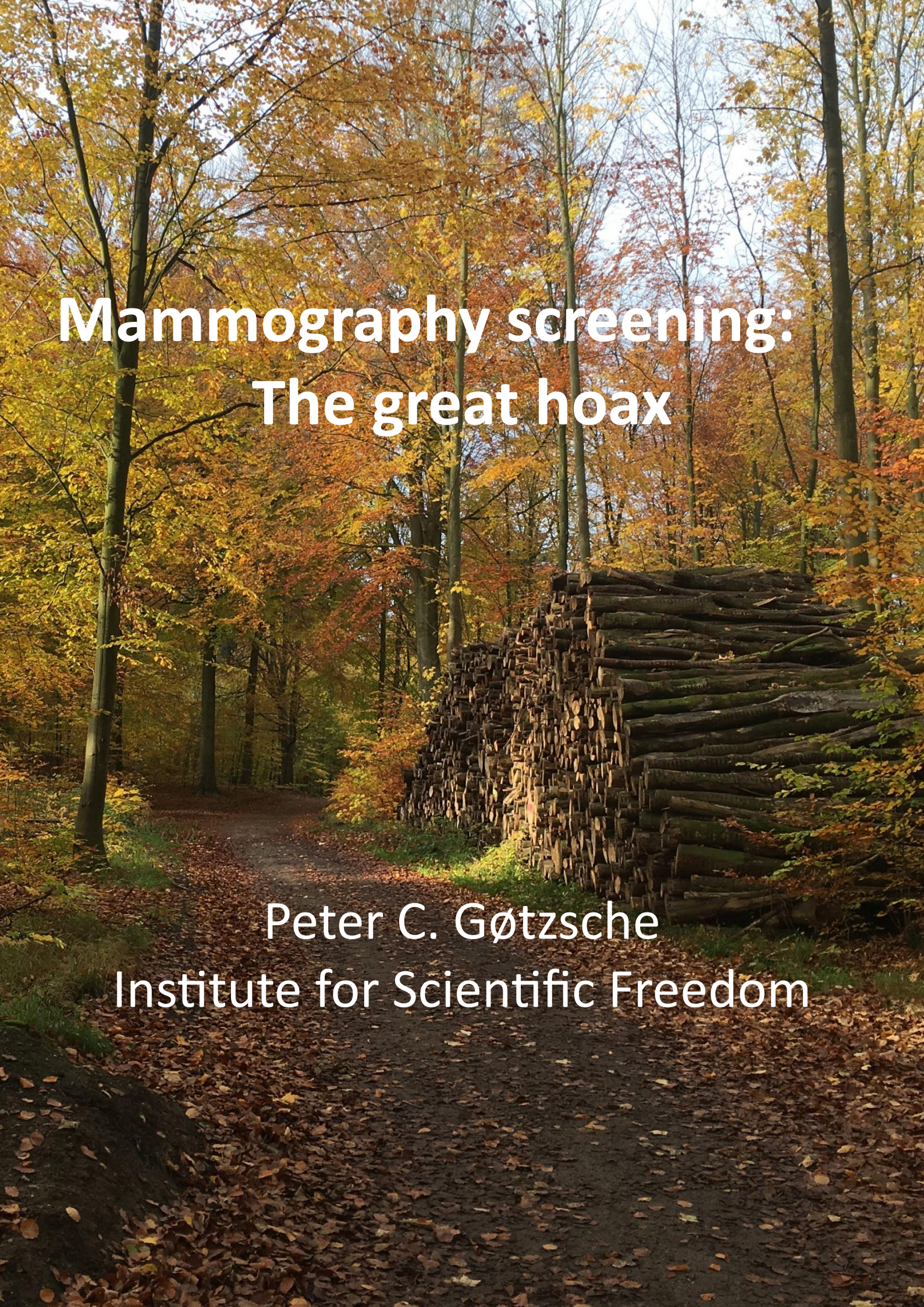

Mammography screening: The great hoax

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Foreword by Hazel Thornton

This book provides an account of an unfinished, unfolding drama that should give concern not only to targeted women but to all citizens generally. It is written by one of the main characters in this melodrama who, together with colleagues in the Cochrane Collaboration, plus many other people elsewhere worldwide, has exposed the injurious unforeseen consequences of pursuing an initially well-intentioned idea for combating the scourge of breast cancer. Unfortunately, as you will see, the programme was too hastily undertaken, propelled by powerful people motivated by additional objectives other than the good of the unsuspecting, targeted women.

Meanwhile, in the intervening three and half decades since that ping of a division bell in the UK House of Commons (1) which resulted in the establishment of the UK National Health Service Breast Screening Programme (NHS BSP), we have seen changes (not for the better) in the culture and conduct generally of citizens, both lay and professional.

We can observe that screening advocates are seemingly unable to honestly and disinterestedly consider the best evidence in order to engage in civilised debate. This has resulted in a great deal of unnecessary harm being inflicted on citizens here and worldwide. In that time, the scaffolding of statistics and science has been fleshed out and clothed by social scientists, ethicists, philosophers, other disciplines and groups, including some of the women themselves - citizens unnecessarily turned into patients by this wilful activity.

You will see that each indexed chapter gives details of content, enabling you to home-in on those aspects that interest you most if delving deeply into data is not your forte. The graphics and other illustrations are very clear and helpful, especially for those readers who haven't studied statistics.

Peter Gøtzsche and I share a common quest - you might even call it an obsession - to overturn the false premise that "finding it early" (and all the costly, harmful activity that goes with it) could "save your life." We are like terriers with a bone, who can`t leave it alone until we have nibbled even closer to the truth. We are both detectives, each in our own way, seeking justice for the millions of women who have, and indeed still are being lured by this apparently sensible proposition to attend for screening.

We approach our sleuthing of this proffered screening stratagem from opposite directions: I, as the Miss Marple, quietly observing and commenting on the (sometimes unseemly) behaviour of the motley cast of characters in this drama; Peter, as the straight-speaking, precise, meticulous, tenacious fact-finding one, with encyclopaedic knowledge and wide grasp of the subject, as you will realise when you follow his account of this remarkable but unfinished saga. I leave it you to find your own fictitious lookalike for him. I, an amateur sleuth; he, the professional one.

Our credentials couldn't be more different. Mine stem from being one of millions of trusting women who fell prey to the invitation that came unbidden through my letterbox from the UK NHS BSP to attend for mammographic screening at my local hospital. This was in 1991, shortly after the programme had been introduced. The "Damascus Road moment" came for me when attending a follow-up appointment two weeks after undergoing an excision biopsy. During that consultation, I was invited to join the UK Trial for the management of screen-detected ductal carcinoma in situ (DCIS): a difficult decision-making proposition for any layperson without the necessary knowhow. The provided information was inadequate, to say the least.

So began my radical conversion of attitude and thought during the two weeks I had been given to decide whether to participate. A self-devised crash course with a very steep learning curve ensued. But that two weeks was enough time for me to realise that I would decline the invitation to that trial with its preposterous potential treatment options, which would have been randomly allocated. I felt like a Black Swan (2) paddling furiously against a sea of unknowns, uncertainties and probabilities. And still paddling (as we all must and are) after more than three decades, sorting the sheep from the goats, the fact from the fiction: a bewildering task. Realising I was but one of many women to be affected by this gratuitous, intrusive invitation, I felt compelled to expose this imposition, so put pen to paper (3). My quest had begun with a bang.

Peter's and my motivation is the same: to prevent perpetuation of this abuse of human rights. Our arguments are based on the best available reliable evidence, systematically and thoroughly reviewed and assembled, showing that the known harms of this medical intervention exceed any potential there might be for benefit.

Our common desire is that every woman should know that every human being in that or similar position, has the right to make up their own mind to give well-informed consent. Clear, unambiguous, unbiased information, based on the best quality available evidence, including the uncertainties, limitations and consequences that can result from agreeing to be mammographically screened, must be made available.

Blind acquiescence to any inducements could cost them dear, as can being led astray by the persuasive, manipulative means used by some of those involved in the screening industry. Availability of suitable adequate information from a trustworthy source other than the promoter is an absolute necessity.

I speak from experience. I was one of the many millions of women who trusted those who invited me. Having been unnecessarily turned from citizen to patient, I became a sceptical sleuth, suspicion aroused by being invited to participate in a trial to find the best way to treat this "new" condition of DCIS (a "pre-cancer" as they described it in the protocol) that was increasingly being found in the screened women.

Women can suffer other harms too: those who receive a false positive or false negative diagnosis; those who are overdiagnosed and overtreated; those who suffer associated social, work and insurance problems, having been unnecessarily labelled "cancer patients," as you will discover when you read this account.

My "retirement" preoccupation, as an Independent Citizen Advocate for Quality in Research and Healthcare, begun in 1991, still intrigues me. As, evidently, it does Peter. What landed on my doorstep, or, perhaps I should say "came through my letterbox," unbidden, was the spur to subsequent action.

