“ALTERNATIVE FACTS”
IN BREAST CANCER SCREENING

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50 YEARS OF MISINFORMATION IN THE EFFORT TO REDUCE ACCESS TO MAMMOGRAPHY SCREENING

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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.
Experts Disagree

Shouldn’t we just “agree to disagree”?
Experts Disagree

Experts can look at the same information and reach different conclusions
A United States naval vessel was barreling through heavy seas at night when a light was seen coming toward it. The captain instructed his signalman to flash the order to the light:
“ALTER YOUR COURSE 10 DEGREES TO STARBOARD”
The signalman sent the message and returned with a reply from the light.

"Change YOUR course 10 degrees to starboard."
This upset and exasperated the captain, so he sent for the signalman and had him send this message:
"This is a United States battleship - I am an admiral in the U.S. Navy - Alter your course 10 degrees to starboard."
The signalman sent the message and returned quickly with the following response:
"I am a boatswain's mate, 3rd class, U.S. Coast Guard - This is a lighthouse - It's your call."
There are truths!
BREAST CANCER SCREENING

THERE ARE FACTS
BREAST CANCER SCREENING

THERE IS ACTUALLY NOW A CONSENSUS BUT IT IS BURIED IN NON-SCIENCE (NONSENSE):

All of the major groups now agree that the most lives are saved by annual screening starting at the age of 40.
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 Cancer Society (ACS) "Screening mammography in women aged 40 to 69 years is associated with a reduction in breast cancer deaths" and that "Women should have the opportunity to begin annual screening between the ages of 40 and 44 years".
CONSENSUS !!

Unfortunately, the inexpert panels (no one on either panel provided care for women with breast cancer) went on to impose their own biases by suggesting that women should delay screening until age 45 (ACS) or age 50 (USPSTF) to reduce the number of recalls from screening!
CONSENSUS !!

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.
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 forties would die whose lives could be saved by annual screening starting at the age of 40.
CONSENSUS !!

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

PERIOD
1. Randomized, controlled trials have, unequivocally, shown a statistically significant mortality reduction for screening beginning at the age of 40.

2. When screening is introduced into general populations the death rate from breast cancer declines.
FIGURE 1
Relative Rate of Breast Cancer Death in the Eight Randomized Trials of Breast Cancer Screening
SCREENING 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.
RCT PROOF THAT SCREENING SAVES LIVES STARTING AT THE AGE OF 40

Effect of mammographic screening from age 40 years on breast cancer mortality in the UK Age trial at 17 years’ follow-up: a randomised controlled trial

Suie M Moss, Christopher Wolfe, Robert Smith, Andrew Evans, Howard Cridle, Stephen W Duffy

Findings Between Oct 14, 1990, and Sept 25, 1997, 160 921 participants were randomly assigned; 53 883 women in the intervention group and 106 953 assigned to usual medical care were included in this analysis. After a median follow-up of 17 years (IQR 16·8–18·8), the rate ratio (RR) for breast cancer mortality was 0·88 (95% CI 0·74–1·04) from tumours diagnosed during the intervention phase. A significant reduction in breast cancer mortality was noted in the intervention group compared with the control group in the first 10 years after diagnosis (RR 0·75, 0·58–0·97) but not thereafter (RR 1·02, 0·80–1·30) from tumours diagnosed during the intervention phase. The overall breast cancer incidence during 17 year follow-up was similar between the intervention group and the control group (RR 0·98, 0·93–1·04).

Interpretation Our results support an early reduction in mortality from breast cancer with annual mammography screening in women aged 40–49 years. Further data are needed to fully understand long-term effects. Cumulative incidence figures suggest at worst a small amount of overdiagnosis.
Breast Cancer Death Rate 1940 - 1990

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
Breast Cancer Death Rate 1940 - 2003

Screening begins

Death rate decreases

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).
39% fewer women now die each year from breast cancer in large part due to screening and earlier detection.

