SCIENCE AND EVIDENCE: EXPOSING THE MISINFORMATION USED TO CONFUSE THE IMPORTANCE OF BREAST CANCER SCREENING

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Nothing to disclose
Can’t experts look at the same information and come to different conclusions?
Experts Disagree ??

The Earth certainly looks flat!!
THERE ARE FACTS
There have been more than 50 years of misinformation in the effort to reduce access to mammography screening.
BREAST CANCER SCREENING

JUST IN CASE – A FEW FACTS

1. There is little if any “overdiagnosis” of invasive breast cancer.
2. No one has ever seen an invasive breast cancer, detected by mammography, “disappear” on its own.
3. Screening reduces the rate of advanced cancers.
4. “False positives” is a misnomer. These are simply recalls from screening for a few extra pictures or an ultrasound.

5. The only “harm” that is affected by delaying screening is the recall rate.

6. Screening is the main reason that deaths have declined. Therapy saves lives when breast cancers are treated earlier.
Mammography screening is one of the major medical advances in the last 50 years. It has undergone greater scrutiny and more challenges than virtually any other medical intervention.

Opposition has persisted for over 50 years despite continually mounting evidence of benefit.
1. There is no benefit from screening – (1960-2009)
2. We can’t possibly screen all women – (1970)
3. The radiation from the mammogram will cause more cancers than will be cured – (1976)
4. There is no benefit from screening women ages 40-49 – (1993)
5. The parameters of screening change abruptly at the age of 50 – (1994-1997)
6. Screening women in their forties should be based on their risk of developing breast cancer (2008).


8. Improved therapy is the reason lives are being saved.

9. Screening doesn’t work because it did not reduce “all cause mortality” in the randomized controlled trials.”
10. Screening doesn’t work because it doesn’t reduce the rate of advanced cancers.

11. Screening everyone is “old fashioned”. We need “value based” screening.

Science has shown, repeatedly, that screening reduces deaths from breast cancer, while specious arguments have been created, and then refuted in an effort to reduce access.
Randomized, controlled trials have, unequivocally, shown a statistically significant mortality reduction for screening for women ages 40-74.
FIGURE 1
Relative Rate of Breast Cancer Death in the Eight Randomized Trials of Breast Cancer Screening

- HIP
- Malmö
- Two-County
- Edinburgh
- Stockholm
- NBSS-1
- NBSS-2
- Gothenburg
- All 0.76 (0.70-0.82)
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All 0.76 (0.70-0.82)
Despite early and, scientifically, inappropriate analyses claiming no benefit, a statistically significant mortality reduction is clear for women ages 40-49.
Although the RCT were never intended to be analyzed by age groups, the data show a benefit from screening women ages 40-49. This was provided to, and ignored by the Panel at the 1997 Consensus Development Conference.
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RCT’S actually underestimate benefit due to “non-compliance” and “contamination”.

When screening is introduced into general populations the death rate from breast cancer declines to an even greater extent.
SCREENING IN CANADA IS SAVING LIVES

Comparing women who participate in screening and those who do not, the death rate for the screened women is 40% (range 27%-50%) lower than expected.

DECLINING BREAST CANCER DEATHS

Observational studies show that the decline in deaths is linked to screening.

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BREAST CANCER SCREENING

IN THE U.S.
Breast Cancer Death Rate 1969-1990

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics
Branch, released April 2006. Underlying mortality data provided by NCHS
(www.cdc.gov/nchs).
Breast Cancer Death Rate 1969-1990

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics
Branch, released April 2006. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).
Breast Cancer Death Rate 1969-2003

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics
Branch, released April 2006. Underlying mortality data provided by NCHS
(www.cdc.gov/nchs).
Breast Cancer Deaths Averted Over 3 Decades

