!! THANKS TO LOUISE MILLER !!

I just want to add my thanks and deep gratitude to Lousie Miller for her extraordinary career studying, improving, and teaching how best to perform breast evaluation and to provide the best care for our patients! Her efforts have greatly improved screening and early detection which has saved hundreds of thousands of lives!

Thank You Louise !

Dan Kopans

1

Thank you for giving me the opportunity to speak with you today.

DISCLOSURES

I am a consultant to DART Imaging which is building Digital Breast Tomosynthesis (DBT) devices for China.

I am on the Board of Malcova which is developing a novel Breast CT System

I receive royalties from IZI Medical for my hookwire localization system.

2

FICTION AND FACTS IN BREAST CANCER SCREENING

Daniel B. Kopans, M.D.

Professor of Radiology
Harvard Medical School
Founder - Breast Imaging Division
Massachusetts General Hospital

3

Unfortunately, the COVID pandemic has exposed the tragic consequences that result from ignoring science and evidence and relying on "alternative facts", misinformation, and ***actual lies***!!.

4

OBJECTIVES

1. To provide multiple examples of misinformation that have been promoted over decades concerning breast cancer screening.

2. To provide facts that have resolved many of the false claims that have been promoted over the decades concerning breast cancer screening.

5

BREAST CANCER SCREENING

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.

6

FALSE CLAIMS !

The "debate" about breast cancer screening has been going on for so long that many (! most) are unaware of the incredible amount of misinformation that has been promulgated over decades that has formed a false foundation for arguments against screening.

7

Decades of "alternative facts" and misinformation have confused the issues surrounding breast cancer screening.

8

FALSE CLAIMS !

Many of you who are new to the issues surrounding breast cancer screening are more likely to believe that the arguments are valid on both sides because they are unaware of the false underpinnings of the "debate".

9

"Experts Disagree"

Shouldn't we just

"agree to disagree"?

10

"Experts Disagree"

Experts can look at the same information and reach different conclusions

11

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:

12

“ALTER YOUR COURSE 10 DEGREES TO STARBOARD”

13

The signalman sent the message and returned with a reply from the light.

"Change *YOUR* course 10 degrees to starboard."

14

This upset and exasperated the captain, so he sent for the signalman and had him send this message:

15

"This is a United States battleship - I am an admiral in the U.S. Navy - Alter your course 10 degrees to starboard."

16

The signalman sent the message and returned quickly with the following response:

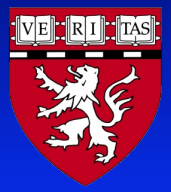
17

"I am a boatswain's mate,
3rd class, U.S. Coast Guard
- This is a lighthouse -

It's your call."

18

There are truths !



19

BREAST CANCER SCREENING

THE EARTH IS NOT FLAT!

20

FALSE CLAIMS !

1950's

21

FALSE CLAIMS !

1950's

"Breast cancer is systemic before you can find it. You cannot find it early enough to make a difference."

(This was the origin of efforts to develop systemic therapeutic agents)

22

FACTS

EARLY DETECTION CAN SAVE LIVES

The Health Insurance Plan (HIP) of New York was the first Randomized, Controlled Trial (RCT) of screening.

HIP proved that screening and earlier detection could detect cancers at a time before successful metastatic spread, and lead to cures.

(Shapiro S. Evidence on Screening for Breast Cancer from a Randomized Trial. Cancer. 1977;39:2772-278)

23

FALSE CLAIMS !

1960's

24

FALSE CLAIMS !

1960's

It is not possible to screen large numbers of women efficiently and effectively

25

FACTS

1970's

The Breast Cancer Detection Demonstration Project (BCDDP) of the 1970's screened more than 250,000 women efficiently and effectively over a 5 year period.

(Baker LH. Breast Cancer Detection Demonstration Project: five-year summary report. CA Cancer J Clin. 1982 Jul-Aug;32(4):194-225.)

26

The Breast Cancer Detection Demonstration Project (BCDDP)

275,401	Women screened
4,443	Cancers detected
3,557	Cancers detected at screening
886	Cancers detected after a normal screen (20%)
1,481	Cancers found only by mammography (42%)
308	Cancers found only by physical examination (9%)

(Baker LH. Breast Cancer Detection Demonstration Project: five-year summary report. CA Cancer J Clin. 1982 Jul-Aug;32(4):194-225.)

27

FALSE CLAIMS !

1970's

28

FALSE CLAIMS !

1970's

The radiation from mammography will cause more cancers than will be cured.

(Bailar, JC. Mammography: A contrary view. Ann Intern Med 1976 84:77-84.)

29

CONSEQUENCE

1970's

Because of the radiation scare the BCDDP stopped screening women ages 40-49.

30

FACTS:

The breast is susceptible to radiation carcinogenesis while it is developing (? High concentration of stem cells?)

Women exposed to high doses of radiation while in their teens had an increased risk of developing breast cancer (Hiroshima and Nagasaki).

31

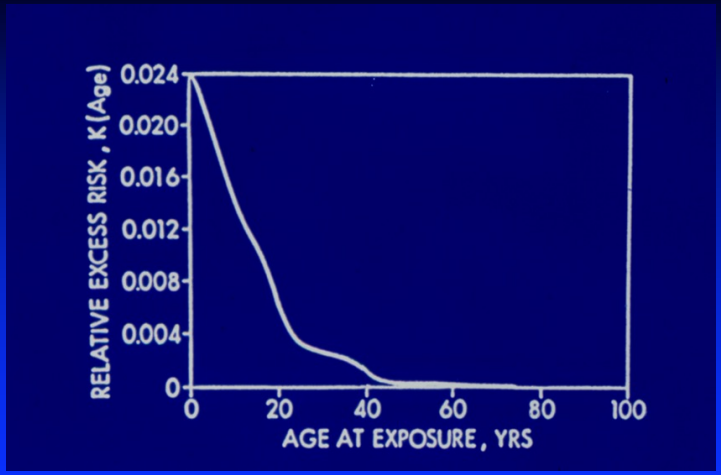
FACTS

Radiation risk to the breast drops rapidly with increasing age. There is little or no excess risk from radiation to the breast after the age of 30 (probably related to terminal differentiation).

(Hancock SL, Tucker MA, Hoppe RT. Breast Cancer After Treatment of Hodgkin's Disease. J Natl Cancer. Inst 85:25-31, 1993)

32

RADIATION RISK DECREASES WITH INCREASING AGE



33

FACTS

RADIATION RISK:

The risk for women ages 40 and over is so small that it is *unmeasurable*.

All the estimates are based on extrapolations from high doses at younger ages and even these risks are well below even the smallest benefit.