274,765 breast cancer deaths averted (women's lives saved) from 1990 to 2014.

22,054 lives were saved in 2014 alone.

Total Number of Female Breast Cancer Deaths Averted From 1990 to 2012

- The blue line represents the actual number of breast cancer deaths recorded in each year.
- The red line represents the number of breast cancer deaths that would have been expected if breast cancer death rates had remained at their peak rate in 1989.

(Courtesy R. Smith, PhD, ACS)
It has been suggested that the decline in breast cancer deaths is due to improvements in therapy.
There certainly have been therapeutic advances, but numerous observational studies have shown that the death rate declines primarily for women who participate in screening.
DECLINING BREAST CANCER DEATHS

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

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


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!
FAILURE ANALYSIS

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.

More than 30,000 women are diagnosed with breast cancer each year among women in their forties.
BREAST CANCER SCREENING
WHY THE CONTROVERSIES?

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.
BREAST CANCER SCREENING
WHY THE CONTROVERSIES?

“ALTERNATIVE FACTS”

“THE BIG LIE”
(Repeat it enough times and they will believe it is fact)

“POST TRUTH”
The arguments against screening have gone from ridiculous:

“Mammography squeezes cancer into the blood causing early death”

to the outrageous.

“Breast cancer would “melt away” if left undetected.
As each new challenge has been addressed, scientifically, opponents dream up new challenges most of which have no scientific basis.
The “debate” is not about the facts, but has been the result of data manipulation, and pseudoscience that has been permitted and perpetuated by bias and failed peer review at the medical journals, and disseminated by an uncritical media.
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)
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
BIASING DATA BY INAPPROPRIATE AGE GROUPING

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.
"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)
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 USPSTF GUIDELINES ARE SCIENTIFICALLY UNSUPPORTABLE

By grouping the data by decades, the USPSTF misled the public –

A woman age 48 is much more like a woman age 52 than she is like a woman age 42.
FACTS:

Why start screening at the age of 40?

The Randomized, Controlled Trials, included women ages 40-74. From the beginning they showed reduced deaths for all women who were invited to participate ages 40-74.
1970’s Bailar falsely claims radiation will cause more cancers than will be cured. BCDDP halts screening women ages 40-49

1980’s HIP showed “delayed” benefit for women ages 40-49 (actually expected due to length bias) misinterpreted as the benefit starts at age 50

1990’s Canadian National Breast Screening Study claimed mammography was leading to earlier deaths among women ages 40-49. Likely due to unblinded allocation process.

1993 Using unplanned retrospective subgroup analysis lacking power, the benefit for women ages 40-49 was not STAT SIG so NCI drops support for screening women ages 40-49
FICTION AND LIES
TO REDUCE ACCESS TO SCREENING (RATS)

1993 – Kerlikowske et al group women 30-49 and average cancer detection rate comparing it to the average for women ages 50-74 suggesting a sudden jump when non exists.

1995 Benefit begins to show up in women 40-49 called “AGE CREEP” – claims they reached age 50 and screening began to work

1997 AGE CREEP recanted. With AGE Trial benefit for women ages 40-49 becomes irrefutable.

2007-2016 RATS effort claims “harms” out weigh the benefit for women ages 40-49. Harms = Recalls from screening (called “false positives”) and “Overdiagnosis”

2007-2017 RATS claim mammographically detected breast cancer would disappear if left undetected.
Fact:

There are no data (NONE !!!!) that 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. Even menopause has no demonstrated effect.

THE USPSTF GUIDELINES ARE SCIENTIFICALLY UNSUPPORTABLE
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

(Kopans et al Rad 1996:200)
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.
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.
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)
BREAST CANCER SCREENING

FICTION

7. Mammography screening leads to false positive studies that lead to biopsies that permanently scar the breast so that when a lesion is palpable the mammogram is useless – (1994)

8. The benefit must appear within 5 years – (1993-1997). If not screening is less effective.

9. The breast tissues are dense prior to the age of 50 hiding most cancers. At age 50 the breasts turn to fat and screening begins to save lives. (1993-1997)

10. There is so little breast cancer among women in their forties that we should concentrate on screening women ages 50 and over – (1994)
11. Age Creep – Women reached the age of 50 and screening began to work.