R. Edward Hendrick, PhD1; Jay A. Baker, MD2; and Mark A. Helvie, MD3

BACKGROUND: From 1975 to 1990, female breast cancer mortality rates in the United States increased by 0.4% per year. Since 1990, breast cancer mortality rates have fallen between 1.8% and 3.4% per year, a decrease that is attributed to increased mammography screening and improved treatment. METHODS: The authors used age-adjusted female breast cancer mortality rate and population data from the Surveillance, Epidemiology, and End Results (SEER) program to estimate the number of breast cancer deaths averted by screening mammography and improved treatment since 1989. Four different assumptions regarding background mortality rates (in the absence of screening mammography and improved treatment) were used to estimate deaths averted for women aged 40 to 84 years by taking the difference between SEER-reported mortality rates and background mortality rates for each 5-year age group, multiplied by the population for each 5-year age group. SEER data were used to estimate annual and cumulative breast cancer deaths averted in 2012 and 2015 and extrapolated SEER data were used to estimate deaths averted in 2018. RESULTS: The number of single-year breast cancer deaths averted ranged from 20,860 to 33,842 in 2012, from 23,703 to 39,415 in 2015, and from 27,083 to 45,726 in 2018. Breast cancer mortality reductions ranged from 38.6% to 50.5% in 2012, from 41.5% to 54.2% in 2015, and from 45.3% to 58.3% in 2018. Cumulative breast cancer deaths averted since 1989 ranged from 237,234 to 370,402 in 2012, from 305,934 to 483,435 in 2015, and from 384,046 to 614,484 in 2018. CONCLUSIONS: Since 1989, between 384,000 and 614,500 breast cancer deaths have been averted through the use of mammography screening and improved treatment. Cancer 2018;0:1-7. © 2018 American Cancer Society.

KEYWORDS: breast cancer, female, mortality rate, screening mammography, therapy, treatment, United States.

Between 384,000 and 614,000 lives have been saved since 1990 based on what the projected mortality would have been.

Figure 3. Surveillance, Epidemiology, and End Results (SEER) age-adjusted mortality rates (per 100,000 women) for women aged 65 to 69 years by year from 1975 through 2015 (blue data points). Dark red data points represent linear extrapolation of the mortality rate to 2016 through 2018 based on the trend from 2006 through 2015. Solid lines represent the 4 different assumptions regarding background (Bkgd) mortality rate trends since 1989. Blue indicates increasing by 0.94% per year since 1989; red, based on a linear fit to mortality rates from 1979 through 1989; green, increasing by 0.4% per year since 1989; orange, constant since 1989.
More than 40% fewer women now die each year from breast cancer in large part due to screening and earlier detection.

**Figure 1.** Age-adjusted US breast cancer mortality rates (per 100,000 women) for women aged 40 to 84 years by year from 1969 through 2015 from the Surveillance, Epidemiology, and End Results (SEER) database.
It has been suggested that the decline in breast cancer deaths is due to improvements in therapy.
DECLINING BREAST CANCER DEATHS

There certainly have been therapeutic advances, but the numerous observational studies have shown that the death rate declines primarily for women who participate in screening.
INCIDENCE OF FATAL CANCERS

Over 50,000 women ages 40-69:

Prescreening data from 1958-1976
Screening era followed over 39 years
1977-2015

Despite all women having access to modern therapy, the incidence of mortality was 60% lower at 10 years and 47% lower at 20 years for women participating in screening compared to those who did not.

ONE FINAL OBSERVATION

The effect of therapy is unclear.

The death rate for men with breast cancer has not declined since 1990 while it has steadily declined for women.
Mammography screening began in the mid 1980’s and the death rate began to fall in 1990. Over the same period, with access to the same therapy, the death rate for men increased, then returned to 1990 levels, and has not fallen since 1990.

THE DIFFERENCE?

WOMEN ARE BEING SCREENED!
ONE FINAL OBSERVATION

What is the difference?

Women are being screened and their cancers detected earlier.
THERE IS ACTUALLY NOW A CONSENSUS BUT IT IS BURIED IN NON-SCIENCE:

All of the major groups agree that the most lives are saved by annual screening starting at the age of 40.
The Panels used results from the National Cancer Institute’s 6 computer modeling groups called:

The Cancer Intervention and Surveillance Modeling Network

“CISNET”
CISNET SHOWS THAT MOST LIVES ARE SAVED BY ANNUAL SCREENING BEGINNING AT 40

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Fig. 1—Percentage mortality reduction from various screening strategies. Note that annual (A) screening from ages 40–84 years (A40–84, solid arrow) is estimated to have 71% greater mortality benefit than biennial (B) screening from ages 50–74 years (B50–74, dashed arrow). Number of mammograms shown on horizontal axis is per 1,000 women screened. Data shown are mean values of six models from [6].

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ACR

USPSTF
The United States Preventive Services Task Force (USPSTF) "found adequate evidence that mammography screening reduces breast cancer mortality in women ages 40 to 74 years."

The American College of Physicians (ACP)

"Screening mammography has been shown to decrease the number of deaths from breast cancer in women ages 40-74."