34

FACTS

RADIATION RISK:

EVEN THE *THEORETICAL* RISK IS OUTWEIGHED BY EVEN THE SMALLEST BENEFIT BENEFIT

1. Feig SA: Hypothetical breast cancer risk from mammography: A reassuring assessment. Breast 5:2-6, 1980.
2. Mettler FA, Upton AC, Kelsey CA, Rosenberg RD, Linver MN. Benefits versus Risks from Mammography: A Critical Assessment. Cancer 1996;77:903-909.
Feig SA, Hendrick RE. Radiation risk from screening mammography of women aged 40-49 years. J Natl Cancer Inst Monogr. 1997;(22):119-24. Review.
3. Hendrick RE. Radiation doses and cancer risks from breast imaging studies. Radiology. 2010 Oct;257(1):246-53.
4. Yaffe MJ, Mainprize JG. Risk of radiation-induced breast cancer from mammographic screening. Radiology. 2011 Jan;258(1):98-105. doi: 10.1148/radiol.10100655. Epub 2010 Nov 16. Erratum in: Radiology. 2012 Jul;264(1):306.
5. Miglioretti DL, Lange J, van den Broek JJ, Lee CI, van Ravesteyn NT, Ritley D, Kerlikowske K, Fenton JJ, Melnikow J, de Koning HJ, Hubbard RA. Radiation-Induced Breast Cancer Incidence and Mortality From Digital Mammography Screening: A Modeling Study. Ann Intern Med. 2016 Feb 16;164(4):205-14.

35

FALSE CLAIMS !

RADIATION RISK

The specter continues to be raised to add uncertainty, but most (even the USPSTF and the ACP) now realize that the risk for women ages 40 and over is inconsequential.

36

FALSE CLAIMS !

1980's

37

FALSE CLAIMS !

1980's

There is no benefit from screening women ages 40-49.

38

ALTERNATIVE FACT

THE ORIGIN OF AGE 50 AS A THRESHOLD FOR SCREENING

Since breast cancer is clearly related to hormones, the HIP investigators wanted to determine if menopause had any influence on their results. Since they had not collected data on menopause,

they used the age of 50 as the average age of menopause.

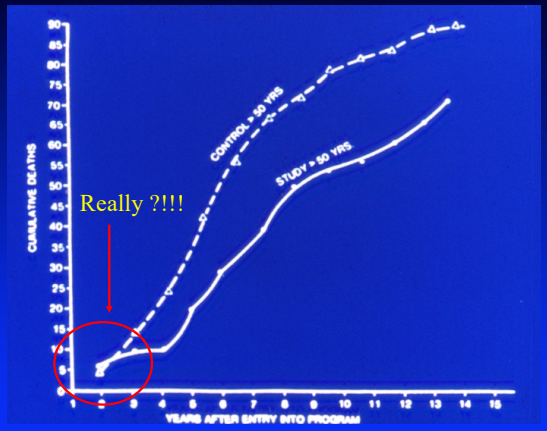
39

MISINFORMATION !

Using the age of 50 as the "average age of menopause", the HIP used unplanned, retrospective subgroup analysis of data lacking statistical power and evaluated women ages 40-49 separately from ages 50-64.

40

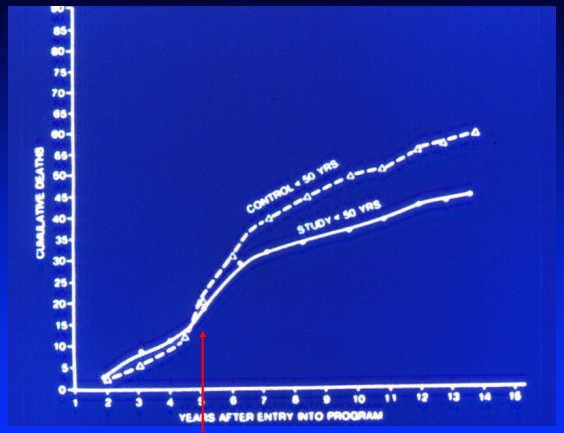
HIP WOMEN AGES 50-64



For women ages 50-64, the data suggested that screening saved lives, immediately!!!

41

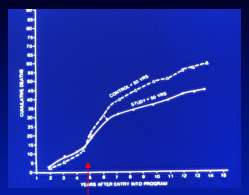
WOMEN AGES 40-49

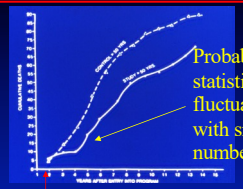


The data suggested that the benefit for women ages 40-49 was delayed, and, therefore, ?? not as robust??

42

HIP DATA WERE MISINTERPRETED





Probably statistical fluctuation with small numbers

40-49 the deaths did not diverge until 5-7 years

50-64 the curves began to diverge immediately

Screening is very unlikely to save lives immediately! The curves for the younger women make scientific sense due to "length biased sampling". The curves for ages 50-64 are likely statistical fluctuation with small numbers.

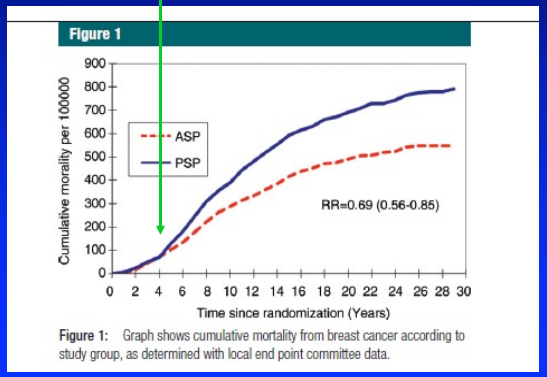
(Kopans DB. Screening for breast cancer and mortality reduction among women 40-49 years of age. Cancer. 1994 Jul 1;74(1 Suppl):311-22.)

43

FACTS

The benefit from screening is not expected to 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



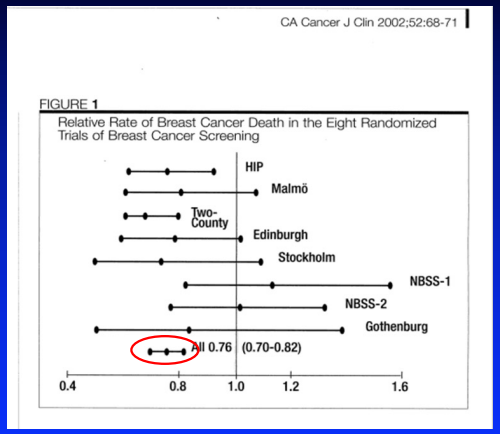
44

THERE IS A BENEFIT FOR ALL WOMEN AGES 40-74

This was finally proven with longer follow-up that provided the statistical power to permit legitimate evaluation of women ages 40-49.