12. 1997 Consensus Development Conference - There is no reason to encourage women in their forties to be screened – (1997)


14. 2000 Gotzsche and Olsen Lancet – There is no benefit from screening for women at any age.

16. The incidence of breast cancer has decreased because of reduced use of hormones - 2007
17. Screening women in their forties should be based on their risk of developing breast cancer (2008).
19. Since mammography does not find the fastest most aggressive cancers it is not very useful (Esserman JAMA 2009)
20. “Screening leads to massive overdiagnosis.

21. Money can be saved by allowing women to die from breast cancer by starting screening at age 50 and screening every two years.

22. Women fifty and over are not reliably returning – Let’s concentrate on them.

23. The screening data are outdated (RCT’s). Improved therapy is the reason lives are being saved.

24. Screening doesn’t work because it did not reduce “all cause mortality” in the randomized controlled trials.”
25. Screening doesn’t work because it doesn’t reduce the rate of advanced cancers.
26. Screening everyone is “old fashioned”. We need “value based” screening.
THE DECADES LONG EFFORT TO REDUCE ACCESS TO 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.
THE “HARMS” OF SCREENING

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

RECALLS FROM SCREENING

1000 women screened

100 (10%/1000) recalled for additional evaluation (which is the same as for Pap testing)

65 (6.5%/1000) have a few images or an ultrasound and told everything is fine.

26 (2.6%/1000) are asked to return in 6 months

19 (1.9%/1000) have an image guided needle biopsy using local anesthesia

5-8/1000 have breast cancer
Opponents of screening seek to deny women access to screening to reduce inconvenience and some anxiety.
ALMOST ALL BREAST CANCERS ARE OVERTREATED

It is not just screen detected cancers, but all breast cancers are overtreated since it is not possible to determine who will actually benefit.

ALMOST ALL BREAST CANCERS ARE OVERTREATED

Only 10% of women treated with systemic therapy under the age of 50 actually benefit from the systemic therapy. Mortality at 15 years is 42.4% for no chemotherapy and 32.4% for poly chemotherapy.

Almost all breast cancers are overtreated

Only 3% of women treated with systemic therapy ages 50-69 actually benefit from the systemic therapy.

Mortality at 15 years is 47.4% for no chemotherapy and 50.4% for polychemotherapy

WE HAVE A MAJOR PROBLEM!

The major medical journals are preventing an open discussion of important medical issues.
The New England Journal of Medicine continues to publish misleading, and scientifically unsupportable material about mammography screening and has, repeatedly, refused to publish analyses that support screening.

Purported to show that screening women in Norway had very little effect on mortality. The paper had only 2.2 years of follow-up. The material was completely specious since the benefit from screening does not begin to appear until 3-5 years after it is instituted.
The benefit from screening does not begin to appear until 3-5 years after it is instituted.

30 year results from the Swedish Two County Trial shows deaths begin to decline 5 years after the start of screening.

They were looking for a decline in deaths after screening was instituted in the national program. They neglected to point out that more than 40% of women were being screened before the national program began. Deaths had already declined due to screening.
MISINFORMATION

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”
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.
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, and extrapolations which were simply incorrect.
In order to dilute the benefit of screening in their analysis, Bleyer and Welch combined DCIS and small invasive cancers calling them “early stage cancer”.