(http://www.acpinternist.org/archives/2012/05/policy.htm)
The American Cancer Society (ACS)

"Screening mammography in women aged 40 to 69 years is associated with a reduction in breast cancer deaths"

"Women should have the opportunity to begin annual screening between the ages of 40 and 44 years"
Experts in screening were specifically excluded from the panels! None of the panelists provided care for women with breast cancer.
Unfortunately, the inexpert panels went on to impose their own biases by suggesting that women should delay screening until age 45 (ACS) or age 50 (USPSTF and ACP). Their claim was this would reduce “overdiagnosis”, “overtreatment”, and “false positives”.
Experts need not apply!

By not having experts on the panels allowed “advisors” (opponents of screening) to influence the outcomes.
INEXPERT PANELS

They claim to have weighed the “harms” (primarily recalls from screening) vs. the “benefits” (lives saved), yet neither group explains:

How many fewer recalls are equivalent to having one woman die, unnecessarily, from breast cancer?
Using the NCI/CISNET models it is estimated that waiting until the age of 45 and going to biennial screening at age 55 (ACS) would mean that 38,000 women now in their thirties would die whose lives could be saved by annual screening starting at the age of 40.
USPSTF PANEL IGNORED ITS OWN RESULTS

Using the CISNET models it is estimated that waiting until the age of 50 and screening every two years (USPSTF) would mean that 100,000 women now in their thirties would die whose lives could be saved by annual screening starting at the age of 40.

Despite treatment, more than 40,000 women still die each year in the U.S. despite therapy.
In a major study at the Harvard teaching hospitals, where women had access to modern therapy, the majority of the women who died from breast cancer, were not participating in screening.

71% of the breast cancer deaths were among the 20% of women who were not participating in screening.

The Harvard study would suggest that many of the women who die in the U.S. each year were not participating in screening.

Why doesn’t our National database (SEER) track how cancers are found?
CONSENSUS !!

The fundamental scientific evidence shows that the most lives are saved by annual screening starting at the age of 40.

PERIOD
BREAST CANCER IS NOT A TRIVIAL PROBLEM FOR WOMEN IN THEIR FORTIES
More than 30,000 women are diagnosed with breast cancer each year while in their forties.
Years of Life Lost to Breast Cancer

There are more years of life lost to breast cancer for women ages 40-49 than women ages 50-59.

BREAST CANCER IS NOT A TRIVIAL PROBLEM FOR WOMEN IN THEIR FORTIES

There are more years of life lost to breast cancer among women ages 40-49 than among women ages 50-59.

Since the issues have not changed, and they have all been addressed, scientifically, the continued use of misinformation to deny women access to screening is either due to a failure to understand the data and legitimate scientific analysis, or a malicious effort to mislead.
The effort to reduce access to screening has been going on steadily for decades. We had “ALTERNATIVE FACTS” before they became mainstream!
There are NO DATA (ZERO) to support the use of the age of 50 as a threshold for screening.

None of the parameters of screening change abruptly at the age of 50 or any other age.
The recall rate from screening decreases gradually with increasing age from 8% to 6% with no abrupt change at age 50 or any other age.

(Kopans et al. The Breast Journal 1998;4)
The percentage of women who are recommended for biopsy is fairly constant with no abrupt change at age 50 or any other age.

(Kopans et al. The Breast Journal 1998;4)
The positive predictive value of a biopsy instigated by mammography goes up with the prior probability of cancer in the population with no abrupt change at any age.

The yield of cancer for all mammographically initiated biopsies patients 40-79 years old.

Age 50

(Kopans et al Rad 1996:20)
ANNUAL BREAST CANCER INCIDENCE (per 1000) BY AGE

CANCERS/1000/YEAR

40-44 45-49 50-54 55-59 60-64 65-69 70-74 75-79 80-84
Fact:
The cancer detection rate increases steadily with increasing age along with the steady increase in breast cancer incidence, reflecting the prior probability of breast cancer that increases with age.

There is no abrupt change at age 50 or any other age.
How to make it appear as if the cancer detection rate changes suddenly at the age of 50.
Compared women ages 30-49 to all women ages 50-70+

(Kerlikowske et al – UCSF-JAMA 1993)

Cancers per 1000 women

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-49</td>
<td>2</td>
</tr>
<tr>
<td>50-70+</td>
<td>10</td>
</tr>
</tbody>
</table>
Compared women ages 30-49 to all women ages 50-70+

(Kerlikowske et al – UCSF-JAMA 1993)
USING A MORE APPROPRIATE COMPARISON (40-49 VS. 50-59) THERE IS LITTLE DIFFERENCE

3 per 1000 for women ages 40-49 and 6 per 1000 for women ages 50-59.

