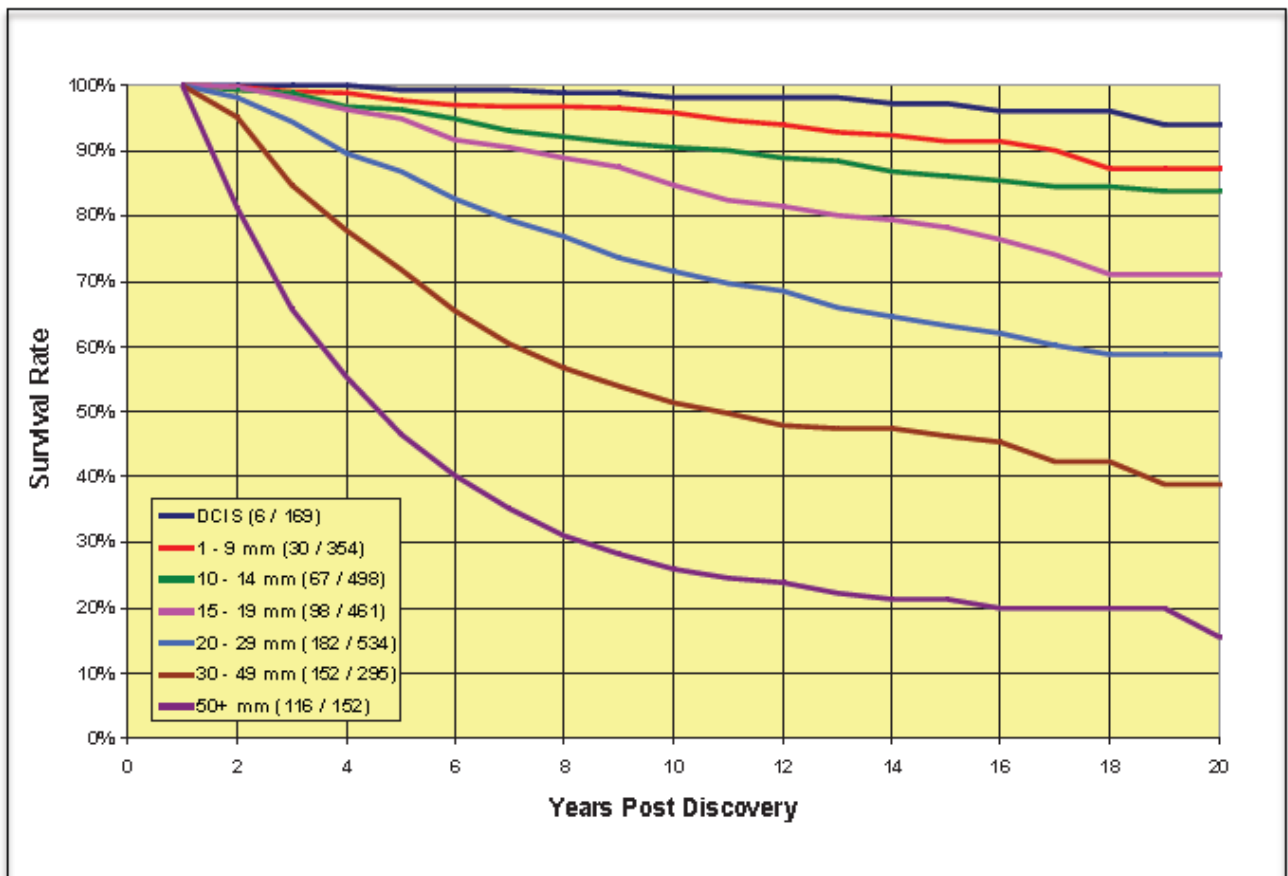
2.6 cm for palpable cancers and 1.5 cm for those cancers that were detected through screening mammography.

Time becomes even more relevant considering that the tumor doubling time has been estimated for most breast cancers at 130 days ^[22].

For those women who receive false negative mammogram results, the tumor is generally not discovered until it is palpable. A diagnosis of clinical (palpable) breast cancer –greater than 2cm and at or more advanced than Stage IIA - generally means that chemotherapy will be recommended in the course of therapy, decreasing the medium to long term survival rate.

The Swedish Two County Trial tracked the mortality rate associated with size of tumor at diagnosis across a span of over two decades. The top curve, representing DCIS, can be used as a proxy for the natural death rate, and we adjust the mortality rate of the other curves using this proxy.

Figure 4: Two-County Trial 20-Year Survival, Death from All Causes. *Adapted from Duffy, et al* ^[23]



Conservative Estimate of Mortality: 7,700 of the Women With False Negatives Will Die Within 10 Years; 77,000 Preventable Deaths in 10 Years

Our first estimate is extremely conservative and assumes that none of the women who receive false negative reports are diagnosed at greater than 3 cm, a scenario which is demonstrably inaccurate. Assuming that half of the tumors are detected between 2 and 2.9 cm (20-29 mm), and half detected between 1.5 and 1.9 cm (15-19 mm), the number of deaths approaches 8,000 within 10 years.