45

FACTS



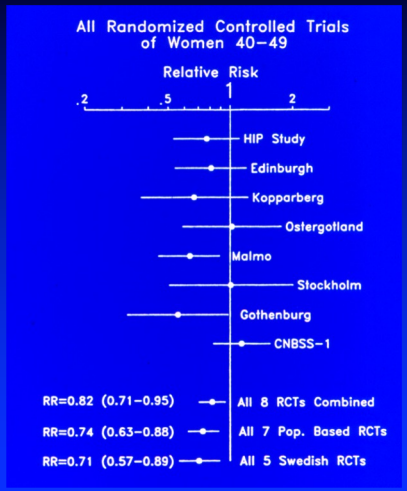
SCREENING SAVES LIVES FOR WOMEN AGES 40-74

46

SCREENING FOR WOMEN AGES 40-49

Although the RCT were never intended to be analyzed by age groups, with longer follow-up, 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

Hendrick RE et al. Benefit of screening mammography in women ages 40-49: a new meta- analysis of randomized controlled trials. Journal of the National Cancer Institute Monograph 22: 87-92, 1997.



47

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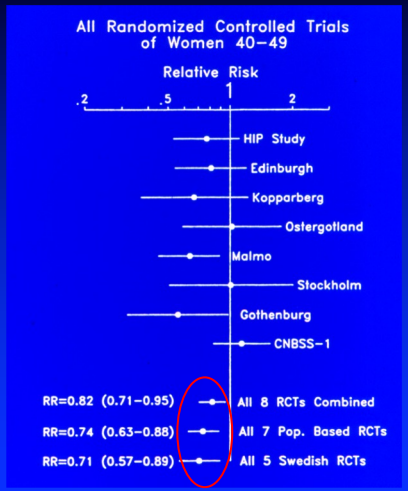

48

FALSE CLAIMS !

1990's

49

PREDETERMINED EFFORT

1993

The NCI held the

"INTERNATIONAL WORKSHOP ON BREAST CANCER SCREENING"

Bethesda, Maryland Feb. 24-25, 1993

to review the data on screening, especially, for women ages 40-49.

50

1993 INTERNATIONAL WORKSHOP ON BREAST CANCER SCREENING WAS LOADED AGAINST SCREENING WOMEN AGES 40-49

1. The Chairperson chosen for the NCI "Workshop" had already written an editorial arguing against screening women ages 40-49.
2. Daniel Kopans, M.D. ***was the only one invited to defend screening for women ages 40-49*** while numerous other invitees argued against screening women ages 40-49
3. The workshop was based on data from the compromised Canadian National Breast Screening Studies (CNBSS), and on an unplanned, retrospective subgroup analysis of the trials which lacked statistical power to permit this.

51

FACTS

1993

Dr. Kopans raised concerns about the Canadian studies:

(Kopans, DB. The National Breast Screening Study of Canada. A Critical Review of the Results for Women Ages 40-49. Presented to the International Workshop on Screening of Breast Cancer, Bethesda, Maryland Feb. 24-25, 1993)

52

FACTS

1993

Dr. Kopans also explained that the other trials were not designed to evaluate women ages 40-49, separately, so, lacking statistical power, grouped conclusions were not valid.

(Kopans DB, Halpern E, Hulka CA. Statistical Power in Breast Cancer Screening Trials and Mortality Reduction Among Women 40-49 with Particular Emphasis on The National Breast Screening Study of Canada. Cancer 1994;74:1196-1203.)

53

INAPPROPRIATE ANALYSIS OF DATA FROM THE RANDOMIZED, CONTROLLED TRIALS OF SCREENING

If statistical power were not important, then only a few people would be needed for any trial!

54

THE INAPPROPRIATE USE OF UNPLANNED RETROSPECTIVE SUBGROUP ANALYSIS OF THE SCREENING TRIAL DATA CREATED FALSE CLAIMS

The trials were not designed to permit subgroup analysis of women ages 40-49 and lacked any statistical power.

(Kopans DB, Halpern E, Hulka CA. Statistical Power in Breast Cancer Screening Trials and Mortality Reduction Among Women 40-49 with Particular Emphasis on The National Breast Screening Study of Canada. Cancer 1994;74:1196-1203.)

55

SCREENING WOMEN AGES 40-49
THE STATISTICAL POWER OF THE TRIALS

To have an 80% power to prove a 25% mortality benefit with a 95% certainty that the result is not due to chance (is statistically significant) with a follow-up of 5 years after the first screen

56

SCREENING WOMEN AGES 40-49
THE STATISTICAL POWER OF THE TRIALS

Would require 1440 cancers in each arm of the trial assuming unscreened controls have an 80% five year survival.

235,294 women would be needed in both arms

Total = 479,588

(Kopans et al - Cancer 1994)

57

THE RANDOMIZED CONTROLLED TRIALS OF SCREENING

HIP	600	4%	1400
Kopke	511	2%	1455
Gabriel	284	2%	6835
Miller	400	8%	747
Shapiro	600	3%	2242
Cuzick	455	8%	900
Edwards	600	8%	1173
NBSS	900	3%	3000
TOTAL			19322

Number of women under age 50 *in all of the RCT's combined*

58

THE RANDOMIZED CONTROLLED TRIALS OF SCREENING

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Kopke	511	2%	1455
Gabriel	284	2%	6835
Miller	400	8%	747
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Cuzick	455	8%	900
Edwards	600	8%	1173
NBSS	900	3%	3000
TOTAL			19322

Just "a bit shy" of the 480,000 needed to prove 25% mortality reduction!!

59

THE RANDOMIZED/CONTROLLED TRIALS

In all of the world's trials, *put together*, there were fewer than half the women needed to permit accurate statistical analysis of the subgroup of women ages 40-49 in the early years of follow-up.

Disregarding the science, health planners advised women and their physicians based on an illegitimate analysis.

60

FALSE CLAIMS !

1993

Ignoring the fundamental scientific facts, the summary of the "Workshop" – written by declared opponents of screening - falsely claimed there was no benefit from screening women ages 40-49.

(Fletcher SW, Black W, Harris R, Rimer BK, Shapiro S. Report of the International Workshop on Screening for Breast Cancer. J Natl Cancer Inst 1993;85:1644-1656.)

61

MISINFORMATION !

1993

Continuing to ignore the facts, the NCI held a series of meetings over the course of the year to prepare the public for a guidelines change using "loaded" panels.

62

FALSE CLAIMS !

False claims were made to support the NCI position.

63

FALSE CLAIMS !

1990's

"Screening will lead to biopsies of benign lesions that will permanently scar the breast so that when a woman has a lump, mammography will be useless."

Paraphrase: Cindy Pearson, Spokesperson - National Women's Health Network. ABC Television - Nightline - March 19,1993 11:30, EDT.

[Kopans DB. Three false claims in a "single breath hold!"]

64

FACTS

1. Mammography is rarely "diagnostic" so saving it to evaluate a lump has little value. It is a screening test.
2. By the time a woman has a lump, the value of early detection has been lost.
3. Properly performed surgery rarely leaves any confusion on subsequent mammograms.

(Slanetz PJ. Giardino AA, McCarthy KA, Hall DA, Halpern EF, Moore RH, Kopans DB. Having Undergone Benign Breast Biopsy Rarely Complicates or Alters Interpretation of Screening Mammography. Am J Roentgenology 1998;170:1539-1541.)

65

FACTS WERE IGNORED !

AT THE END OF 1993

The NCI Board of Scientific Counselors told NCI to continue screening women ages 50 and over annually.