With overlapping confidence intervals there is no significant difference.
MORE APPROPRIATE AGE GROUPING BY DECADE

Kerlikowske et al - JAMA 1993

AGE BY DECADES

CANCERS PER 1000 SCREENED
BIASING DATA BY INAPPROPRIATE AGE GROUPING

Kerlikowske et al - JAMA 1993

AGE BY DECADES

CANCERS PER 1000 SCREENED

30-39 40 49/50 59 60-69

AGE BY DECADES

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Kerlikowske et al - JAMA 1993
BIASING DATA BY INAPPROPRIATE AGE GROUPING

Kerlikowske et al - JAMA 1993

The data were made to appear to change abruptly at the age of 50.
INAPPROPRIATE DATA GROUPING CAN BE GREATLY MISLEADING

"The yield [of cancers] of the first mammogram was five times higher in women 50 years of age and older (10 cancers per 1000 studies compared with 2 cancers per 1000 studies)...

Clearly mammography is much more efficient in detecting breast cancers in older women."

(Sox - Annals of Int Med:1995)
HOW YOU WERE MISLED

FACT: Opponents of screening women ages 40-49 have repeatedly grouped them together as if they are a uniform group and compared them to the group of all women ages 50 and over as if they are a uniform group. This also takes factors that change gradually with increasing age and makes them appear to change suddenly at the age of 50.
The age of 50 has been imbued with importance by scientifically unjustified subgroup analyses, and dichotomous data grouping that makes steady changes appear to change at the age of 50. Investigators should know better.
Age grouping has been used to make data that actually change gradually with increasing age appear to change suddenly at the age of 50.

Reality = continuous gradual change

Dichotomous grouping

USPTSF = group by decade
The suggestion that any of the parameters of screening change abruptly at the age of 50 is a myth that is unsupported by any science. Women should be informed, and investigators should cease grouping data to make age 50 appear as if it has any true importance.
MAMMOGRAPHY SCREENING

RADIATION RISK
One of the recurring issues that has been used to dissuade women from mammography screening is the concern over risk of carcinogenesis from radiation.
RISKS AND BENEFITS

The Origin of The Breast Cancer Radiation Fear

In 1976, Bailar suggested that radiation from mammograms would cause more cancers deaths than would be cured.

(Bailar, JC. Ann Intern Med 1976 84:77-84)
Bailar was off by at least an order of magnitude.

The concerns did lead to valuable improvements in technology and a marked reduction in mammographic doses, but exaggerated concerns have persisted.
Misinformation has been perpetuated in journals that are monitored by the media. Susan Love, a “media expert” wrote in the Journal of The American Medical Association, that for every 20,000 mammograms the radiation would cause one breast cancer – just a statement – no reference.

(Lee Davis D, Love SM. Mammographic Screening. JAMA 1994;271:152-153.)
Any exaggerated estimate of radiation risk from mammography was reinforced by Berry in his summary of the Consensus Development Conference in 1997 on mammography screening for women in their forties. This was passed to the public by the media.

RADIATION RISK TO THE BREAST IS TRIVIAL COMPARED TO THE BENEFIT

The major problem with mammography screening is not the radiation risk, which is unmeasurable and small, but, rather, the repeated dissemination of misinformation.
“Large studies have found that earlier mammograms save almost no lives; since the radiation can cause cancer it therefore makes sense to minimize them”

Sharon Begley – Newsweek Dec. 10, 2009
Fact:

Radiation risk to the breast is related to the age at exposure, and drops off rapidly with increasing age.

(NCRP Report No. 149; 2004)
RADIATION RISK DECREASES WITH INCREASING AGE
Fact:
Women treated for Hodgkins disease, with mantle radiation, while in their teens, have a 35% chance of developing breast cancer. The same treatment after the age of 30 results in no excess breast cancer.

RADIATION RISK TO THE BREAST IS AGE RELATED

The undifferentiated breast, in teenage women (and younger), is susceptible to radiation carcinogenesis.

There are no direct data (it is all extrapolated) to show any risk from mammograms for women ages 40 and over.
BREAST CANCERS MAY BE INTIATED EARLY IN LIFE

The developed breast (cellular differentiation) appears to be much less susceptible to radiation carcinogenesis.

? Concentration of stem cells ?
RADIATION RISK TO THE BREAST IS AGE RELATED

The theoretical risk from mammograms, extrapolated from high dose data, is outweighed by even a small benefit.

Hundreds of millions of mammograms have been performed since 1980. If mammograms were causing cancer, the incidence would be increasing among women in their fifties. The incidence of breast cancer has decreased in these women.
THE “HARMS” OF SCREENING

A pejorative term introduced by those interested in reducing access to screening.
THE “HARMS” OF SCREENING

“FALSE POSITIVES”

The effort to reduce access to screening has emphasized the “harms” of screening. These are dominated by the “false positives”.