There is legitimate debate about DCIS, but there is no justification for combining it with small invasive lesions.
THE “NORDIC COCHRANE CENTER” & THE DARTMOUTH INSTITUTE HAVe PROMULGATED MISINFORMATION BY MISUNDERSTANDING FUNDAMENTALS

Expected Change in Incidence with Screening

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.
THE “NORDIC COCHRANE CENTER” & THE DARTMOUTH INSTITUTE HAVE PROMULGATED MISINFORMATION BY MISUNDERSTANDING FUNDAMENTALS

Once screening participation is stable, the incidence will return to an increasing “baseline” if the prescreening incidence had been increasing.
Screening begins

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, San Jose/Monterey Counties, California, and Utah).
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”
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 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.
MISINFORMATION

Bleyer and Welch failed to acknowledge that the incidence of invasive breast cancer had been increasing steadily not by 0.25%, but by 1% per year since at least 1940.

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

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.


In 1940 there were 60 invasive cancers/100,000 rising to 100/100,000 in 1980. If this 1% per year increase continued then there should have been more than 130/100,000 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.
Screening begins

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

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

1940

60/100,000
If the correct extrapolation is used (1% per year) then there should have been 132 women with cancer/100,000 women in 2008.

SEER estimates there were 128.

Bleyer and Welch are incorrect.
The incidence is actually lower than expected showing that there is no overdiagnosis of invasive cancers!
Bleyer and Welch are incorrect.

Not only was there no overdiagnosis, but there were fewer invasive cancers than expected following the start of national screening in the mid 1980’s (as many as 16/100,000 if APC was 1.3%).

It is likely that the removal of DCIS lesions over the years has resulted in fewer invasive cancers.
It is likely that with longer follow-up the removal of moderate and lower grade DCIS will further reduce the number of invasive cancer in the future.
Not only is there no overdiagnosis of invasive cancers, but there were fewer than expected. This may be because DCIS has been removed over preceding years.
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

Age-Adjusted SEER Incidence Rates
By Cancer Site
All Ages, All Races, Female
1975-2009 (SEER 9)
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.
MISINFORMATION

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.

MISINFORMATION

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 be withdrawn. Its conclusions should not be used to establish screening guidelines.
Despite having been discredited years ago as a compromised trial, the CNBSS reported a 25 year follow-up and concluded that there was no benefit from mammography screening for anyone ages 40-59.

Proper design and execution of RCT is critical.
RANDOMIZED/CONTROLLED TRIALS

Randomization must be blinded
SUCCESSFUL RANDOMIZATION
SUCCESSFUL RANDOMIZATION
SUCCESSFUL RANDOMIZATION

Them same number will die of cancer over time.
SUCCESSFUL RANDOMIZATION

If fewer women die in the screened group over time, then efficacy can be shown.
RANDOMIZATION
BIAS

CHANCE OR
COMPROMISED
PROCESS
RANDOMIZATION

BIAS

CHANCE OR
COMPR O ISED
PROCESS
BIASED ALLOCATION IMBALANCE LEADS TO APPARENT EXCESS DEATHS
Author of Canadian Breast Cancer Study Retracts Warnings

A major study designed to dispel the doubts about the value of mammographic screening in women ages 40 to 49 has instead raised the index of uncertainty. Leaks of preliminary data from the Canadian National Breast Screening Study have periodically seeped into the news over the last year, informing readers that women ages 40 to 49 who underwent mammography as part of a physical examination had a higher death rate.

Anthony B. Miller, M.B., F.R.C.P., a University of Toronto epidemiologist, presented preliminary results of his study in April 1991 at the Second International Cambridge Conference on Breast Cancer Screening. At that time, the data indicated a 52% increase in breast cancer mortality in the group of women ages 40 to 49 who were screened.

In subsequent newspaper articles, Miller and his colleague Cornelia Baines, M.D., were quoted offering putative physiologic mechanisms for their findings. In one, they said cancer cells were squeezed into the bloodstream under the pressure of the mammographic plates. In another, they said the excess deaths may have been in women who harbored the still unidentified gene for ataxia telangiectasia, which is thought to increase the risk of radiation-induced breast cancer.
RCT’S require blinded allocation which was totally violated in the CNBSS:

1. All women had a CBE first so they knew who had palpable lesions (cancers) and positive axillary nodes
2. Women were allocated on open lists so that lines could be skipped to insure a woman was placed in the mammography group.