The National Cancer Advisory Board (NCAB) told NCI to NOT change any of the guidelines!

66

FACTS IGNORED !

1993

At the end of 1993, and *for the first time in its history, the NCI ignored the advice of the National Cancer Advisory Board (NCAB),*

NCI dropped support for screening women ages 40-49 and advised women ages 50 and over to be screened every two years.

67

FALSE CLAIMS !

1994

Even Congress protested but to no avail:

House Committee on Government Operations.

"Misused Science: The National Cancer Institutes Elimination of Mammography Guidelines for Women in Their Forties."

Union Calendar No. 480. House Report 103-863. October 20, 1994.

In testimony before Congress the NCI Director said the NCAB recommendation was "not unanimous"!!

IT HAD BEEN 13 to 1 !!!!

68

FALSE CLAIMS

In order to bolster NCI's position, statements were made, and papers were published to make it seem as if there was a sudden change in data that occurred at the age of 50 when there are none.

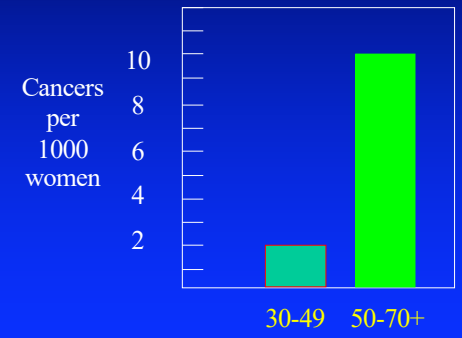
(Kerlikowske K, et al. Positive Predictive Value of Screening Mammography by Age and Family History of Breast Cancer. JAMA 1993;270:2444-2450.)

69

A SIMPLE WAY TO BIAS CONCLUSIONS

(Kerlikowske et al – UCSF-JAMA 1993)

Compared women ages 30-49 to all women ages 50-70+



70

A SIMPLE WAY TO BIAS CONCLUSIONS

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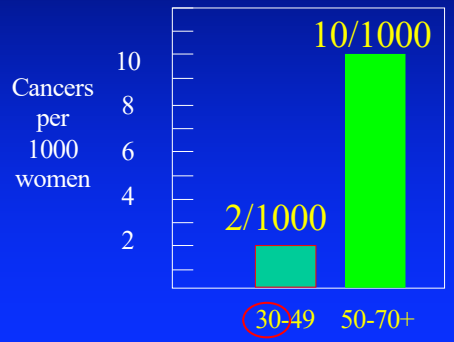
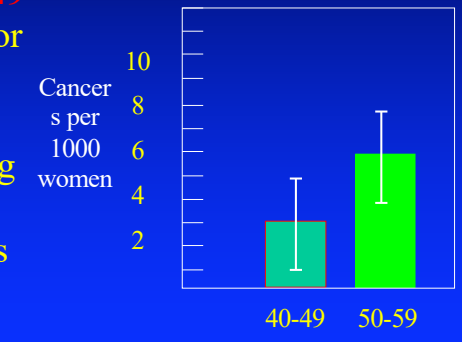


71

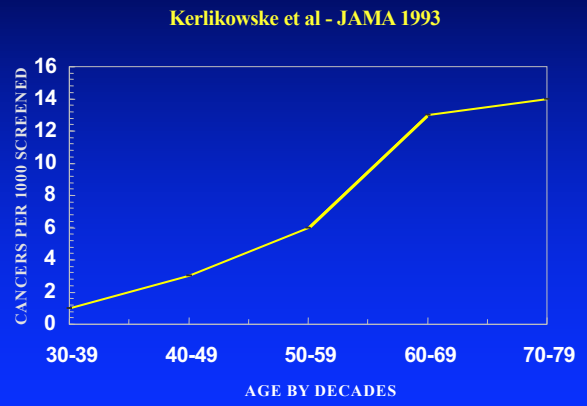
USING A MORE APPROPRIATE COMPARISON (40-49 VS. 50-59) THERE IS LITTLE DIFFERENCE

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



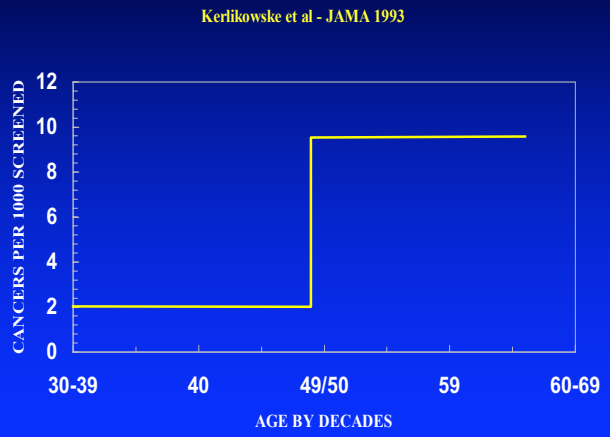
72

MORE APPROPRIATE AGE GROUPING BY DECADE



73

BIASING DATA BY INAPPROPRIATE AGE GROUPING AND AVERAGING



74

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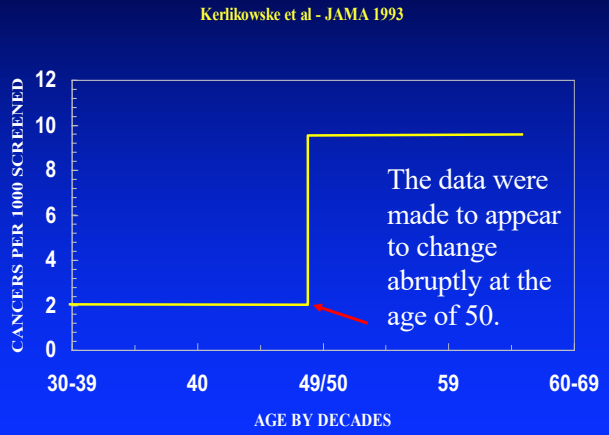


75

FALSE CLAIMS!!

1995

Based on the Kerlikowske paper the false claim was spread by the Dartmouth Institute

"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)

76

FACT

Opponents of screening women ages 40-49 have repeatedly grouped them together and averaged the data as if they are a uniform group and compared them to the group of all women ages 50 and (3 decades) over as if they are a uniform group.

This takes factors that change gradually with increasing age and makes them appear to change suddenly at the age of 50.