What they fail to explain is that most “false positives” are women who are recalled from screening for additional evaluation and do not have cancer.
1000 women screened

100 (10%) recalled for additional evaluation
(which is the same as for Pap testing)
65 have a few images or an ultrasound and nothing is found.
26 are asked to return in 6 months
19 have an image guided needle biopsy using local anesthesia
5-8 have breast cancer
19 women out of 1000 have an imaging guided needle biopsy under local anesthesia and 20-40% are found to have breast cancer.

Before there was imaging and surgeons biopsied areas of clinical concern, the yield of cancers was lower (15%) and palpable cancers are larger and later stage, and less likely to be cured than those detected by mammography.

(Spivey GH, Perry BW, Clark VA, & et al, Predicting the Risk of Cancer at the Time of Breast Biopsy. The American Surgeon 1982;48 No.7: 326-332)
WE HAVE A MAJOR PROBLEM!

The major medical journals are preventing an open discussion of important medical issues, and the media have been taught that we are a biased vested interest.
Journals such as:

The New England Journal of Medicine
The Annals of Internal Medicine
The Journal of the American Medical Association
“The Journal of the National Cancer Institute”
(which is not the NCI’s journal)

Have refused to publish work supporting screening while publishing papers opposing screening (particularly for women ages 40-49)
THE “HARMS” OF SCREENING

The argument to reduce access to screening now revolves around the “Harms” of screening.

1. “False Positives”
2. “Overdiagnosis”
3. “Overtreatment”
“OVERDIAGNOSIS” AND “OVERTREATMENT”
It is a diversion to blame these on screening.

Pathologists determine the diagnosis. It is up to them to correctly identify potentially lethal cancers.

Treatment is decided by oncologists who know that they have to overtreat many women because they cannot accurately predict who will benefit.

Blaming screening for “overdiagnosis” and “overtreatment” is like blaming the engines in our cars for traffic accidents!
THE “HARMS” OF SCREENING

The only “harm” that can be reduced by delaying screening are the “false positives” and this is a misnomer. Women are not being told that they have cancer when they do not. These are simply “recalls” from screening when women are reassured that everything is fine. They are, pejoratively, called “false positives”!
The claim is that screening finds cancers that would never become clinically significant. The panels that seek to limit screening argue that these cancers would go away on their own so that waiting until the age of 50 and screening every two years will reduce "overdiagnosis" and hence the "overtreatment" of these fake cancers.
Those seeking to limit access to screening argue that there are “fake” cancers that would go away if left undetected. This is beyond nonsense.

There have been a handful of cancers that have gone away on their own (“miracles” certainly not a common event). Some of the women still died from their “disappearing” cancers!
“FAKE BREAST CANCERS”

The hypocrisy is that the effort is to reduce access to screening despite the fact that the miraculously disappearing cancers were all clinically evident!

Perhaps we should stop treating clinically evident cancers because they may disappear on their own!
There is not a single credible report of an invasive breast cancer, detected by mammography “melting away” on its own. If this occurred as frequently as 30-50% of the time someone should have at least seen a few cases!!
OVERDIAGNOSIS

If there is any ‘overdiagnosis’ from screening it can only be measured from the randomized, controlled trials, and they have suggested that it is, at most, under 10%, and more likely less than 1%.

Claimed that due to screening in 2008 alone:
"breast cancer was overdiagnosed in more than 70,000 women; this accounted for 31% of all breast cancers diagnosed"
BIAS IN THE MEDIA

The next day the New York Times, which has a long history of bias against mammography screening, published an Op Ed piece by Dr. Welch with no rebuttal.

The New York Times
The Opinion Pages

OP-ED CONTRIBUTOR
Cancer Survivor or Victim of Overdiagnosis?
By H. GILBERT WELCH
Published: November 21, 2012
Hanover, N.H.
MISINFORMATION

The NEJM paper had no scientific merit and should not have been published.