There are many types of researchers (3): Peter and I are certainly different, but we converge on the aim of seeking justice, and getting as near to the truth as we can, in order to prevent further harm being done to the many women who unwittingly fall prey to the promised lure of "saving your life." I too, had fallen for it in my ignorance and gullibility. It is not an easy task for citizens or patients: They will need to work hard to acquire understanding of many aspects of research activity, preferably when they are well, if they want to effectively participate in the shared responsibility and debate. Or, indeed, avoid the regret of accepting that imposed invitation in the first place (4,5). They will also need to be keen observers of behaviour.

Living contentedly encompasses health of mind and spirit as well as that of the body. Well-balanced use of head, heart, and hand = equilibrium. We are not machines. You will

read that screening asymptomatic citizens can cause not only damage to the body but also, as researchers have found, considerable anxiety, sometimes long-lasting, especially in falsely diagnosed women and those diagnosed with DCIS. Also, for those who wonder if they made the right decision on receiving that gratuitous invitation. Mammographic screening is an imperfect tool. It can result in false positives; false negatives; overdiagnosis leading to disfiguring and toxic overtreatment; and numerous consequential social difficulties.

Passions run high when it comes to the breast screening controversy, as you will find when you read this dramatic "trip through the uncertainties," with its cast of hundreds, that Peter Gøtzsche has set out for you. Over to you! What do you think? Doubts are essential to honest thinking.

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Abbreviations

CI: Confidence interval.

DCIS: Ductal carcinoma in situ.

IARC: International Agency for Research on Cancer, the cancer agency of the World Health Organization.

NHS: National Health Service in the United Kingdom.

UK: United Kingdom.

1 Breast screening – the facts, a summary

> *If women don't go to screening, they will reduce their risk of becoming a breast cancer patient by one third and their risk of losing a breast by one fourth.*

Mammography screening is one of the most controversial and most expensive interventions ever introduced in healthcare. It became nation-wide in several countries in the late 1980s based on two randomised trials that were not reliable. When additional trials appeared, some of these also had shortcomings.

Screening leads to substantial overdiagnosis, which is the detection of cancers that would not have been identified in someone's remaining lifetime without screening. This is the most serious harm of screening. As it is not possible to distinguish between dangerous and harmless cancers, they are all treated as if they were dangerous.

A special case is carcinoma in situ. These are cell changes that are not cancer. They are rarely detected without screening, and most cases do not develop into invasive cancer. However, as they are often diffusely spread in the breast, their detection leads to mastectomy similarly often as for invasive cancer.

Some healthy women who are overdiagnosed will die from the treatment they receive, e.g. radiotherapy and chemotherapy. This is one reason why breast cancer mortality is not a reliable outcome. Total cancer mortality, including breast cancer, is more reliable. All-cause mortality is the only mortality outcome that is guaranteed free from bias.

The adequately randomised trials did not show an effect of screening on breast cancer mortality whereas the suboptimally randomised trials – those of poor quality - showed an effect. The adequately randomised trials did not find an effect of screening on total cancer mortality, including breast cancer (risk ratio 1.00, 95% confidence interval 0.96 to 1.04) or on all-cause mortality, (risk ratio 1.01, 95% confidence interval 0.99 to 1.04).

Mammography screening does not save lives. And it does not spare the women more aggressive surgery but leads to more mastectomies and more lumpectomies.

Screening also harms many women through false positive findings. At least 25% of the women (about 50% in USA) will be recalled because the mammogram has raised a suspicion of cancer that is later rejected. Several years after having experienced this, many women still suffer from anxiety.

Official announcements about screening including invitations to screening are often misleading and is contradicted by the science. Much of the research literature about screening is also flawed. This makes people confused. They don't know what to believe. It is a sad fact that hundreds of millions of women have attended screening without knowing it doesn't work and could harm them. This disregard of the principles for informed consent and national laws may be the biggest ethical scandal ever in healthcare.

My book is about this. It intends to provide clarity in a controversial area. The violation of women's human rights is the main reason why I have done so much research on mammography screening; why I published a mammography screening book in 2012; and why I have now updated it.

I didn't have any interest in mammography screening and knew very little about it when the Danish National Board of Health asked me to review the screening trials in 1999.

Like others with a strong research background, I was shocked by what I found and my first publication in *The Lancet* in 2000, which was a review of the trials, started a debate that went on for the next 12 years. It died out when a review of the trials was published in 2012

by a so-called independent group, also in *The Lancet*. This review is not reliable, and I shall explain why.

The science is clear. As mammography screening is harmful, it should be abandoned. The only remaining question therefore is: How long shall we wait before this happens?

If you are a woman in the screened age group, there is something you can do. What is most important for all cancers is to prevent their occurrence. It is very easy for you to decrease your risk of becoming a breast cancer patient. If you don't go to screening, you will reduce this risk by one third and the risk of losing a breast by one fourth.

2 How two Nordic health agencies sustained the hoax

> *Don't skip this chapter, as it gives you a rare insight into how health policies are made, using Machiavellian methods in Denmark and Sweden, with disregard for the evidence.*

My work in mammography screening began in 1999 when the Danish National Board of Health asked me to review the randomised trials of mammography screening. There were seven trials, and four of them had been carried out in Sweden.

Lack of effect of screening in Sweden

The first Swedish trial, the Two-County trial, was published in *The Lancet* in 1985 by László Tabár and colleagues.[1] It reported a 31% reduction in breast cancer mortality.

Screening was introduced in Sweden the same year, and it became more widespread in the United States and Australia. In the UK, it started in 1988.

It was therefore unexpected when general practitioner Göran Sjönell and clinical pharmacologist Lars Ståhle reported in 1999 in Läkartidningen (*Swedish Medical Association Journal*) that in Sweden, breast cancer mortality was only 1% lower than expected without screening.[2]

People did not realise in 1985 that the only two trials of mammography screening that had been completed and published, the other and earlier one being from New York, were both unreliable and exaggerated the effect, as I shall explain later.

What ensued in Sweden was not pretty. Accusations of misleading statistical analyses, poor understanding of the basics of cancer screening, poor science and of damaging the good reputation of Sweden swirled around, and screening advocates repeated their criticism even after Sjönell and Ståhle had explained to them that it was unwarranted.

What I have called the "you're not one of us" and the "everybody agrees" tricks were also used, and there were speculations about Sjönell and Ståhle's motives. The ultimate trump card, "you are killing my patients," was also used. Those who raise questions about screening are responsible for the death of many women.

All the critics of Sjönell and Ståhle's paper had vested interests and the Swedish Board of Health, which had started and supported the Two-County trial, made an inexcusable error. The Director of the Swedish Board of Health, Nina Rehnqvist, and two professors from the same institution, Måns Rosén and Ingvar Karlberg, noted that the ten-year survival of patients with breast cancer was better in those counties that started screening early than in those that started late.[3]

Anyone with the slightest knowledge of screening knows that such a comparison is misleading. The purpose of screening is to find cancers earlier than if found clinically. So, when the clock starts earlier, it will guarantee that the ten-year survival looks better even if screening doesn't lower breast cancer mortality.

Counties starting screening early will also have more overdiagnosed cases of harmless cancers that would never have threatened the women's lives than counties starting late, and when these women are included in a ten-year survival estimate, it becomes misleading. By definition, the ten-year survival for these women is 100%, unless they die from other causes. These two biases are called lead-time bias and length bias, respectively.

In their reply to the criticism, Sjönell and Ståhle mentioned that there was 30% over-diagnosis during the first six years after screening started, and when they adjusted their calculation for this problem, the counties in the Two-County trial had a ten-year survival that was *lower* than the average for the whole country![4]

Machiavellian methods in health policy in Denmark

In Denmark, the attitude to mammography screening had been very erratic.[5] In 1989, the Board of Health issued a whole book[6] that recommended screening based on only three trials. In 1994, additional trials had been published that were less convincing, and a new thick report appeared that was undecided.[7]

Neutral observers criticised publicly that, strangely, a third heavy report recommended screening in 1997, although no new results had been published.[8] Further, there was no attempt at quality assessment of the trials and a flawed trial from Edinburgh was included even though it was so poorly randomised that it couldn't provide reliable data. We excluded this trial when we published our first Cochrane review four years later.[9] In the study group, 53% of the women belonged to the highest socio-economic level compared to only 26% in the control group, and screening was associated with a 26% reduction in cardiovascular mortality, which cannot be correct.

The controversy in Denmark that started in 1999 after Sjönell and Ståhle's paper was not a question of understanding and debating the science but of who had the most power and could raise the strongest emotions.[10] [11] Breast surgeon Mogens Blichert-Toft from Rigshospitalet and the Danish Breast Cancer Group did not understand the uncertainties of screening and described his own arguments as logical and factual, and other people's arguments as non-factual, although the reality was quite the opposite. He also played the "you are killing my patients" card, saying that opponents of screening wished that Danish women continued to die from the disease.

The Danish Medical Association was more sensible and contacted the Danish National Board of Health with its worries because of the disappointing results in Sweden.