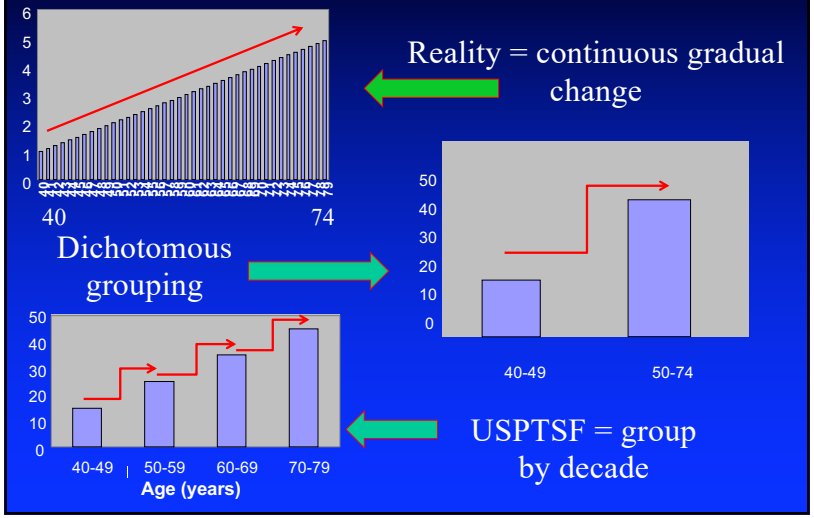
77

FACTS

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.

78

Age grouping has been used to make data that actually change gradually with increasing age appear to change suddenly at the age of 50.



79

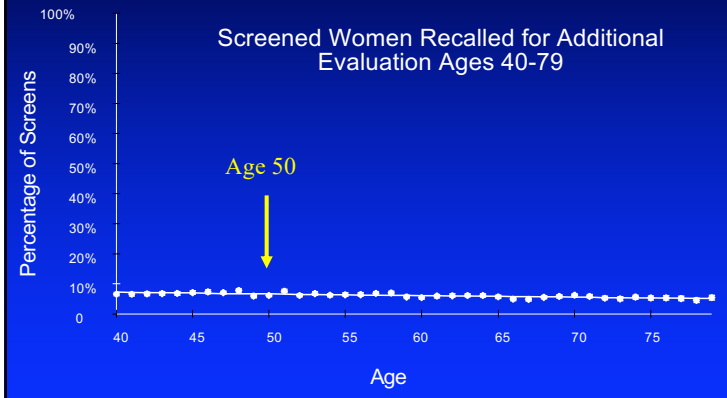
FACTS

NONE of the parameters of screening change abruptly at the age of 50 or any other age.

There are ***no data*** that support the use of the age of 50 as a threshold for initiating screening.

80

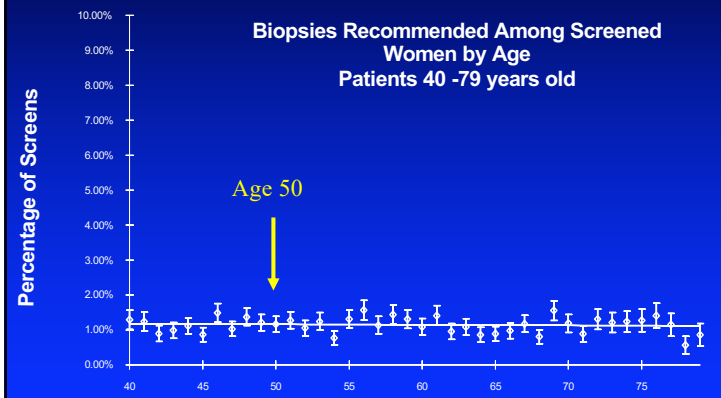
The recall rate from screening decreases gradually with increasing age from 8% to 6% with no abrupt change at age 50 or any other age



(Kopans et al The Breast Journal 1998;4)

81

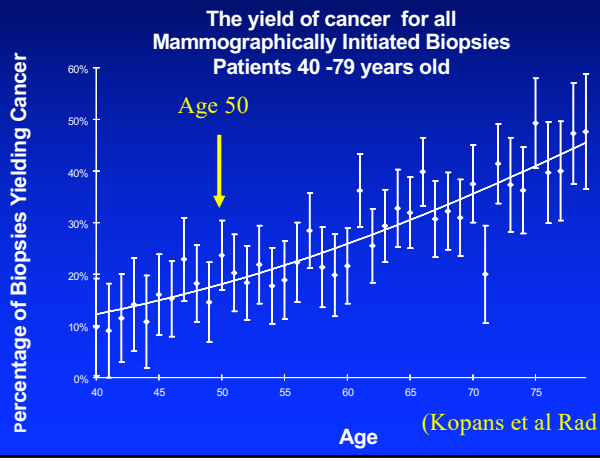
The percentage of women who are recommended for biopsy is fairly constant with no abrupt change at age 50 or any other age.



(Kopans et al The Breast Journal 1998;4)

82

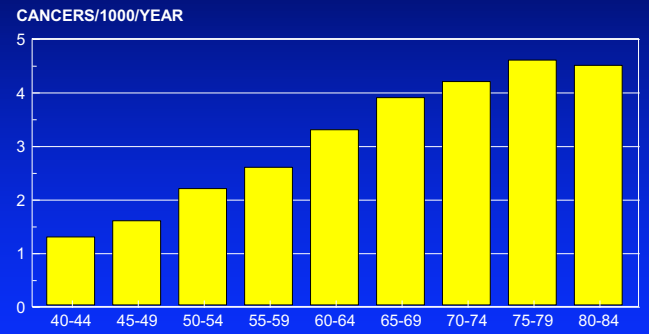
The positive predictive value of a biopsy instigated by mammography goes up with the prior probability of cancer in the population with no abrupt change at any age.



(Kopans et al Rad 1996:200)

83

ANNUAL BREAST CANCER INCIDENCE (per 1000) BY AGE



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.

85

FALSE CLAIMS !
MISINFORMATION !

The artificial and false threshold for initiating screening using the age of 50 has persisted in the effort to reduce access to screening, despite there being no science-based data to support its use.

86

MORE MISINFORMATION !

1997

Under a new Director, and based on nearly constant pressure, with longer term follow-up from the RCT's, the NCI agreed to hold a Consensus Development Conference (CDC) entitled:

"Breast Cancer Screening for Women Ages 40-49"
January 21-23, 1997

87

ANOTHER RIGGED PANEL !

1997

The CDC was supposed to be independent of the NCI, but the same person who organized the 1993 Workshop, organized the 1997 CDC and, once again, loaded the participants. The "Jury" included at least 3 individuals with more than $1 million in NCI grants ("beholding" to the NCI) to determine if NCI guidelines were incorrect.

88

FACTS

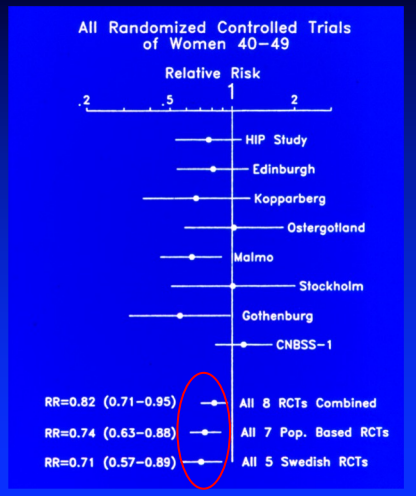
The CDC was provided with clear proof that screening reduced deaths for women ages 40-49.
With longer follow-up (increasing statistical power) the mortality reduction in the RCT's was as high as a "statistically significant" 44% in Gothenberg!