1. They did not have direct patient information but relied on registry summaries.
2. They faulted mammography even though they had no idea which women had mammograms and which women had their cancers detected by mammography.
3. They, inappropriately, combined DCIS and small invasive cancers calling them “early breast cancer” to dilute the results for invasive cancers.
In addition to not having direct patient data, the paper was based on assumptions, estimates, extrapolations, and “guesses” which were simply incorrect.
With stable screening annual incidence returns to slightly above prescreening levels (leadtime and new prevalence cancers) with cancers at a smaller size.
What some analysts have misunderstood is that the “baseline” prescreening incidence has been increasing and continued to increase during the screening era.
Once screening participation is stable, the incidence will return to an increasing “baseline” if the prescreening incidence had been increasing.
Screening begins
Use of mammography in the U.S. among women 40 years of age and over

Gradual increase in participation causes a long “prevalence peak”
Use of mammography in the U.S. among women 40 years of age and over


Use plateaus 1999
Utilization of mammography

Gradual increase in participation causes a long “prevalence peak”
Utilization of mammography

Plateau in utilization ends "prevalence peak" with return toward baseline

Bleyer and Welch used data from 1976-1978 to estimate what the baseline breast cancer incidence would have been had screening not been initiated.
Bleyer and Welch used data from 1976-1978 to estimate what the incidence of breast cancer would have been in 2008 had screening not been initiated in the 1980’s.

They ignored the fact that many women were screened after Happy Rockefeller and Betty Ford had breast cancers diagnosed in 1974 and then screening stopped. This was the most unreliable period in the SEER database.

They also ignored 40 years of data.
SEER began in 1973. Bleyer and Welch used data from ‘76-’78 to estimate that the baseline breast cancer incidence would have increased by 0.25% per year if screening had not been initiated.

Bleyer and Welch estimate 0.25% per year baseline increase.
Bleyer and Welch claim that, since there were more cancers diagnosed in 2008 than they estimated should have occurred in the absence of screening, the excess must be “fake” cancers that would have never been clinically evident.
Bleyer and Welch failed to acknowledge that the incidence of invasive breast cancer had been increasing steadily not by 0.25%, but by 1.3% per year since at least 1940.

In fact, the incidence of invasive breast cancer had been increasing by 1-1.3% each year from 1940 to 1980 prior to any national screening.
THE INCIDENCE OF BREAST CANCER HAD BEEN INCREASING FOR DECADES

Introduction of mammography
Promotion of breast self-exam
Introduction of adjuvant chemo/hormonal Rx

Breast cancer incidence and mortality rate per 100,000
Every published estimate of the incidence of breast cancer prior to the start of the SEER registry has relied on the data from the Connecticut Tumor Registry.

STEA DILY INCREASING BACKGROUND INCIDENCE OF UNSCREENED WOMEN IN DENMARK

The Incidence of Fatal Breast Cancer Measures the Increased Effectiveness of Therapy in Women Participating in Mammography Screening

László Tabár, MD; Peter B. Dean, MD; Tony Hsiu-Hsi Chen, PhD; Amy Ming-Fang Yen, PhD; Sam Li-Sheng Chen, PhD; Jean Ching-Yuan Fann, PhD; Sherry Yueh-Hsia Chiu, PhD; May Mei-Sheng Ku, MSc; Wendy Yi-Ying Wu, PhD; Chen-Yang Hsu, PhD; Yu-Ching Chen, MD; Kerri Beckmann, PhD; Robert A. Smith, PhD; and Stephen W. Duffy, MSc

The Incidence of Fatal Breast Cancer/Tabár et al

2% APC continues in non-participants
2% APC prior to any screening
The BASELINE incidence of breast cancer has been increasing since 1940.

CONNECTICUT TUMOR REGISTRY INVASIVE CANCERS 1940-2015

Baseline APC = 1.3% per year

Ad hoc screening after Betty Ford and Happy Rockefeller dx with breast cancer

Pre screening era

Participation plateaus – return toward baseline

APC = 0.7% per year

Below baseline when it should be above. ? Due to removal of DCIS over the years?

Extended prevalence peak as more and more women participate in screening

Data courtesy of:
1940-1972: Connecticut Tumor Registry
“OVERDIAGNOSIS“ IS GROSSLY OVERESTIMATED

In 1940 there were 60 invasive cancers/100,000 rising to 100/100,000 in 1980. If this 1.3% per year increase continued then there should have been more than 143/100,000 in 2008 yet there were only 128/100,000.
In fact, using Bleyer and Welch’s approach, and the correct numbers, there were actually fewer invasive cancers in 2008 than would have been expected.
40 year trend 1% per year increase in baseline for invasive cancers.

The incidence is actually lower than expected showing that there is no overdiagnosis of invasive cancers!

Screening begins in 1940.