	10 Year Mortality		10 Year Mortality		Total Deaths Per Year
	15-19 mm	.13	20-29mm	25%	
Number of False Negatives	20,300	.13	20,300	.25	7,700

Moderate Estimate of Mortality: 10,150 of the Women With False Negatives Will Die Within 10 Years; Over 100,000 Preventable Deaths in 10 Years

In a moderate scenario, we assume that all of the women who receive false negative mammograms have cancer detected at 2.6 cm, which is the average size of palpable tumors detected by Mathis et al^[23]. The 10 year survival rate for tumors discovered at 20-29 mm is approximately 75% (accounting for the natural death rate of the DCIS curve).

	10 Year Mortality		10 Year Mortality			Total Deaths Per Year
	20-29mm	25%	30-49mm	55%	50+mm 30%	
Number of False Negatives	40,600	.25	0	.55	0 .30	10,150

In this scenario, there is a 10 year mortality rate of 25% among the 40,600 women who received false negative mammogram results; 10,150 of these women would die as a result of the false and misleading mammogram results.

Aggressive Estimate of Mortality: 14,700 of the Women With False Negatives Will Die Within 10 Years; 147,000 Preventable Deaths in 10 Years

For a more aggressive estimate we assumed that 50% of cancers were discovered between 2 and 2.9 cm (20 – 29 mm), 35 % between 3 cm and 4.9 cm (33 mm – 49 mm), and 15% at 5 cm (50 mm) or greater. While this is a more aggressive estimate, it is still realistic. The total mortality in 10 years (14,700) falls within our initial upper threshold of 18,760.

	10 Year Mortality		10 Year Mortality		10 Year Mortality		Total Deaths Per Year
	20-29mm	25%	30-49mm	55%	50+mm	30%	
Number of False Negatives	20,300	.25	14,210	.55	6090	.30	14,700

The three scenarios contemplated above provide a fair range of deaths associated with false negatives. Because the time horizon was limited to 10 years, the range of estimates remains somewhat conservative, as using a 15 or 20 year time horizon would greatly increase mortality.

Conclusion

Any screening mechanism that enables earlier cancer detection (when the tumor is smaller, or “pre-clinical”) will achieve the important end result of mortality reduction. With a complex disease process as exhibited with breast cancer, it is natural that early detection may require multiple screening modalities.

Mammography is the current standard baseline for breast cancer screening, but it does not work equally well for all women.

This wide variation in effectiveness and the fact that mammograms alone are ineffective for 40% of the population has been systematically withheld from millions of women patients. Over 15 million women with high BTDR receive false and misleading mammogram reports claiming that their results are “normal” when there is irrefutable and long-standing evidence that the mammogram cannot detect cancer with any degree of reasonable certainty in this population.

In October 2011, this Institute filed a Citizens Petition requesting that the FDA Commissioner fully and adequately implement the patient notification statute of the federal Mammogram Quality Standards Act. This statute mandates that mammogram results be communicated directly to women patients in language easily understood by a layperson. Information regarding a woman's BTM is obtained from the mammogram, and BTM is directly related to the mammogram's ability to detect cancer. This information and the need for some women to obtain adjuvant screening should be disclosed in the letter to the patient.

There is no defensible, rational basis for withholding this information from women. Withholding this information violates all medical ethical principles as well as the statutory requirements of the Mammogram Quality Standards Act of 1992. Because women are not provided critical information regarding their own health, they have routinely been denied the right to make informed medical decisions and to advocate on their own behalf.

The Institute for Health Quality and Ethics is a non-profit organization dedicated to protecting the rights of all people to make fully informed medical decisions. We seek to promote a system of quality healthcare which supports the dignity and rights of all people based on ethical considerations.

The Institute is not affiliated with any political party or religious persuasion. We welcome your thoughts and feedback.