The Canadian National Breast Screening Study (CNBSS)

The Data Clearly Show Compromise of Random Allocation:

1. Significant excess of women with advanced cancers in the screening arm
2. More deaths in the screening group in first 10 years
3. Greater than 90% 5 year survival in the control women while background in Canada was only 75%. Impossible without moving cancers from control to screening arm.
Not only did the CNBSS violate the fundamental requirements of RCT, but these were trials of mammography screening. You would expect that the quality of the mammograms would be high, but they were, in fact, poor to unacceptable for much of the trials.
Documented poor quality mammography.

1. Old devices (10 years old in Vancouver) at least 1 second hand.
2. No grids
3. No training for techs – used straight lateral not MLO
4. No training for the radiologists
5. Mammo size cancers = 1.9 cm Controls = 2.1 cm
Documented poor quality mammography.

"..in my work as reference physicist to the NBSS, [I] identified many concerns regarding the quality of mammography carried out in some of the NBSS screening centers. That quality [in the NBSS] was far below state of the art, even for that time (early 1980's). “

(Yaffe MJ. Correction: Canada Study. Letter to the Editor JNCI 1993;85:94).
Poorly Positioned Mammogram
Cancer Is Now Much Larger And Visible A Year Later
Cancer missed due to poor positioning

Cancer is now much larger and visible a year later.
No Grid
Same Day Same Patient With A Grid – The Cancer Is Obvious
No grid – even a large cancer is hard to see

Same patient, same day with a grid – the cancer is obvious
Images provided by Martin Yaffe, PhD. Reference Physicist Canadian National Breast Screening Study
The CNBSS claimed they showed major overdiagnosis.

Over-diagnosis

At the end of the screening period, an excess of 142 breast cancer cases occurred in the mammography arm compared with control arm (666 v 524) (fig 4⇓). Fifteen years after enrolment, the excess became constant at 106 cancers. This excess represents 22% of all screen detected invasive cancers—that is, one over-diagnosed breast cancer for every 424 women who received mammography screening in the trial.
OVERDIAGNOSIS ????
Since mammography finds cancers years in advance you can’t just look at the screening period. The CNBSS data show for total cancers:

<table>
<thead>
<tr>
<th>Year of study</th>
<th>Mammography arm (n=44,925)</th>
<th>Control arm (n=44,910)</th>
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<tr>
<td></td>
<td>No of cancers detected</td>
<td>Mean size (cm)</td>
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<tr>
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<td>253</td>
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</tr>
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<td>Subtotal years 11-25</td>
<td>2,070</td>
<td>—</td>
</tr>
<tr>
<td>Subtotal years 6-25</td>
<td>2,564</td>
<td>—</td>
</tr>
<tr>
<td>Total years 1-25</td>
<td>3,250</td>
<td>—</td>
</tr>
</tbody>
</table>

Mammography arm

Control arm
NO MAJOR OVERDIAGNOSIS

In fact, there was no 22% “overdiagnosis” but it was less than 4%.

If the correct numbers are used the CNBSS data show there were only 117 more cancers in the screening arm than the control arm \([3250 - 3133 = 117]\) which is only a 4% \([117/3133 = 0.37]\) overdiagnosis rate and not the 22% claimed by the CNBSS.
The CNBSS results have been ignored in Canada. The provinces have continued to support breast cancer screening and just reported there has been a major decline in breast cancer deaths as a result.
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.