60/100,000
Long prevalence peak

60/100,000

1940

Screening begins

40 year trend 1% per year increase in baseline for invasive cancers

Bleyer and Welch estimate 0.25% per year baseline increase

Cancer sites include invasive cases only unless otherwise noted.
Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130). Regression lines are calculated using the Joinpoint Regression Program Version 3.5, April 2011, National Cancer Institute.
Incidence source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).
Bleyer and Welch are incorrect.
The incidence is actually lower than expected showing that there is no overdiagnosis of invasive cancers!
REMOVING DCIS FROM THE POPULATION REDUCES THE NUMBER OF FUTURE INVASIVE CANCERS

It is possible that, with longer follow-up, the removal of moderate and lower grade DCIS will further reduce the number of invasive cancer in the future.
Bleyer and Welch claimed that there had been little if any reduction in advanced breast cancers over the time period (hence little benefit).

Actually, had they used the Connecticut Tumor Registry data

“At an APC [Annual Percentage Change] of 1.3%, late-stage breast cancer incidence decreased by 37%.”

More than 40 experts in breast cancer (including oncologists, surgeons, and several organizations) signed a letter to the editor of the New England Journal calling for a withdrawal of the Bleyer and Welch paper.

The NEJM refused to publish the letter.
Etzioni et al calculated that if Bleyer and Welch are correct, then American radiologists were finding invasive cancers, on average, 9 years prior to their becoming clinically evident. Even the most optimistic studies suggest a “leadtime” of 2 to at most 4 years.

Bleyer and Welch are wrong.

There have now been 3 separate analyses that show that the conclusions of the Bleyer and Welch paper in the NEJM are incorrect.

The paper should have been withdrawn. Its conclusions should not be used to establish screening guidelines.
The “Panels” advise that delaying screening until age 50, and then biennially will reduce “overdiagnosis” (detecting “fake” cancers).
The only way that delaying screening will reduce “overdiagnosis”, if it even exists, is if the “fake” cancers disappear before age 50 or between biennial screens.
No one has ever seen a mammographically detected breast cancer regress or disappear on its own.

In my informal survey of more than 2,000 breast imagers, no one has ever seen this happen.
“…among 240 untreated screen-detected invasive breast cancers, none disappeared or regressed.”

“…among 239 untreated cases of screen detected DCIS, none disappeared or regressed”.

Total = 479

Since, mammographically detected, breast cancers don’t disappear, delaying screening until the age of 50, or screening every two years will not reduce “overdiagnosis” [if it exists at all]. They will be there no matter when you start screening or how long you wait between screens.

The ONLY “harm” that delaying screening until the age of 50 or screening every two years will reduce is “recalls” for additional evaluation, most of which prove to be negative and women are told that everything is fine.

BREAST CANCERS DON’T DISAPPEAR
Reducing access to screening will only reduce “recalls”, but if women now in their thirties wait until the age of 50 and are screened every two years, as many as 100,000 will die whose lives could be saved by annual screening starting at the age of 40.

None of the groups seeking to reduce access have explained how many fewer recalls “balance” allowing one woman to die an avoidable death by delaying screening?!
MORE “ALTERNATIVE FACTS”

THE CLAIM THAT SCREENING DOESN’T REDUCE THE INCIDENCE OF LATE STAGE CANCERS IS FALSE!
DECLINE IN ADVANCED DISEASE WITH SCREENING


DECLINE IN ADVANCED DISEASE WITH SCREENING


“rates for early-stage and late stage tumors diverged in the early 1980s, also consistent with earlier detection over time.

“Breast cancer mortality rates declined 31.6%, slightly more than estimates from randomized screening trials [1, 2]. Thus, the mortality benefit of early detection and intervention seem firm.”


William F. Anderson · Ismail Jatoi · Susan S. Devesa

REGIONAL AND DISTANT DISEASE DECLINED AS MORE AND MORE WOMEN PARTICIPATED IN SCREENING

Fig. 1 Female breast cancer mortality and incidence trends in Connecticut by stage and twelve 5-year time periods of diagnosis (1943–1947 to 1998–2002). Note: ‘Total’ includes in-situ and invasive breast cancers.
Screening begins after Betty Ford and Happy Rockefeller are diagnosed with breast cancer.