Screening in Denmark took place in only two areas, corresponding to 20% of the population, and many politicians, including the minister of health, had doubts about screening. However, a majority was in favour of spreading screening to the whole country, and a voting about screening was just five weeks away.

I was the Director of the Nordic Cochrane Centre and was respected for my expertise in randomised trials and in research methodology. I had also lectured in Theory of Medicine for medical students at the University of Copenhagen for 11 years. I was therefore not surprised when the Board of Health asked me to review the mammography screening trials.

I didn't have the slightest interest in mammography screening and the only thing I knew about it was that the Swedish trials had been criticised for using suboptimal randomisation methods and that the issue was controversial.

My statistician, Ole Olsen, and I were astonished when we started our work and learned that the evidence for screening was so poor. We took a break with our other projects and finished our report in just four weeks, as it would have been futile to deliver it after the politicians had voted yes or no to screening.

There were seven trials and we found major problems with most of them. In five trials, the randomisation procedures had been inadequate; in the four Swedish trials, the number of included women and number of deaths varied between different reports of the same

trial; in a trial from Stockholm, the same women were counted twice; and in the trial from New York, the same number of cancers were found in the two groups, which suggested that its large effect on breast cancer mortality could not be correct.

In our report, we discussed the problems with biased assessment of cause of death and therefore also analysed total mortality, which had not been reduced with screening.

We noted that epidemiologist Lennart Nyström and colleagues had published a meta-analysis of the Swedish trials in 1993 where they mentioned that the relative risk for total mortality was 1.00.[12] However, they failed to mention that they had adjusted their analysis for age differences at baseline between the screened group and the control group, and they did not respond adequately to the criticism that was raised in relation to this in letters to the editor (see more about this later). We pointed out that, without Nyström's age adjustment, the Swedish trials showed a significant 6% increase in total mortality, and we noted that there must have been many other imbalances than that for age.

We mentioned that, in contrast to what was usually claimed, screening had not led to less but increased use of radical treatments including mastectomies because of an over-diagnosis of 25-35%. We furthermore noted that data from the United States had shown that 49% of screened women would experience at least one false positive mammogram during ten screening rounds and that 19% would have a biopsy taken.

We noted that it is most relevant for women to know the absolute effect of screening and not the relative effect. If we don't know what the risk of dying is, it is like seeing that a dress is for sale with a 25% discount without knowing what the original price was.

We said that the Swedish trials had reported a reduction in breast cancer mortality after 12 years from 0.5% to 0.4%, i.e. an absolute reduction of 0.1%, which meant that if there was any effect of screening, it must be very small. We also noted we couldn't confirm the numbers in the 1997 report from the Board of Health that claimed a reduction from 5% to 4%. This exaggeration of 10 times originated from an obviously inadmissible extrapolation till the women became 80 years old and assuming they didn't die from other causes.

We concluded that the scientific basis for introducing mammography screening was very uncertain; that it had not been documented that screening does more good than harm; and that we could not exclude the possibility that screening does more harm than good.

The erroneous 1% absolute benefit would come up time and again, also in articles by screening advocates in other countries. In Denmark, the Board of Health made precisely the same error in 2001 when it published a report recommending screening for colorectal cancer.[13] Official authorities rarely admit they have made an error; they prefer to make fools of themselves. After much pressure during a very long time from independent scientists, assisted by a professor of biostatistics, the Board issued a press release saying it was possible to calculate the mortality reduction in other ways!

The mammography screening debacle in 1999 was a lesson that politicians are often badly served by the institutions they have created and by the specialists whose salaries they provide. People tend to control and distort the information to serve their own interests and to avoid losing face. It is regrettable that this also applies to national boards of health, which I shall describe next.

Our 11-page report was factual and evidence-based and, as just noted, had elements of criticism of the Board's own 1997 report. When we delivered it to the Board of Health on 12 May 1999, it was immediately censored. The next day we received another version from its

Director, Einar Krag, where he had deleted our summary on the first page and replaced it by his own very short overall judgement on the last page.

It is very uncommon not to start a report with a summary, and it didn't apply to the Board's own 1997 report. Furthermore, our conclusion, that we couldn't exclude the possibility that screening does more harm than good, was gone, even though we said the same in our Cochrane review two years later. Krag's conclusion was that it was very important to perform a careful meta-analysis after Cochrane standards.

His tactic was the same as in an episode of *BBC's* famous "Yes Minister" series from the 1980s:

"How to discredit an unwelcome report. Stage one: Refuse to publish in the public interest saying … you are waiting for the results of a wider and more detailed report, which is still in preparation. (If there isn't one, commission it; this gives you even more time)."

Krag shelved our report, which he classified as a "non-paper" that could not be accessed through the Freedom of Information Act. But he didn't know that we had sent our report with a messenger to save time. This meant it had been officially registered in the system and could not become non-existent. He therefore had to change his tactics.

He drafted a letter to the Board, which he asked me to sign as if I had written it. It said something about "misunderstandings" but there were no misunderstandings. I removed the misleading sentences – which would have undermined our work – before I signed the letter, which I felt forced to do. I had no funding for my centre, and I worked on getting it from the government, as the centre couldn't survive in the long run based only on project funding. It would not be wise to be seen as "non-cooperative" with the major authority on health in the country as the funding would come from the ministry of health.

The interference by a public agency with a scientific assignment went too far. We were forced to make a third version of our report where our remark that the Board's 1997 report had exaggerated the benefit by a factor of 10 was gone. In handwritten comments to our report, someone had remarked that our statement undermined the Board's credibility. It surely did, but it was deserved, in a matter of great importance for public health. Our remark that it is usually claimed that screening with mammography leads to less radical treatments, which the Board's own report falsely stated, was also removed.

The infallibility of the Board of Health must never be questioned. We felt it was like living in a dictatorship state where it is not allowed to criticise the ruler. The independence of the Nordic Cochrane Centre was widely respected, also in political circles, but here, we had come too close to those who held the power over healthcare.

Krag had promised us he would send our report to the minister, but on the day of the voting, the minister said he had been informed that our report was only provisional. There was nothing provisional about it, but Krag had dubbed it provisional and a "working paper" after having seen our findings and conclusions, just as in "Yes Minister."

There were other curiosities. According to the Board, the minister was informed about our report three days before the voting, but the minister said he first heard about it on the radio on the day of the voting.

We had seriously doubted whether our report would make it to the ministry, but we kept quiet. We were afraid of making powerful enemies by stepping into sensitive political decision processes and ruining Krag's plan.

But we had told some of our colleagues about our troubles, and one of them did not keep quiet. Three days after the politicians had voted yes to screening, Krag's manipulations became front-page news.[14] The journalist mentioned that the Board of Health was in

possession of a report that doubted the effect of screening; that the Board had shelved it; and that "The truth about health is unwelcome."[15]

This caused a speaker on health in parliament to talk of Machiavellian methods, and he asked who decided what politicians were entitled to know about.

The affair was greatly embarrassing for the Board. My letter to the Board, and Krag's manipulated one, were reprinted in full length in the newspaper.

Three weeks later, the same journalist published a damning, very long article, "Cheating with mammography."[16] She told me that while working on it, a member of the advisory group the Board of Health had established on breast screening had told her that it would be dangerous for her to write about it and that she would be punished.

As the cat was now out of the bag, the Health Technology Assessment agency (HTA) at the Board of Health decided to send our original, non-redacted report to those who requested it. In a letter to the editor of Läkartidningen (*Swedish Medical Association Journal*), which the editor showed to me, the agency stated that the report had never had a secrecy stamp on it. This was not an honest remark. The Board had done everything it could to keep it secret.

Many neutral observers noted that the conclusions in the Board's 1997 report were misleading, and one remarked that it was comical to read that although false positive diagnoses – suspicions about cancer that were later rejected - could lead to temporary anxiety, this could not be detected in blood samples. He asked if this was what the doctors were supposed to tell their anxious patients.

There were also conflicts of interest. Five of the six experts in the Board's advisory group came from the Danish Breast Cancer Group, which had advocated screening since 1987 and received an income of DKK1000 from the counties for every new breast cancer patient.

It is not an exaggeration to speak of Machiavellian methods, and top politicians in the counties didn't take the lack of independent advice lightly. They asked what motivated the Board to change its recommendations between its 1994 and 1997 reports but didn't get a satisfactory answer.

A year after these events, my own hospital, Rigshospitalet, the major hospital in the country, which had introduced screening in 1991, wished to close it down, but the politicians wouldn't allow this.

After we had finished our report, we acquired funding from the Board's HTA agency to do a Cochrane review, and the HTA agency wrote to the Danish Medical Association that it couldn't give a reply before the Cochrane review was finished, which was expected to take quite a while ...

The Machiavellian methods continued. Even though the Board had funded our Cochrane review under the assumption that we were independent scientists, they tried hard to manipulate us, and our academic freedom was constantly under attack.