89

SCREENING FOR WOMEN AGES 40-49

Although the RCT were never intended to be analyzed by age groups, with longer follow-up, 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

Hendrick RE et al. Benefit of screening mammography in women ages 40-49: a new meta- analysis of randomized controlled trials. Journal of the National Cancer Institute Monograph 22: 87-92, 1997.



90

FALSE CLAIMS !

1997

The CDC, ignoring the data that they had been convened to review, claimed that there was no benefit from screening women ages 40-49.

91

FALSE CLAIMS REVERSED!

1997

Fortunately, the National Cancer Advisory Board (NCAB) reviewed the data and, in March of 1997, NCI, once again, supported screening starting at the age of 40.

Then NCI stopped developing guidelines!

92

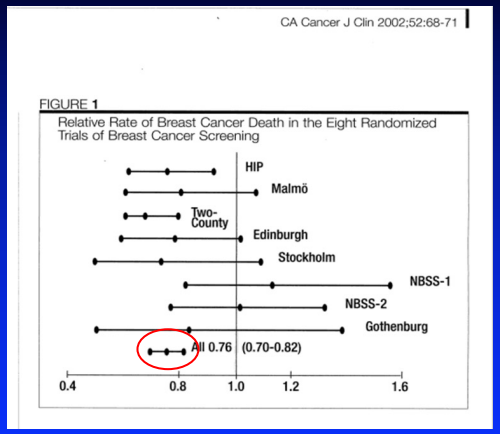
FACTS

Mammography has been proven to reduce deaths for women ages 40-74

PERIOD!!

93

FACTS



SCREENING SAVES LIVES FOR WOMEN AGES 40-74

94

FALSE CLAIMS !

2000

It was, falsely, claimed that there is no benefit from screening women at any age!

(Gotzsche PC, Olsen O. Is Screening for Breast Cancer with Mammography Justifiable? Lancet 2000;355:129-134.)

95

MISINFORMATION !

2001

The 2000 paper, which lacked any validity, caused a furor so [*incredibly*] the authors got a "do over" and republished their false claims in 2001! [Against peer review]

(Olsen O, Gotzsche PC. Cochrane Review on Screening for Breast Cancer with Mammography. Lancet 2001;358:1340-1342.).

96

FACTS

Multiple reviews cited all the errors in 2000/2001 Gotzsche and Olsens claims

Duffy SW. Interpretation of the Breast Screening Trials: A Commentary on the Recent Paper by Gotzsche and Olsen. The Breast 2001;10:209-212.

Freedman DA, Petitti DB, Robins JM. On the Efficacy of Screening for Breast Cancer. International Journal of Epidemiology 2004 ;33 :43-55

Knottnerus JA. Report to the Minister of Health, Welfare, and Sport. The Benefit of Population Screening for Breast Cancer with Mammography. Health Council of the Netherlands. P.O. Box 16052 NL-2500 BB The Hague. Publication No. 2002/03E.

Kopans DB. The Most Recent Breast Cancer Screening Controversy About Whether mammographic Screening benefits Women at Any Age: Nonsense and Nonscience. AJR 2003;180:21-26

but the misinformation added to the confusion.

97

FACTS

As Head of the Nordic Cochrane Center Gotzsche got to promote his false analysis

The "Cochrane Collaboration" had been a highly respected, independent group that reviewed treatment trials

Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2013 Jun 4;(6):CD001877. doi:10.1002/14651858.CD001877

98

FALSE CLAIMS !!!

Gotzsche discounted all the trials that showed a benefit and claimed that the Malmo Trial and the Canadian Trial were the only "fairly well done trials" and they showed no benefit.

The CNBSS???!!!!

Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2013 Jun 4;(6):CD001877. doi:10.1002/14651858.CD001877

99

FALSE CLAIMS !!!

Not only is it scientific nonsense to discard the results from trials simply because you "don't like them", but contrary to Gotzsche's claim, the Malmo trial showed a benefit including for women ages 40-49, yet Lancet still published the papers against peer review.

(Andersson I, Janzon L. Reduced Breast Cancer Mortality in Women Under Age 50: Updated Results From the Malmo Mammographic Screening Program Monogr Natl Cancer Inst 1997;22:63–67)

100

FALSE CLAIMS !!!

The authors claimed that the Canadian Trial [they overlooked the fact that they were actually two separate trials] was one of the "two trials with adequate randomisation methods".
!!!

101

FACTS ABOUT THE CNBSS

They ignored the fact that the CNBSS data are hopelessly corrupted. They violated the fundamental requirements for randomized, controlled trials.

1. The volunteers each had a clinical breast examination (CBE) prior to allocation and the findings were provided to the coordinators.
2. Women were assigned on open lists so that women could be assigned out of random order.
3. The data clearly showed that nonrandom allocation occurred.

102

FACTS ABOUT THE CNBSS

FACTS ABOUT THE CNBSS

1. Only 32% of the cancers in the screening arm were found by mammography alone (10% fewer than the 40% found in the BCDDP 10 years earlier!).
2. A statistically significant excess of women with palpable advanced cancers were assigned to the screening arm.
3. There were more women with lymph node positive cancers assigned to the screening arms.
4. The size of the cancers found by rigorous CBE was larger in the screening arms than women having "usual care" in the control arms.

103

FACTS ABOUT THE CNBSS

The Canadian trials were far from "adequate".

They are a major example of how NOT to perform a Randomized Controlled Trial!

104

FACTS ABOUT THE CNBSS

In 2021 I gave a virtual talk in Canada "What Canadians Need to Know About the Canadian Breast Screening Studies" outlining all of the concerns. I was contacted by a technologist from the studies who confirmed the suspicions that I had raised.

105

FACTS ABOUT THE CNBSS

The CNBSS results are unreliable. I joined with the Canadian experts, based on all of the facts, to urge the ethics committee at the University of Toronto to withdraw the corrupted studies, but they ignored the facts and refused to do so.

106

FALSE CLAIMS !

2007 AND BEYOND!!

Concerns were raised over the "harms" of screening.

1. Recalls from screening for a few extra pictures or an ultrasound were pejoratively called "false positives".
2. It was [falsely] claimed that mammography screening led to "overdiagnosis" which led to "overtreatment".

107

FALSE CLAIMS !

The promoters of "overdiagnosis" claimed that since a tiny number of **clinically evident** breast cancers have miraculously disappeared on their own, without treatment, that this is true of many screen detected cancers and, consequently, we should limit access to screening!

108

FALSE CLAIMS !

Despite the fact that no one has ever seen a screen detected cancer disappear on its own, this ***nonscience*** has stuck !!! Women have been told to delay screening until the age of 50 with the false implication that many cancers will have disappeared, reducing "overdiagnosis".

109

FALSE CLAIMS !

2007

In 2007 the American College of Physicians, out of the blue, promoted new guidelines:
Wait until the age of 50 and then screen biennially.