REGIONAL AND DISTANT DISEASE DECLINED AS MORE AND MORE WOMEN PARTICIPATED IN SCREENING.
REGIONAL AND DISTANT DISEASE DECLINED AS MORE AND MORE WOMEN PARTICIPATED IN SCREENING

Screening begins after Betty Ford and Happy Rockefeller are diagnosed with breast cancer.
Screening begins after Betty Ford and Happy Rockefeller are diagnosed with breast cancer.
NOTE THAT THE OVERALL INCIDENCE OF INVASIVE CANCERS WAS INCREASING STEADILY GOING BACK TO 1940 SO THE RELATIVE DECLINE IN REGIONAL AND DISTANT DISEASE WAS EVEN GREATER
The authors claimed that the shift to smaller cancers related to mammography screening was, predominantly “overdiagnosed” cancers since the rate of metastatic disease was only slightly reduced.
The authors, incorrectly, decided that the underlying incidence in the absence of screening was defined by the period 1975-1979.
They claimed that in the absence of screening the incidence of cancer would have been a flat line and would have been the same in 2012 as in 1977 (red line).
The actual increase in underlying incidence was 1 - 1.3% per year which is similar to what is seen in the prescreening period from 1979-1982 (green).
If the correct extrapolation is used there is no overdiagnosis (green line). There are actually fewer cancers than expected, likely due to the removal of DCIS lesions preventing them from becoming invasive.
If the correct extrapolation is used the rate of metastatic disease should have increased at the same rate as the other invasive cancers (blue line). This means that the rate of metastatic disease has declined dramatically (red line).
Not only was the conclusion of this paper scientifically unsupportable, but the lead author left Dartmouth having been found guilty of plagiarism!
In 2012 Welch argued that the baseline incidence of breast cancer would have increased by 0.25%-0.5% per year. In this paper for the same time period he claimed it was 0.0%!

Same data, same journal different numbers!

Great peer review at the NEJM!
“ALL CAUSE” MORTALITY
“ALL CAUSE” MORTALITY

If you don’t know what you are talking about it might be a good idea to not talk about it!
One of the more recent pseudo issues raised by those seeking to reduce access to screening is the claim that the 30% reduction in breast cancer deaths in the RCT’s did not, significantly, reduce deaths from all causes.
“ALL CAUSE” MORTALITY

In treatment trials it is important to look at deaths from all causes because your treatment might reduce breast cancer deaths, but cause deaths from other problems.

eg. Breast radiation therapy caused deaths from heart damage.
However, in treatment trials, since everyone has breast cancer, the vast majority of deaths will be due to breast cancer and not from other “all causes” so that a reduction in breast cancer deaths is likely to reduce total (“all cause”) deaths.
In screening trials that evaluate a normal population, a very small number of women develop breast cancer, and an even smaller number die. Most deaths in the trial will be due to causes other than breast cancer.
“ALL CAUSE” MORTALITY IS THE LATEST "NONSCIENCE"

Each year only, approximately, 3% of deaths in the general population are due to breast cancer. A 30% reduction in breast cancer deaths will only reduce, “all cause”, total mortality by 1%. You would need approximately 2.5 million women in a trial to show this reduction as significant.

“ALL CAUSE” MORTALITY THE LATEST "NONSCIENCE"

If you look at women diagnosed with breast cancer in RCT’s (so that they are like treatment trials), reducing breast cancer deaths, significantly, reduces all cause mortality.

!! CAUTION !!

“RISK BASED” SCREENING

And

“VALUE BASED” SCREENING

are stealth efforts to reduce access to screening.
There are two interpretations of “RISK BASED SCREENING”.

1. The ACR and the SBI advise that all women be screened annually starting at the age of 40 with very high risk women beginning at younger ages depending on risk. Women with a lifetime risk of 25% or more should consider alternating mammography with MRI every 6 months.
CAUTION!!

“RISK BASED” SCREENING

2. Groups want to limit screening to women who will develop breast cancer (as if no one ever thought of doing that before). They want to ONLY screen high risk women.
2. Only 10% of women who are diagnosed with breast cancer each year have a BRCA1 or 2 mutation. Another 15% have a family history or other elevator of risk.
!!CAUTION!!

“RISK BASED” SCREENING 2:

It is “pie in the sky” to suggest that screening can be tailored based on risk.

1. The randomized, controlled trials were not stratified by risk so there is no proof that screening only high risk women will save any lives.
"RISK BASED" SCREENING 2:

It is “pie in the sky” to suggest that screening can be tailored based on risk.

2. If we only screen high risk women, 75% of women who develop breast cancer each year will not benefit from early detection.
FACT:
Screening has, consistently, shown a decrease in breast cancer deaths for all women of approximately 30%.

USPSTF SHOWS THAT MOST LIVES ARE SAVED BY ANNUAL SCREENING BEGINNING AT 40
The Bottom Line

Most women who develop breast cancer are not at increased risk.

All women are at risk and annual screening, beginning at the age of 40, should be encouraged for all women.
“Women should be helped to understand the risks of screening; weighing benefits and risks should be done by women, not for women.”