At a meeting with the Board's breast cancer advisory group, we were told bluntly that the credibility of our centre would hardly be supported by the report we had written, and we were urged to include surgical expertise when we evaluated the trials for our Cochrane review. We were fed up with all the attempts at censoring our science, and I replied that we didn't need surgeons, as we were not going to operate on the breasts ourselves.

When the issue of including appropriate experts came up again, I responded that we had learned how to read and didn't need help with this. The head of the HTA agency, Finn Børlum Kristensen, drafted the minutes from the meeting, which said that we would do what we could to stop the public debate about our report and that we would not criticise the

Board of Health's expert advice. We had not agreed to this and we therefore demanded the gagging statements be removed from the minutes.

These meetings were dreadful. At the last meeting, we were asked which experts we collaborated with. We corresponded extensively with the trialists and other experts but declined to give this information, as it would have led to renewed pressures about whether those people were the "right" ones.

I had no doubt that those on the other side of the table found us stubborn and irritating. But we had not embarked on a consensus report or a political document. It was science. Pure, unadulterated science.

Later, I wrote to the Board of Health and asked what evidence its working group had used when it declared in the summary of its 1997 report that the number of women who will have a mastectomy will decrease. I explained that there was no reference for this pivotal statement and that we had found the opposite in the randomised trials. I copied Kristensen on my letter, and he wrote back declaring firmly that my request didn't fall under the agreement we had made with his institute to review the trials!

He also questioned the appropriateness of a Cochrane centre contacting a country's uppermost scientific authority on health asking for the evidence behind a statement in a report, and he asked whether there was a need to discuss the activity profile of my centre with its advisory board.

To have come so close to the uppermost power circles in healthcare and to see how policies in matters of life and death affecting the whole population were made was one of the biggest shocks in my entire career.

There was a double irony in this. My letter to the Board of Health was prompted by a letter from a member of its own advisory group, Henning Mouridsen from the Danish Breast Cancer Group, who said I was wrong about screening leading to more mastectomies, but he didn't explain why. Furthermore, the Board had itself asked us to read their report when we reviewed the trials, which we had dutifully done. The Board did not answer my letter, which I felt was very arrogant. The Board works on behalf of Danish citizens and my question was very relevant for Danish citizens.

Our 2000 *Lancet* review of the trials ignited a fierce debate

In Krag's view, Danes were not entitled to learn about our findings. My view was that the whole world should know about them. Olsen and I therefore submitted a paper to *The Lancet* less than four weeks after the Board of Health had stonewalled our report.

Six months later, I informed Kristensen that we would publish our findings in *Lancet* and that we would hold a press conference two days before. Kristensen was very worried about this and referred to a non-existing "common understanding" about mammography screening, arguing that the important scientific debate could not possibly be part of the public debate when our paper had not been published. We cancelled the press conference, which didn't help soothe Kristensen's concerns, as *Lancet* published its own press release.

Lancet's editors were so convinced that screening was a bad idea that they wanted us to "end the tale" even though there had been screening for 12 years in the UK.

In Sweden, they also used Machiavellian methods. The Swedish experts who were critical of screening mostly aired their reservations in private, out of fear of being threatened or ridiculed by László Tabár, the primary investigator for the Two-County trial.

Some wondered how it was possible for a physician from Hungary to become the main investigator and was entrusted with carrying through the biggest research endeavour ever undertaken in Sweden. Tabár had only five publications in English-language journals before he embarked on the trial, and he hadn't done a randomised trial before.

Mammography screening had become a feminist issue in Sweden in the 1980s. Women from all political parties joined ranks and demanded screening, and the Swedish Board of Health that had supported Tabár's study protected him against criticism right from the beginning.

Our message in Lancet was simple (a 95% confidence interval means that we are 95% confident that the true risk lies within this interval. If the interval crosses 1.00, the risk is not statistically significant):[17]

Findings Baseline imbalances were shown for six of the eight identified trials, and inconsistencies in the number of women randomised were found in four. The two adequately randomised trials found no effect of screening on breast-cancer mortality (pooled relative risk 1.04 [95% CI 0.84–1.27]) or on total mortality (0.99 [0.94–1.05]). The pooled relative risk for breast-cancer mortality for the other trials was 0.75 (0.67–0.83), which was significantly different (p = 0.005) from that for the unbiased trials. The Swedish meta-analysis showed a decrease in breast-cancer mortality but also an increase in total mortality (1.06 [1.04–1.08]); this increase disappeared after adjustment for an imbalance in age.

Interpretation Screening for breast cancer with mammography is unjustified. If the Swedish trials are judged to be unbiased, the data show that for every 1000 women screened biennially throughout 12 years, one breast-cancer death is avoided whereas the total number of deaths is increased by six. If the Swedish trials (apart from the Malmö trial) are judged to be biased, there is no reliable evidence that screening decreases breast-cancer mortality.

We considered it scientific misconduct that Nyström had adjusted his analysis for age but had not informed about this in his meta-analysis. Readers would not have expected any adjustment to have been made in a meta-analysis of hundreds of thousands of women in which adjustments would not change anything, provided the trials had been properly randomised.

We wrote in our *Lancet* paper that Petr Skrabanek obtained the mortality rates from Nyström in 1993 and drew attention to the increased mortality in the screened groups (relative risk 1.06).[18] In his reply, Nyström did not mention the imbalance in age, but defended the relative risk of 1.00 reported in his meta-analysis by comparing the observed number of deaths in the screened groups with the expected number in the population.[19] He also noted that the relative risks for total mortality in the individual trials were 0.98, 0.98, 0.99, 1.00, and 1.00, which is quite impossible when the pooled risk is 1.06.

Then, another commentator wrote that "a more precise and apt comparison is that between the mortality rates in the exposed and control groups."[20] In response to this indisputable fact Nyström wrote that he preferred standardised relative risks to crude relative risks.[21] This reply makes no sense at all. The whole idea with randomisation is to make unbiased analyses possible, but it was another three years before Nyström admitted publicly that he had adjusted his analysis of total mortality for age.[22]

We reported in *Lancet* that screening led to 35% more breast operations and 23% more mastectomies. As I shall document in the rest of this book, this crucial fact, that screening leads to more breasts being removed, has been fiercely denied ever since by screening advocates.

There were only two adequately randomised trials, one from Malmö and one from Canada (sometimes described as two trials, as they covered two different age groups, with slightly different designs).

We noted in our paper that the Canadian trial had been subjected to much more criticism than other trials, no doubt because it had the most negative result, but the criticism had been rebutted. It is telling for the lack of reason in this area that this trial was by far the best-documented one.

Particularly the quality of the mammography had been much criticised, whereby the Canadian researchers got punished for having published data on their quality control, which did not exist for the other trials. Screening advocates continued to propagate untruthful and malicious statements about the quality of the mammography repeatedly, also after their errors had been pointed out to them. Ironically, the truth is that the tumours detected by screening in the Canadian trial were smaller, on average, than those in the Swedish trials.[23]

Our *Lancet* paper raised a media storm, and we found ourselves talking to radio and television stations from all over the world all the time. *Lancet's* press officer, Richard Lane, aptly described what happened:[24]

"Some sections of the press questioned *The Lancet's* judgement in publishing such a controversial review, which was roundly criticised by many 'experts' … If you read the press reports at the time, however, and some of the vitriolic comments from leading figures in the cancer organisations, you might have been forgiven for thinking that Gøtzsche had committed professional suicide. In this case, the spin came not from the scientists, but from certain areas of the media, who were helped on their way by 'expert' outside comment. These commentators, presumably for reasons of self-interest, had to condemn the study, even though they couldn't disprove it by offering alternative evidence."

A scientific analysis of the press coverage in the UK was revealing.[25] There had been a lot of smoke, some errors and virtually no relevant substance in the comments from "experts" and proponents for the screening programme who were unquestioningly cited as authoritative. This was surprising, as journalists are usually critical about motives when they cite politicians.

It was a total defeat for evidence-based medicine and common sense. Each article had at least one reference to an "expert" and the core content was usually completely irrelevant, e.g. the data cited most frequently were number of cancers found and their size, and breast cancer mortality rates for the whole nation. Number of lives saved was also commonly reported, as quoted in documents from the UK Screening Programme, with no explanation how it was derived, and ignoring that screening doesn't save lives, as total mortality was unaffected by screening.

The most frequently cited information item from *Lancet* was from an opposing editorial[26] by Harry de Koning, a leading figure in the Dutch screening programme. He said we had ignored other factors which likely could be more important for lowering the mortality rate through screening. He did not explain what he meant by this cryptic remark, or how such other factors "through screening" could change our negative result into a positive one. This would seem impossible, as we based our analysis on the randomised trials, the most reliable evidence we have. But it very often happened that screening advocates resorted to wishful thinking when they didn't like the data, and that others cited it as if it constituted evidence.

There were many testimonials from women, even though they cannot prove anything about the effect of screening.

The most aggressive comments were from the United States. The head of a Long Island breast cancer advocacy group noted that to stop screening was "like murder." The Americans boasted they did the best screening in the world and the British said the same.