"CONCLUSIONS: Although few women 50 years of age or older have risks from mammography that outweigh the benefits, the evidence suggests that more women 40 to 49 years of age have such risks."

(Armstrong K, et al. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. Ann Intern Med. 2007 Apr 3;146(7):516-26.)

110

FALSE CLAIMS !

2009

In 2009 the US Preventive Services Task Force, closely allied with the ACP, promoted new guidelines:

Wait until the age of 50 and then screen biennially.

(US Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009 Nov 17;151(10):716-26, .)

111

FALSE CLAIMS !

2012

Mammography Screening leads to massive "overdiagnosis"

112

FALSE CLAIMS !

2012

It was claimed that in 2008 alone there were *70,000* breast cancers that would have disappeared if left undiagnosed by mammography.

(Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. N Engl J Med. 2012 Nov 22;367(21):1998-2005)

113

MORE DECEPTION

Analyses that should have never passed peer review were published that ignored the facts and falsely made it appear as if there is massive overdiagnosis!

114

FACTS

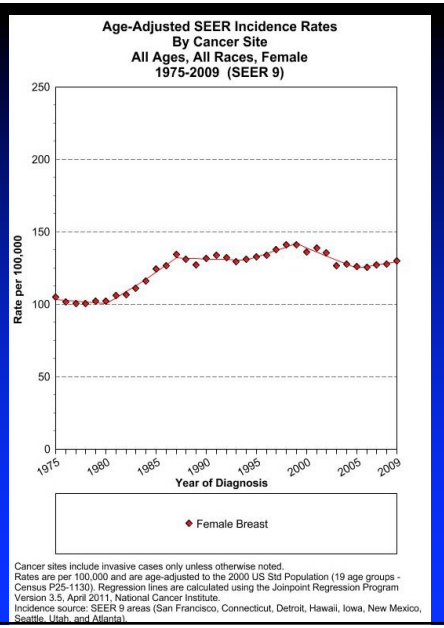
The arguments that claim that mammography leads to massive "overdiagnosis" are based on the claim that the incidence of breast cancer would have remained stable (a flat line) had screening not begun in the mid 1980's.

115

Incidence of invasive breast cancer

SEER data

1974-2008



116

MISINFORMATION

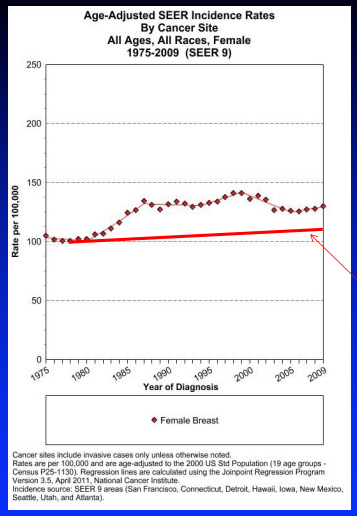
Bleyer and Welch used data from 1976-1978 to estimate what the incidence of breast cancer would have been in 2008 had screening not been initiated in the 1980's. They wrote:

"We called this estimate the "best guess."

"***Best Guess***" in the New England Journal of Medicine!!??

117

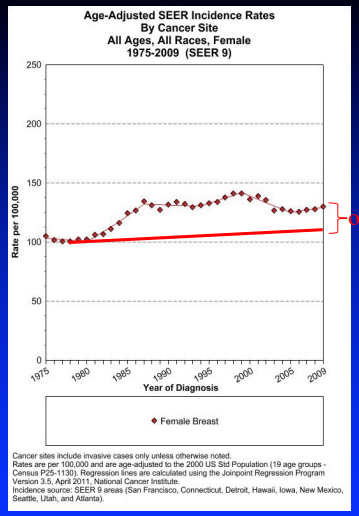
SEER began in 1973. Bleyer and Welch used data from '76-'78 to estimate that the baseline breast cancer incidence would have increased by 0.25% per year if screening had not been initiated



Bleyer and Welch estimate 0.25% per year baseline increase

118

Bleyer and Welch claim that, since there were more cancers diagnosed in 2008 then they estimated should have occurred in the absence of screening, the excess must be "fake" cancers that would have never been clinically evident.

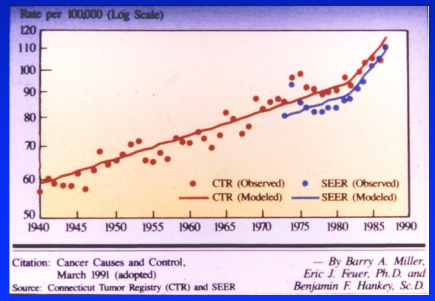


overdiagnosis

119

MISINFORMATION

Bleyer and Welch ignored the fact that many women were screened over this period after Happy Rockefeller and Betty Ford had breast cancers diagnosed in 1974.
They also ignored 40 years of data.

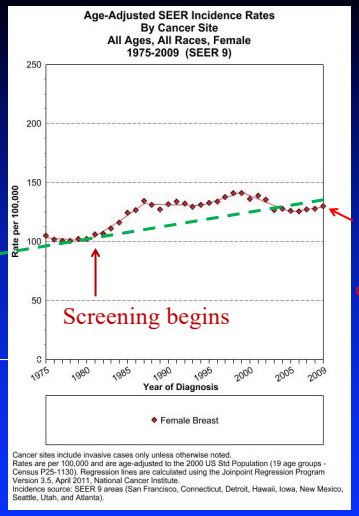


120

Had they used 40 years of a steady increase in incidence….

60/100,000

1940



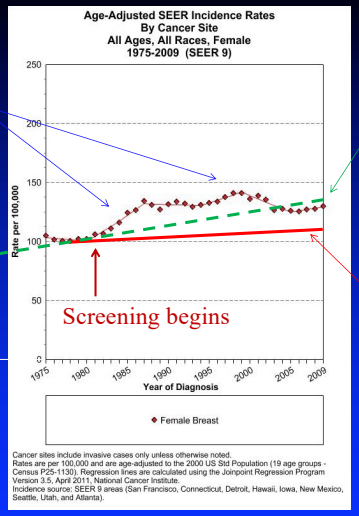
Not only is there no overdiagnosis of invasive cancers, but there were fewer than expected. This may be because DCIS has been removed over preceding years

121

Long prevalence peak

60/100,000

1940



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

Bleyer and Welch estimate 0.25% per year baseline increase

122

FACTS

Not only is there no "overdiagnosis" of invasive cancers, but there have been fewer cancers than would have been expected had the 30 year (1940-1970) trend continued with a 1-1.3% per year increase. This makes sense since screening had removed DCIS lesions likely preventing some of them from progressing to invasive cancers.

123

FALSE CLAIMS !

"Screening doesn't work because it doesn't reduce the rate of advanced cancers".

(Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. N Engl J Med. 2012 Nov 22;367(21):1998-2005)

124

FACTS

If the correct baseline is used (increasing at 1-1.3% each year) then all the "overdiagnosis" arguments disappear.