<table>
<thead>
<tr>
<th>Region</th>
<th>SMR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>0.58</td>
<td>0.54 to 0.62</td>
</tr>
<tr>
<td>Manitoba</td>
<td>0.60</td>
<td>0.52 to 0.68</td>
</tr>
<tr>
<td>Ontario</td>
<td>0.73</td>
<td>0.68 to 0.78</td>
</tr>
<tr>
<td>Quebec</td>
<td>0.59</td>
<td>0.55 to 0.64</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>0.41</td>
<td>0.33 to 0.48</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>0.64</td>
<td>0.54 to 0.74</td>
</tr>
<tr>
<td>Newfoundland and Labrador</td>
<td>0.67</td>
<td>0.42 to 0.91</td>
</tr>
<tr>
<td>Summary (random)</td>
<td>0.60</td>
<td>0.52 to 0.67</td>
</tr>
</tbody>
</table>

The “debate” is not about the facts, but has been the result of data manipulation, and pseudoscience that has been permitted and perpetuated by bias and failed peer review at the medical journals, and disseminated by an uncritical media.
There is not a single credible report of an invasive breast cancer “melting away” on its own. If this occurred as frequently as 50% of the time someone should have at least seen a few cases.

The “Nordic Cochrane Center” has promulgated misinformation.
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%.

“RISK BASED” SCREENING:

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.

2. If we only screen high risk women we will miss 75-90% of women who develop breast cancer each year.
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.

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].
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.
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. If breast irradiation causes 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.
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.
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.

There seems to be no end to the non-science.
It is unclear why there has been such a determined and relentless effort to reduce access to screening that has been based on misinformation and the misinterpretation of data.
Periodically, a possible motive ‘slips out”, when physician “analysts” drop into their “better health care argument” that insurance companies should not be graded on the number of women screened and should not have to pay to support screening.
“...mammography screening .... The time has come for it to stop being used as an indicator of the quality of our health care system.”

“...as our society debates whether to continue to require insurance companies to pay for mammograms,“

(http://www.forbes.com/sites/peterubel/2015/09/08/has-mammography-created-an-epidemic-of-pseudo-survivorship/)
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 1976-1978.
They claimed that in the absence of screening the incidence of cancer in 2012 would have been the same as in 1977 (red line).
The actual increase in underlying incidence was 1% per year which is seen in the period 1979-1982 (green).
If the correct extrapolation was 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).
Results: A representative sample of the 108 actively practicing Society of Breast Imaging fellows (n = 42 [39%]) participated, each reporting outcomes data from his or her entire screening mammography practice.

Among all practices, 25,281 screen-detected invasive breast cancers and 9,360 cases of screen-detected ductal carcinoma in situ were reported over the past 10 years. Among these cancers, there were 240 cases of untreated invasive breast cancer and 239 cases of untreated ductal carcinoma in situ, among which zero were reported to have spontaneously disappeared or regressed at next mammography.


BREAST CANCERS DON’T DISAPPEAR
“…among 240 untreated screen-detected invasive breast cancers, none disappeared or regressed.”

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

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.

CONSEQUENCES OF VARIOUS GUIDELINES

For women age 40:

Lifetime deaths averted

ACR: 29,369
ACS: 22,829
USPSTF: 17,153

For women age 40 Lifetime deaths averted

ACR vs. USPSTF and ACS

ACR - USPSTF  
29,369 – 17,153 = 12,216

ACR - ACS:  
29,369 - 22,829 = 6,540

“…unless breast cancers actually can regress and disappear (which no one has ever observed for an invasive cancer found by mammography), delaying the age at which screening is started and extending the time between screens will have no effect on “overdiagnosis”, since “overdiagnosed” cancers still will be present at the age of 45 or 50 and still will be present whether screening is annual or biennial.

“Women should be helped to understand the risks of screening; weighing benefits and risks should be done by women, not for women.”

The effort to reduce access to mammography screening is a major medical disgrace that has gone on unchecked. Several of the high profile medical journals have promoted their undeclared biases by censoring the publication of legitimate science while publishing scientifically unsupportable material that has misled physicians and the public.

THIS NEEDS TO STOP!
Mammography screening is not the ultimate answer to breast cancer. It does not find all cancers and does not result in a cure in all cases, but it is available today and is saving thousands of lives each year.

While we await a cure, or a safe way to prevent breast cancer (neither is on the horizon) it makes no sense to reduce access to screening.