The level of the debate was very low. Iben Holten from the Danish Cancer Society described our research as an "opinion piece" that expressed attitudes, called it unscientific in prime-time television news, and used the "everybody agrees" trick.[27] The politician behind the proposal of introducing screening in the whole of Denmark declared that it would be sufficient for him if screening could improve the condition for only four patients.

Mogens Blichert-Toft characterised what we had written as "pure misinformation," based on "wrong assumptions" that "cannot be used for anything."[28] He also said: "I have never met a woman who was sorry that we found a small tumour rather than a large one."[29]

Walter Schwartz, head of Fyn's breast screening unit, dismissed our findings of overdiagnosis entirely, saying it didn't happen where he worked. He also noted that in his experience, fewer of the small tumours had metastasised than the large ones. True, but this cannot tell us anything about screening, and overdiagnosis is a fact whether Schwartz opens his eyes or not.

An even poorer argument, offered by cancer charities and politicians, was that the trials were outdated. If that is the case, we don't have any reliable evidence that screening works.

A biostatistician, Irwin D Bross, wrote to me that our results got a lot of attention in the United States, mostly furious denunciations by enraged oncologists, but their critique of our statistical methods was amusing, "since they are nearly all statistical illiterates." A French journalist did not understand statistics either and described us as intellectual statistical masturbists.[30]

Cornelia Baines, one of the two primary investigators for the Canadian screening trial, wrote to me that many of the US and Canadian screening experts who dismissed our research in media interviews – using every belittling adjective one can imagine – had not even read our paper. She also described her own experiences after she had reported the results of her own trial. She received anonymous phone calls and letters telling her she was a murderer; that she should commit suicide; and that she was personally responsible for the deaths of thousands of women.[31] At lectures sponsored by the American Cancer Society, she had been called a fraud, dishonest and unethical.

After our paper was published, a female editor sent us ten letters we should respond to. Back then, all letters in *Lancet* started with "Sir." I reacted to this chauvinism by asking her whether we needed to reply with "Sir" when we wrote to a lady and when the debate was about a disease in women. The editors were not moved, but the century-long habit of using "Sir" disappeared from *Lancet* letters three years later. The letters and our reply took up six pages,[32] which was more than our article, but they were not particularly interesting.

The Swedish Board of Health continued to be dishonest. Måns Rosén and Magnus Stenbeck published one of the most curious articles I have ever seen.[33] The results were too good to be true for Sweden and outright false for the Netherlands. They used a fourth-grade polynomial to control for age effects in their logistic regression model and provided no information about the model, its assumptions, or coefficients, whether it provided a good fit with the data, or explained why they didn't use simple regression.

I showed in my 2012 book about mammography screening that with a fourth-grade polynomial, you can get almost any result you want.[34] You can, for example, take a straight line and bend it in almost any fashion, by choosing appropriate coefficients. If the coeffi-

cients are changed to just a minor degree, the result can change from a 20% effect to a 620% effect.

Torture your data till they confess, as they say in America.[35]

Because of our *Lancet* paper, the US National Breast Cancer Coalition invited me to give a talk at their annual meeting in Washington DC in May 2001.

It was one of the most moving moments in my career. I had checked where the exit doors were, so that I could escape if hundreds of women started to throw tomatoes and eggs at me, but there was no need: I received a standing ovation.

I could have cried. These brave women who fought so hard against their breast cancer welcomed being informed about the benefits and harms of screening from a researcher who had no conflicts of interest.

In 2002, the coalition wrote on its website:[36] "There is insufficient evidence to support blanket recommendations for or against screening mammography in any age group of women ... NBCC believes that there are public health interventions that could save more lives and use fewer health care resources than mammography screening programs."

Today, the position of the coalition is that "screening mammography of all women has demonstrated only a modest, if any, benefit in reducing breast cancer mortality and that the harms associated with screening outweigh those benefits. No individual woman can be assured that screening mammography will prevent her from dying of breast cancer."[37]

3 Editorial misconduct in the Cochrane Collaboration

This chapter describes how what was once an idealistic organisation introduced censorship when the editors, who believed in mammography screening, did not like the results of a systematic review that told them screening causes serious harms.

In 2001, Ole Olsen and I became the victims of serious editorial misconduct.[38] It was the biggest scandal in Cochrane's eight-year history. We were looking forward to publishing our Cochrane review of mammography screening, which was eagerly awaited by decision makers all over the world, but, despite protracted negotiations, the Cochrane Breast Cancer group denied us the possibility of publishing the major harms of screening, overdiagnosis and overtreatment. We therefore published a research letter and the full review in *Lancet*,[39] which was much more of a Cochrane review than the stymied review published in the *Cochrane Library* at the same time.[40]

Our 2001 *Lancet* review and the censored Cochrane review

Lancet's editor-in-chief, Richard Horton, noted in a scathing editorial,[41] that even in the best organisations raw evidence is sometimes insufficient to influence opinion; that our conclusions were unwelcome; that the Cochrane editors insisted that changes, we disagreed with, be made to the review if it was to be published in the *Cochrane Library*; and that interference by Cochrane editors to insert what the authors believed to be invalid analyses eroded their academic freedom.

Horton also wrote that that there is no reliable evidence from large, randomised trials to support screening mammography programmes and that editors who insist on inappropriate analyses that seem to support a particular point of view hurt not only themselves and the institution they represent but also the credibility of the science they claim to value.

Three days before the deadline for publication of our Cochrane review, the Cochrane editors added a misleading result in the abstract about a non-existing benefit of screening when all the trials were lumped (see below), and they excluded data showing that screening increased mastectomies, lumpectomies and the use of radiotherapy, even though inclusion of these data was envisaged in the protocol of the review they had themselves published.

We noted in our *Lancet* research letter that the best trials failed to find an effect of screening on deaths ascribed to breast cancer, relative risk 0.97 (95% confidence interval 0.82 to 1.14) after 13 years (a non-significant 3% reduction), whereas the remaining trials with poor-quality data found a marked effect, relative risk 0.68 (0.58 to 0.78) (a 32% reduction).

We explained that, given the strong heterogeneity (the two confidence intervals didn't even overlap), results from the two quality groups should not be combined. This is the correct approach to take, and it is also the method recommended in the Cochrane Handbook of Systematic Reviews,[42] but the Cochrane Breast Cancer group forced us to lump all the results, which yielded a misleading estimate of a significant 20% reduction in mortality from breast cancer, relative risk 0.80 (0.71 to 0.89).

Our actions carried high costs. We made enemies, and some of our colleagues felt we had hurt Cochrane. However, others commended us for our courage, including the collaboration's founder, Sir Iain Chalmers, who told me in no uncertain terms that this should be seen as a learning process for the Cochrane Breast Cancer Group.

I hadn't doubted for a moment that we did the right thing. Our loyalties should not be with people with vested interests, but with the women. By displaying the data openly, women and policymakers could judge for themselves if screening was a good idea.

As a result of our previous *Lancet* review,[43] from 2000, the Cochrane Breast Cancer Group had come under great pressure and criticism. People had resigned from advisory committees and the editors had received letters of complaint and were subjected to pressures requesting that we should be prevented from completing our review. The group is based in Australia, and I noticed that the National Breast Cancer Centre in Australia, which supports screening, funded the group and that this funding had disappeared the year after our Cochrane review was published.

The review process was a mess. We had over 100 email exchanges with the editors; the review led to tensions and disagreements within the group and some editors didn't know what others were doing; and we were left with two sets of disagreeing peer reviews and editorial recommendations that would be impossible to reconcile. I tried to sort things out by visiting two of the editors but that didn't help either.

The demands to our review increased all the time, and in mid-June 2001, the two key editors, John Simes and Nicholas Wilcken from Australia, told us bluntly that they couldn't accept our review for publication. They ended their letter on a strange note, telling us that until our review was accepted as a Cochrane review, we shouldn't list our affiliation as the Nordic Cochrane Centre, because "Our experience following your publication in the *Lancet* last year indicates that this can be misleading."

This was bizarre. Simes and Wilcken had no right to require this, and omission of our affiliation could have been regarded as scientific misconduct. Furthermore, in our 2000 *Lancet* paper, the word Cochrane appeared only as our affiliation and in our search strategy, which was impossible to avoid.

As Simes and Wilcken were coming to the UK Cochrane Centre in Oxford later the same month, I arranged a meeting with them, in which two more editors, Mike Clarke and Davina Ghersi, also participated. During that meeting, Olsen and I felt the editors had embarked on a process that would never stop, as in Kafka's novel *The Trial*.

Despite being frustrated, I was very polite and accommodated the editors' wishes,[44] but the situation only got worse. The editors stopped responding to emails, even those from Mike Clarke who agreed with us that screening leads to more aggressive surgery. We had discussed at length the biases that could have affected our estimate of overtreatment and had also mentioned that carcinoma in situ (cell changes that are not cancer) is often treated by mastectomy, but the editors flatly denied this indisputable fact.