1. There has been a shift to smaller and lower stage cancers
2. There are fewer cancers than would have been expected (! DCIS removed).
3. The rate of advanced cancers has declined

125

FACTS

Mammography screening REDUCES the rate of advanced cancers.

1. Anderson WF, et al. Assessing the impact of screening mammography: Breast cancer incidence and mortality rates in Connecticut (1943-2002). Breast Cancer Res Treat. 2006 Oct;99(3):333-40.

2. Tabár L, et al. Insights from the breast cancer screening trials: how screening affects the natural history of breast cancer and implications for evaluating service screening programs. Breast J. 2015 Jan-Feb;21(1):13-20.

3. Yen AM, et al. Long-term incidence of breast cancer by trial arm in one county of the Swedish Two-County Trial of mammographic screening. Cancer. 2012 Dec 1;118(23):5728-32. doi: 10.1002/cncr.27580. Epub 2012 May 17

126

FACTS

Mammography screening REDUCES the rate of advanced cancers.

4. Foca F, et al. Decreasing incidence of late-stage breast cancer after the introduction of organized mammography screening in Italy. Cancer. 2013 Jun 1;119(11):2022-8. doi: 10.1002/cncr.28014. Epub 2013 Mar 15.

5. Tabár L, et al. What is the optimum interval between mammographic screening examinations! An analysis based on the latest results of the Swedish two-county breast cancer screening trial. Br J Cancer. 1987 May;55(5):547-51.

6. Swedish Organised Service Screening Evaluation Group. Effect of mammographic service screening on stage at presentation of breast cancers in Sweden. Cancer. 2007 Jun 1;109(11):2205-12

127

FACTS

Mammography screening REDUCES the rate of advanced cancers.

7. Oberaigner W, et al. Reduction in advanced breast cancer after introduction of a mammography screening program in Tyrol/Austria. Breast. 2017 Apr 15;33:178-182.

8. Puliti D, et al. IMPACT COHORT Working Group.. Advanced breast cancer rates in the epoch of service screening: The 400,000 women cohort study from Italy. Eur J Cancer. 2017 Feb 18;75:109-116.

9. Malmgren JA, et al. Impact of mammography detection on the course of breast cancer in women aged 40-49 years. Radiology. 2012 Mar;262(3):797-806. doi: 10.1148/radiol.11111734. PubMed PMID: 22357883

128

FACTS

Mammography screening REDUCES the rate of advanced cancers.

10. Smith RA, et al. The randomized trials of breast cancer screening: what have we learned! Radiol Clin North Am 2004;42(5):793–806

11. Fracheboud J, et al. National Evaluation Team for Breast cancer screening (NETB). Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. Br J Cancer. 2004 Aug 31;91(5):861-7.

12. Helvie MA, et al. Reduction in late-stage breast cancer incidence in the mammography era: Implications for overdiagnosis of invasive cancer. Cancer. 2014 Sep 1;120(17):2649-56.

FALSE CLAIMS !

Screening doesn't work because it doesn't reduce

"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!

"ALL CAUSE" MORTALITY

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.

133

"ALL CAUSE" MORTALITY THE LATEST "NONSCIENCE"

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.

134

"ALL CAUSE" MORTALITY THE LATEST "NONSCIENCE"

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.

135

"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.

(Tabar L, Duffy SW, Yen MF, Warwick J, Vitak B, Chen HH, Smith RA. All-cause mortality among breast cancer patients in a screening trial: support for breast cancer mortality as an end point. J Med Screen. 2002;9(4):159-62.)

136

"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.

(Tabar L, Duffy SW, Yen MF, Warwick J, Vitak B, Chen HH, Smith RA. All-cause mortality among breast cancer patients in a screening trial: support for breast cancer mortality as an end point. J Med Screen. 2002;9(4):159-62.)

137

BREAST CANCER SCREENING

!! CAUTION !!

"RISK BASED" SCREENING

And

"VALUE BASED" SCREENING

are stealth efforts to reduce access to screening.

138

RISK BASED SCREENING

There are two interpretations of

"RISK BASED SCREENING".

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.

139

RISK BASED SCREENING

CAUTION!!

"RISK BASED" SCREENING

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.

140

RISK BASED SCREENING

!!CAUTION!!

"RISK BASED" SCREENING 2:

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

The randomized, controlled trials were not stratified by risk so there is **no proof that screening only high risk women will save any lives.**

141

RISK BASED SCREENING

!!CAUTION!!

"RISK BASED" SCREENING 2:

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

If we only screen high risk women, 75% of women who develop breast cancer each year will not benefit from early detection.

142

FACT:

Screening has, consistently, shown a decrease in breast cancer deaths for all women of approximately 30%.

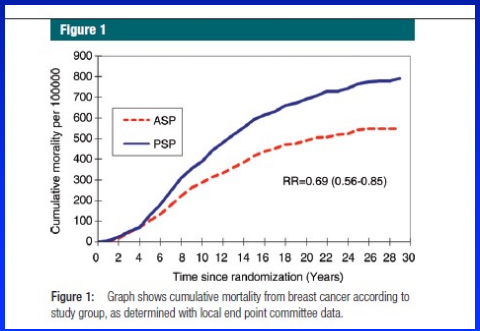


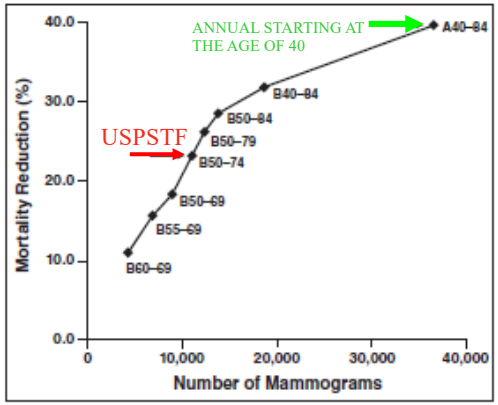
Figure 1: Graph shows cumulative mortality from breast cancer according to study group, as determined with local end point committee data.

Tabár L, Vitak B, Chen TH, Yen AM, Cohen A, Tot T, Chiu SY, Chen SL, Fann JC, Rosell J, Fohlin H, Smith RA, Duffy SW. Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades. Radiology. 2011 Sep;260(3):658-63.

143

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].



144

BREAST CANCER SCREENING

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.

145

BREAST CANCER SCREENING

CONCLUSION

The history of breast cancer screening has been confused by the publication and promulgation of misinformation that has been refuted by science and evidence.

It is time for this to stop!

146

BREAST CANCER SCREENING

Finally, in 2024, the US Preventive Services Task Force (USPSTF) listened to the facts from me and others and once again support what they have recognized for years

–

Screening Saves Lives for women ages 40 and over!

147

BREAST CANCER SCREENING

AS WE BEGIN 2026

There are, unfortunately, continuing efforts to limit access to screening.

148

BREAST CANCER SCREENING

CONCLUSION

There are no data that support the use of the age of 50 as a threshold for screening. The science and evidence show that the most lives are saved by annual screening starting at the age of 40.