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End Notes

1. American Cancer Society. *Cancer Facts and Figures 2011*. (Atlanta: American Cancer Society, 2011).
2. P.C. Stomper, D.J. D'Souza, P.A. DiNitto, M.A. Arredondo. "Analysis of parenchymal density on mammograms in 1353 women 25-79 years old," *American Journal of Roentgenology* 167:5 (1996): 1261-1265.
3. L. Tabar, B. Vitak, T.H. Chen, et al. "Swedish Two-County Trial: impact of mammographic screening on breast cancer mortality during 3 decades," *Radiology* 260:3 (2011): 658-63.
4. L. Tabar and P.B. Dean. "30-years of experience with mammography screening: a new approach to the diagnosis and treatment of breast cancer," *Breast Cancer Research* 10 (Suppl 4) (2008): S3 (doc:10.1186/bcr2163).
5. L. Tabar, S.W. Duffy, F. Vitak, et al. "The natural history of breast carcinoma," *Cancer* 86 (1999): 449-62.
6. K.L. Mathis, T.L. Hoskin, J.C. Boughey, et al. "Palpable presentation of breast cancer persists in the era of screening mammography," *Journal of the American College of Surgeons* 210:3 (2010): 314-18.
7. Mammography Quality Standards Act §900.12(c)(2) (Communication of mammography results to the patients).
8. American College of Radiology, *Breast Imaging Sample Lay Letters*, American College of Radiology. <http://www.acr.org/accreditation/mammography/mammosampleletters.aspx> (May 15, 2010).
9. Agency for Health Care Policy and Research. *Communicating Mammography Results to Women*, Agency for Healthcare Research and Quality, <http://www.fda.gov/downloads/RadiationEmittingProducts/mammographyqualitystandardsactandprogram/Guidance/ucm114151.pdf> (August 26, 2011).
11. Public Act No. 09-41, An Act Requiring Communication of Mammographic Breast Density Information to Patients. Amending Section 1. Section 38a-503 of the Connecticut General Statutes. Approved May 20, 2009, effective October 1, 2009.
12. S.L. Steenbergen, J. Weigert, "The Connecticut experiment: the role of ultrasound in the screening of dense breasts," Radiological Society of North America 2011 Scientific Assembly and Annual Meeting, (Chicago, IL), November 27-December 2, 2011.
13. K. Greenberg, R. Hooley, R. Stackhouse, et al, "Ultrasound screening in women with mammographically dense breasts," Radiological Society of North America 2011 Scientific Assembly and Annual Meeting, (Chicago, IL), November 27-December 2, 2011.
14. J.N. Wolfe, "Risk for breast cancer development determined by mammographic parenchymal pattern," *Cancer* 37:5 (1976): 2486-2492.
15. J.N. Wolfe, "Breast patterns as an index of risk for developing breast cancer," *American Journal of Roentgenology*, 126:6 (1976): 1130-1137.
16. American College of Radiology (ACR). *Breast Imaging Reporting and Data System (BI-RADS™)*. 3rd ed. (Reston, VA, American College of Radiology, 2003).
17. L. Tabár, C.J. Fagerberg, A. Gad, et al, "Reduction in mortality from breast cancer after mass screening with mammography: randomized trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare," *Lancet* 8433 (1985): 829 -32 .
18. N. Arora, T. A. King, L. M. Jacks, "Impact of breast density on the presenting features of breast cancer," *Annals of Surgical Oncology* 17:S (2010): 211-18.
19. N. F. Boyd, H. Guo, L. J. Martin, et al, "Mammographic density and the risk and detection of breast cancer," *New England Journal of Medicine* 356:3 (2007): 227-36.
20. E. D. Pisano, et al, "Diagnostic performance of digital versus film mammography for breast cancer screening," *New England Journal of Medicine* 353:17 (2005): 1773-83.
21. E. D. Pisano, H. E. Hendrick, M. J. Yaffe, et al, "Diagnostic accuracy of digital versus film mammography: exploratory analysis of selected population subgroups in DMIST," *Radiology* 246:2 (2008): 376-83.

22. J. Michaelson, S. Satija, R. Moore, et al, "Estimates of breast cancer growth rate and sojourn time from screening database information," *Journal of Women's Imaging* 5:1 (2003): 11-19.
23. S. W. Duffy, L. Tabar, B. Vitak, et al, "Tumor size and breast cancer detection: what might be the effect of a less sensitive screening tool than mammography?" *Breast Journal* 12 (2006): 91-5.
24. L.L. Humphrey, M. Helfand, B.K. Chan, S.H. Woolf. "Breast cancer screening: a summary of the evidence for the US Preventive Services Task Force," *Annals of Internal Medicine* 137(5 part 1) (2002):347-360.
25. M.T. Mandelson, N. Oestreicher, P.L. Porter, et al. "Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers," *Journal of the National Cancer Institute* 92:13 (2000): 1081-1087.
26. T.M. Kolb, J. Lichy, J.H. Newhouse. "Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations," *Radiology* 225:1 (2002):165-175.
27. P.A. Carney, E.A. Sickles, B.S. Monsees, et al. "Identifying minimally acceptable interpretive performance criteria for screening mammography," *Radiology* 255:2 (2010): 353-61.
28. D.S. Buist, P.L. Porter, C. Lehman, S.H. Taplin, E. White. "Factors contributing to mammography failure in women aged 40-49 years," *Journal of the National Cancer Institute* 96:19 (2004): 1432-1440.
29. P.A. Carney, D.L. Miglioretti, B.C. Yankaskas , et al. "Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography," *Annals of Internal Medicine* 138 (2003): 168-175.
30. K. Kerlikowske, D. Grady, J. Barclay, et al. "Effect of age, breast density and family history on the sensitivity of first screening mammography," *Journal of the American Medical Association* 276:33-8 (1996).
31. R.D. Rosenberg, B.C. Yankaskas, L.A. Abraham, et al. "Performance benchmarks for screening mammography," *Radiology* 241:1 (2006):56-66.