In the UK, 29% of ductal carcinoma in situ lesions are treated with mastectomy, compared with 26% of invasive cancers.[45] The lesions are often multifocal, which adds to debunking the myth that early detection by screening prevents mastectomies.[46] It doesn't, and the increase in mastectomies seems impossible to avoid.

Shortly before our paper came out, John Simes contacted Horton, as he had heard there would be an editorial. He was anxious and disputed almost everything Horton told him about the process. He even lied when he said that we had not disagreed with the changes he had enforced on us. We sent Horton copies of email messages that verified that everything we had told him was correct.

However, a year later, the other key editor, Nicholas Wilcken, also lied. He repeated the false statement that the editors had not insisted on changes.[47]

An anonymous commentator in *BMJ's* Minerva section wrote: "Given the apparent lack of evidence for breast screening programmes, Minerva wonders why women are under such pressure to attend." So did we.

Those who peer reviewed our research for *Lancet* did not provide helpful arguments but denigrated our research with comments like,

"It strikes me as very strange and disturbing, that the Cochrane Collaboration allowed these two authors to conduct an overview of this topic. It would have served Public Health better had an independent group of authors been commissioned to conduct this review of such an important topic,"

"To publish this communication would sully the good name of *The Lancet*,"

"It would be imprudent in the extreme to publish further unsubstantiated allegations,"

"I see nothing publishable here,"

"Gøtzsche et al. will undermine their own credibility."

We got the point. It is professional suicide to publish top-class research, both for the researchers and the journal, if it disturbs a sacred cow.

Horton wrote to us afterwards: "Well done, if I may say, for being so brave to stick by the science, and not to be swayed by the desire to confirm what many hoped for." He added:

"What I see happening is direct *ad hominem* assaults on anybody who dissents from the pro-mammography line, irrespective of the data offered. Jack Cuzick said to me last Friday that your review was an example of context-free statistics. I replied that you had spent a good part of the last 2 years deep in these data – you probably knew the trials better than anybody. But what he seemed to be saying was that one only has the right to comment on screening if one takes a pro-screening line."

A peer reviewer once asked: "What do you mean when you say that you read forty centimetres of literature?" (Ole Olsen, our secretary Tine Bjulf and Peter C Gøtzsche)

Horton was right. No one in the whole world knew these trials and their weaknesses as well as we did. We had been through a huge amount of literature (see photo above), comprising 222 articles, letters and unpublished reports, some of which were in Swedish; we had read the most important papers several times; and we had corresponded extensively with the trialists and many other knowledgeable people.

It is telling that when we published a review according to Cochrane standards and using meta-analysis, Cuzick called it "context-free statistics." He was asked by *Lancet* 11 years later to review my mammography screening book, which confirmed his bias (see Chapter 10).

The same day our paper came out, radiologist Peter Dean from Finland, a mentor for László Tabár, sent a vitriolic mass email to 128 recipients. Dean misquoted our research to the extreme. He guessed Horton would lose his job because he had supported us; he spread the lie that our paper was not peer-reviewed; and he said that he didn't know if Horton had expertise in evaluating mammography screening studies, or had knowledge of breast cancer biology, to say nothing of radiology, or even if he was a physician.

Perhaps Horton didn't exist? Dean would have had his heyday during the Inquisition, where he could have sentenced people like Horton and me to be burned at the stake.

A month before we published our 2001 review, professor of statistics Nick Day from Cambridge, UK, sent an email to Iain Chalmers, which was an attempt at censoring our work. He first criticised our 2000 *Lancet* paper:

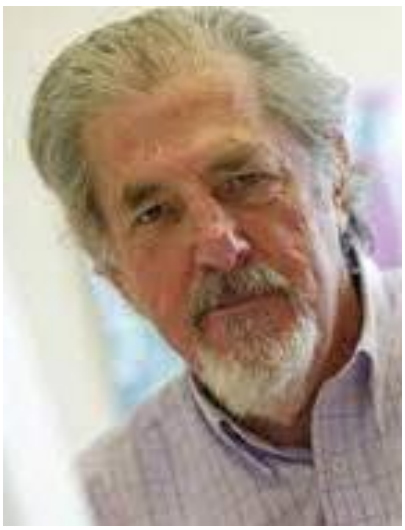
"This paper, I'll call it the GO paper, is not simply controversial, it contains a number of serious statistical mistakes which invalidate its conclusions, and uses a selective approach to the studies and data it assesses. It is a worthless piece of work which if it had been produced by one of our masters students, would have been sent back with demands for a complete rewrite."

Pretty interesting comment, as we made no statistical errors and reviewed the data in a systematic fashion according to the best available standards.

He asked Chalmers to intervene and ended his letter this way: "The immense benefits brought by the [UK] Cochrane Centre will be undermined if its name is associated with incompetent and tendentious reviews such as the GO paper."

Nick Day told the *Philadelphia Inquirer* half a year later when our review had come out that it was "total nonsense, and it is a scandal, first, that it was published and, second, that it has had the impact it has."[48]


Peter Dean


Nick Day


Daniel Kopans

Screening advocates get nervous when they cannot control the narrative, and Day had a problem, which was not a small one. He co-authored the first publication of the Two-County trial in *Lancet* in 1985, and Anthony Miller, one of the two primary investigators for the Canadian trial, told me that Day visited Tabár in Sweden for a weekend and performed the statistical analyses. As Miller said, Day cannot have exerted much quality control, but must simply have believed the data Tabár gave him.

I suppose that, by 2001, Day must have realised that this was a serious threat to his credibility.

US radiologist Daniel Kopans was also unrestrained in the *Philadelphia Inquirer*: "If you take all the studies that show the Earth is round and reject them, then the Earth is flat. That's what they have done."[49] He opined that I knowingly ignore the scientific method in order to further my own agenda; that I am intellectually deficient; that I am on a crusade; that perhaps it is "An all-consuming hatred and jealousy of László Tabár" who carried out an "impeccable trial facilitated by meticulous Swedish record keeping;" and that my influence "has resulted in women's unnecessary deaths."

Kopans has described himself as someone who almost dropped out of medicine because he didn't feel competent, and as someone who slept through statistics in medical school.[50] A 1997 article in *Science* by Gary Taubes quoted scientists who described Kopans's tactics as "intellectual terrorism" or "scientific McCarthyism," and a director of the National Cancer Institute said that Kopans employs "a pattern of inflammatory, accusatory approaches that are antithetical to the requirements of scientific discourse."

We were not impressed by our opponents. As you will see in this book, the most dishonest group of people are Stephen Duffy, László Tabár and Robert Smith (a staunch supporter of mammography screening from the American Cancer Society). They often published together, and their level of debate is similar to that of Kopans. In a letter in *Lancet*,[51] they noted that our review was "riddled with misrepresentation, inconsistency in the treatment of the randomised trials, and errors of method and fact," and that our "alleged inconsistencies" in numbers in different reports of the Two-County trial would have been understood by a competent meta-analyst.

I would say the opposite. Because we were competent and careful, we spotted all these inconsistencies, which were not alleged but real. We have published six different sets of numbers for randomised women in the Kopparberg part of the study and five different sets for the Östergötland part,[52] and tumour data and breast cancer deaths do not add up either, as I shall explain later.

I replied in *Lancet* that Tabár tried to blame his co-workers for the inconsistencies we identified, which is inappropriate because he had co-authored several of the papers, for example those that reported *fewer* deaths from breast cancer with *increasing* follow-up than those identified initially by a blinded endpoint committee.[53] I also noted that Tabár's main trial report was inconsistent with the trial protocol and a later thesis and that this finding reinforced our conclusion that the published data are of poor quality and very likely flawed.

Circling the wagons

Norwegian screening advocates also had a loose regard for truth. When we published our review in *Lancet* in 2001,[54 55] the cancer research community was in uproar and Steinar Thoresen, the leader of the Norwegian screening programme, remarked that we were on a

crusade against screening; that we didn't know what we were talking about; that the technique used in the trials could not be compared with modern-day techniques; and that *Lancet* had become a "popular science magazine."[56] In another newspaper, Thoresen described our work as "unadulterated nonsense," "unlimited naiveté," and we were undermining our trustworthiness.[57] He also said, "by the way, no one in the international research community has any confidence in the movement [The Cochrane Collaboration]."

Norwegian experts "burned with rage" and Rolf Kåresen, medical director and breast surgeon at Ullevål Hospital, insinuated that our conclusion in *Lancet* was completely wrong and that we knew it was wrong – a pretty libellous statement.[58]

A year earlier, pathologist Jan Mæhlen had invited me to lecture on mammography screening at the annual meeting for the Norwegian Society of Pathologists in Oslo. This also led to violent verbal attacks from Thoresen and Kåresen. A Norwegian newspaper reported that Thoresen had presented such derogatory remarks about our work during the meeting that many attendants had perceived it as unprofessional.[59] Thoresen expressed no regrets that he created a bad atmosphere.

Two weeks later, Thoresen and Kåresen published a long article attacking our research,[60] to which I responded.[61] They characterised my criticism of the trials as totally one-sided and based on my own definitions of negative aspects of screening. I was also criticised for having excluded a positive study from the Netherlands. We had indeed excluded it – but it was a case-control study, and we only included randomised trials. Moreover, case-control studies are notoriously unreliable and screening experts have agreed that they cannot be used to evaluate the effect of screening.[62]

Thoresen and Kåresen described as particularly erroneous and serious our claim that more women will lose a breast when there is screening and said that when one of them asked at the meeting if I had literature that could document this, he received no answer. This was not true. I showed on a slide that there was a 20% increase in mastectomies in the randomised trials and on another slide that carcinoma in situ may be treated by mastectomy.

They claimed that new studies had shown that radiotherapy does not increase mortality from heart and lung diseases. Such studies don't exist. Yet, because I had mentioned this harm, they doubted my "academic honesty."

They concluded with the "you are killing my patients" mantra, claiming it was a serious concern that a few researchers in a groundless and demagogic way can influence women to abstain from screening.

The Norwegian Cancer Registry had declared that screening would reduce breast cancer mortality by 50%,[63] and Thoresen referred to this in 1998.[64] Thirteen years on, we still hadn't seen any reduction.[65]

In 2006, Thoresen went on leave "to seek new challenges" after it was revealed that he had received a lot of money from the drug-maker Merck into his personal bank account, which he had failed to declare, although the director of the Cancer Registry had repeatedly warned at meetings he attended that such payments should be declared.[66] He single-handedly negotiated a deal for the HPV vaccine with Merck for Norway. The previous Norwegian minister of health remarked that such financial transactions are called corruption.[67]

Thoresen continued to publish papers listing his address as the Norwegian Cancer Registry, even though he was by now research director at GlaxoSmithKline and lectured medical students at the University of Bergen in a professorship position financed by them.[68]

When this was revealed in a newspaper, Thoresen was defended by the director of the Cancer Registry, Frøydis Langmark, who attacked the journalists that broke the story.[69] She claimed that the education of students would not be influenced by this arrangement.

When Jan Mæhlen and Per-Henrik Zahl noted in a newspaper that many women are overdiagnosed, Thoresen strongly rejected their findings.[70] He said that the proportion of women with metastases had been halved since the programme was introduced, which can only be true if there is massive overdiagnosis of harmless cancers.

A physician working with diagnosing breast cancer declared that it wasn't necessary to give information about the negative aspects of screening because there weren't any.[71]

How can the doctors we trust to inform women be so unprofessional?

Because of our criticisms of the trials, the Swedish Board of Health and the Swedish Cancer Society arranged an international meeting in Stockholm in February 2002. Almost all the attendees were screening advocates, and the atmosphere wasn't friendly towards those who didn't share their views. This is the only time I have met with Tabár, and I used the opportunity to ask him crucial questions about this trial. He refused to reply to any of them, which is remarkable, as the money for his trial had come from the Board of Health and from the Swedish Cancer Foundation.

I heard so many curious and invalid arguments at the meeting that I sent a summary of my own minutes to the director of the Board of Health, Nina Rehnqvist, pointing out the errors even though I knew I wouldn't accomplish anything.

Even the lead investigator for the Malmö trial, Ingvar Andersson, whom I otherwise respected, showed misleading numbers on this occasion. He concluded that screening didn't increase the rate of mastectomies because there were nine fewer mastectomies in the screened group than in the control group in his trial between 1984 and 1988. However, the trial started in 1978, and the total number of mastectomies during all the nine years the trial ran were 424 and 339, respectively,[72] i.e. there were 25% more mastectomies in the screened group than in the control group.

One cannot just cherry-pick a time period long after screening started and get anything reliable out of this. Particularly at the prevalence screen, there is a large excess of mastectomies.

Other researchers were similarly disingenuous. In 2002, epidemiologist Olli Miettinen and others published a most bizarre research letter in *Lancet*,[73] which was followed by an equally curious letter by other researchers who quoted it in a comment to our Cochrane review.[74] US statistician Donald Berry and I explained why Miettinen's research was flawed,[75] but that didn't have any effect on him. He and his co-workers now said: "So grossly does Gøtzsche misrepresent the principles we adduced that they need to be reasserted," where-after they repeated their mistakes.[76] Not even six months later, when other researchers described their errors again, did they admit they were wrong.[77]

They had performed a remarkable act of hocus pocus. They pointed out that the effect of screening only appears after some delay and then used data from the Malmö trial in the time window 8–11 years after the trial started and concluded that screening reduced breast cancer mortality by 55%. But the fact is that this trial did not find an effect of screening.

They might equally well have looked at the interval 3–6 years after randomisation, when there was an *increase* in breast cancer mortality of 58%. Obviously, the only legitimate analysis is to use all the available data from 0 to 11 years. Their method defies logic, as the women cannot come to the interval 8–11 years without having survived the first 8 years.

The second letter, in the *Cochrane Library*, was also strange. Benjamin Djulbegovic and Iztok Hozo declared that we had made "elementary analytical errors" and that it was wrong to pool data at a fixed time point (e.g. after seven years, which is entirely legitimate). They used Miettinen's faulty method, pooled the Canadian and the Malmö trials, and hoopla, reported a reduction in breast cancer mortality of 39%. They even suggested that Miettinen's cherry-picking method should be used in other systematic reviews in cancer.

We noted that we didn't understand how they could have used data from the Canadian trials for their calculations, as we couldn't find useful data for Miettinen's method in the reference they gave.[78] Anthony Miller wrote to Djulbegovic and informed him that he had never published data in a form that would enable anyone to perform a "Miettinen-type" analysis.

It is difficult to understand why experienced researchers would publish such nonsense. Are they so dumb that they cannot see the flaw in their method, or are they cynical and cheat deliberately because they want to create fictitious support for screening? Excuse me for being blunt, but I cannot see any other possibilities.

What we do know is that some screening advocates are deliberately dishonest. For example, Anthony Miller once wrote to me that, "as Kopans is well aware, we have responded to all his points already in the scientific media, but he chooses to ignore this."

Denmark continued to provide a rare insight into how health policies are made, with a glaring disregard for the scientific evidence to arrive at a preconceived and politically desirable conclusion.

The Association of Danish Counties asked the Board of Health to reconsider its recommendations on screening, noting that it had not been documented that screening leads to better survival, whereas we had documented that screened women will experience more operations and more radiotherapy. The association demanded a written report from the Board of Health on its interpretation of our research.

The director of the Board of Health replied that it was not the Board's obligation to comment on every publication in *Lancet*, even though its authors are Danish, ignoring that the Board had funded our research to learn more about screening!

A week later, the Board declared that it would look at data from screening programmes in several countries, as there "are many other data [than those from randomised trials] that can contribute to the evaluation of screening." This is like first using a strong lamp, and when you don't like what you see, you shift to a weak lamp, hoping you don't see it any longer.

In February 2002, the Board published a report that is a masterpiece in manipulation.[79] The dirty tricks included ignoring some of our most important observations and mentioning "positive experiences" with the Swedish programme that had been communicated in a 1997 report from the Swedish National Board of Health. There was no reference to this report, and I was unable to find it.

The truth is that there were no "positive experiences" from Sweden apart from those based on flawed research. The Board denied that screening increases mastectomies; that radiotherapy of healthy, overdiagnosed women increases deaths from heart disease; and that cause-of-death assessments inevitably are biased in favour of screening, even when blinded end-point committees are used.

The Board made other serious errors. It dismissed our finding of overdiagnosis with the inappropriate argument that these particular data were not accepted by the Cochrane

Breast Cancer Group in our Cochrane review. But we published these data in *Lancet*. What's wrong with that?

Although the Malmö trial didn't find an effect of screening, the Board alluded to Miettinen's flawed research letter in *Lancet* and even had the audacity to note in its conclusion that it is noteworthy that we had declared that the Malmö trial showed no effect, when Miettinen's analysis showed an effect.

This information was not part of the draft report we had seen in advance of the meeting at the Board of Health we participated in. It was inserted later, and the final report was quite different from the draft report. We didn't get an opportunity to point out the many errors in the final report because it wasn't sent to us before it was finalised and sent to the Association of Danish Counties.

In Norway, Germany, the United States and elsewhere, we were accused of killing women.

In the United States, there were a few glimpses of sanity, however. The *New York Times* published a series of articles critical of mammography screening and took issue with all the hype noting that the reaction of the cancer establishment "had been to call on higher authority – itself."[80]

An independent panel of US medical experts writing for the National Cancer Institute's website concluded that there is insufficient evidence to show that mammography screening reduces deaths from breast cancer.[81] One of the panel members was Donald Berry, who said to *BMJ* that it was difficult to question an enormous mammography industry: "Screening programmes bring in patients."[82]

This was perceived as so threatening that ten leading medical organisations published a full-page advertisement in the *New York Times* in support of screening using the "you are killing my patients" argument.[83]

The usual untruthful comments and serious manipulations with the data dominated the public discourse. I wrote a regular column on science in a newspaper, and in 2003 I did a piece on cancer screening. This provoked a reaction from chief physician Iben Holten from the Danish Cancer Society.[84] She argued that there was no documentation that the cause-of-death assessment was sometimes erroneous. Holten is a pathologist, and if there is anything pathologists know, it is that determination of cause of death is error prone, particularly in patients with cancer.

Our 2001 meta-analysis started a flurry of meta-analyses, none of which were of high quality. As an example, in 2002, the US Preventive Services Task Force listed under harms only false positive tests, unnecessary anxiety, biopsies and cost.[85] It is misleading to talk about unnecessary biopsies when screening increases both tumourectomies and mastectomies.

A 2007 practice guideline from the American College of Physicians cited our *Lancet* review, but not for its data on overdiagnosis.[86] Instead, a flawed observational study from Florence by Stephen Duffy and others was taken as evidence that screening *decreases* the risk of mastectomy.[87] This was statistical alchemy.

In March 2002, Nyström and colleagues published an updated meta-analysis of the Swedish trials in *Lancet*, which responded to some of the concerns we had raised.[88] However, although Nyström had data on all cancer deaths, he didn't report on cancer mortality. One of our most important findings had been that screening doesn't reduce cancer mortality (including breast cancer), which is expected if screening works. We had written in *Lancet*

that the relative risk for total cancer mortality was 1.02 (95% CI 0.95 to 1.10) in the two trials with adequate randomisation and 1.00 (0.91 to 1.10) in the trials with poor-quality data.[89]

Nyström had published such data in 1996, where he reported a 2% increase in total cancer mortality, which became a 2% decrease after he had adjusted the data for the age imbalances.[90]

There were major problems with numbers in Nyström's 2002 meta-analysis. There were more randomised women than in his 1993 meta-analysis, which shouldn't be possible because both meta-analyses were based on exact age at randomisation and the age range was the same. Thousands of women were included in the analysis although their age was below the defined age for inclusion, and groups differed substantially in size, although the randomisation should have created groups of the same size.

About the possible differences in socio-economic factors at baseline in the Östergötland part of the Two-County trial,[91] Nyström et al. explained that no pre-trial background data were collected in the Swedish trials.[92] This cannot be true, unless Tabár lied when he reported that the randomisation in Östergötland was stratified for socio-economic factors.[93]

Peter Dean continued to spread falsehoods and *ad hominem* attacks,[94 95] and David A Freeman, a distinguished US statistician, and his colleagues made elementary statistical errors and other errors, which I pointed out.[96 97 98 99 100]

Publication of entire Cochrane review obstructed for five years

When the letters criticising our review were published in 2002, Richard Horton alerted readers that big issues were at stake:[101]

"Some senior scientists have said to me that this debate should not be taking place in public. Screening mammography is, they argue, too important for women's health to have its image damaged by questioning the technique's efficacy and safety."

He noted that, to avoid accusations of censorship, "let the scientists doing the review publish what they wish to say – it is, after all, their work ... That way … the public sees science as a truly collaborative process, in which differences of opinion are not only respected, but also welcomed."

So true, but Cochrane had already abandoned the idealistic principles it was based on when it started 1993 and had introduced censorship.[102] In 2001, my research team assessed the quality of Cochrane reviews.[103] We identified major problems in 15 of 53 new reviews (29%), and what particularly stood out was that the evidence did not fully support the conclusions in nine reviews (17%). All the problematic conclusions gave a too favourable picture of the experimental intervention.

The Cochrane leadership was vehemently against us publishing our observations. We had informed our Cochrane colleagues well ahead of publication, which was to our own disadvantage, as the Cochrane Steering Group put pressure on us not to publish the results. I was summoned to a Steering Group meeting to explain why we wanted to publish and said that, since we belonged to an organisation that constantly assesses and critiques others' research and points out when inconvenient results are being suppressed, it would be wrong to suppress our own results, which would also be an act of censorship.

I furthermore noted that it would demonstrate Cochrane's strength that we were willing to criticise ourselves and explained that it was important for patients, doctors and others to know that conclusions of Cochrane reviews should be viewed with caution, and that they needed to read more than just the conclusion.

As it turned out, nothing untoward happened to Cochrane. In fact, our paper benefited Cochrane and led to other quality improvement initiatives than ours being undertaken. But later, Steering Group co-chair Jim Neilson noted that many in the Collaboration felt our review was misleading because it was out of date (which was not correct), embarrassing, and potentially damaging, and that one entity almost lost external financial support.[104]

In science, we hold people accountable for what they publish, and it is not relevant if this is embarrassing for some people. And we could not have foreseen that one entity's funding would come into question.

The chair of The Cochrane Collaboration Steering Group, Peter Langhorne, arranged a telephone conference in November 2001 to resolve our dispute with the Cochrane Breast Cancer Group. He was keen to avoid further damage to the collaboration and therefore asked me to disclose our reply to a letter the Cochrane editors had sent to *Lancet* about the dispute. I replied that suppression of academic freedom could be far more damaging to the collaboration and noted that I had already received the editors' letter from *Lancet* and had responded to it. I felt it would be inappropriate for me to circulate my reply to the conference attendees, as Langhorne requested.

When he insisted, I noted that Horton had made it very clear to me that in his view, the collaboration "should not, repeat not" ask me to disclose the contents of my letter. He noted that "It smacks of censorship and I know of no example where one protagonist has had the right to review the comments of another protagonist pre-publication."

The teleconference went well but the process of updating our review was stonewalled by the Cochrane Breast Cancer Group editors. They ignored all emails, even those from Langhorne. In March 2003, 1½ years later, we had still not heard anything from the Cochrane editors. Therefore, we submitted a revision of our review, which was now out of date, as additional, important data had appeared in the Swedish 2002 meta-analysis.

I sent more emails but got no reply. In September 2003, I told Langhorne that data from the United States and the United Kingdom confirmed the results the Cochrane Breast Cancer Group had not allowed us to publish in 2001 – namely, that screening causes about 30% overdiagnosis and overtreatment. I added that the pro-screening lobby had consistently tried to suppress and even ridicule this important information. I also warned that the longer it took, the more the suspicion of censorship would grow.

The next day, I received an email from the group's two key editors, Simes and Wilcken, who mentioned two peer reviews, but they were not enclosed, only a summary of them. Therefore, we could not reply to them, and we could not even tell if they were written recently or some time ago, as they were undated.

We were told that the two anonymous peer reviewers strongly recommended against publication; that our review was not acceptable for publication; and that further revision of the review was unlikely to resolve the issues.

That was a smart move. By denying us the possibility of updating our review, the group could withdraw the published review at a later stage with the argument that it was outdated.

The editors' complete denial of the most important harm of screening continued. They talked about "unsubstantiated claims of harm" and remarked that in the longer run the number of surgical procedures would tend to become the same in the control groups as in the screened groups. They did not document anything, and their wishful thinking was plainly wrong.

I informed Langhorne about the permanent roadblock the same day, and he offered to contact the collaboration's newly appointed publication arbiter, David Henderson-Smart.

I also contacted my good friend, Drummond Rennie, editor of *JAMA* and co-director at the US Cochrane Center, who said that "unless Cochrane makes it as a scientific enterprise, it cannot and should not survive."

The Cochrane editors noted in their rejection letter that international working parties had reassessed the evidence and had concluded that screening was of value. I remarked that this was a judgement and not a scientific statement, and that Cochrane reviews are about presenting the scientific evidence on benefits and harms and letting the readers make up their own minds. They are not policy documents.

Langhorne and Henderson-Smart advised me that I should ignore the editors' rejection and submit a revision, with a reply to the comments. I did this in November 2003, but it took another three years before our review was published.

The group's arrogance was unbelievable. They continued to ignore us. Then, a second publication arbiter, Kay Dickersin, director of the US Cochrane Center, became involved. In December 2004, I received three peer reviews from Wilcken, which, yet again, were undated. They were excellent and remarkably consistent, and it would be easy for us to respond to them. But we didn't get the opportunity: "It is with regret that we inform you that on the basis of this feedback, the CBCG is unable to accept the review update."

This was a horrific abuse of a monopoly situation. The rejection at this stage, with no possibility of appeal, was not only inappropriate; it also went against Cochrane principles. The reviewers were positive and there wasn't the slightest objective reason for rejection.

By now, the two publication arbiters had had enough of this and involved the Cochrane Collaboration Steering Group. Five months later, we were asked to reply to the comments and to submit a new version. But the Cochrane editors blocked us again. Three days before we submitted the revised review in November 2005, they informed me that our review would be peer reviewed again. I replied that I had understood that it was now up to the editors to look at our paper.

Again, the delay was grotesque, and repeated requests, both from me and from Dickersin, to get a reply from the group led nowhere. It took another seven months before we got the unexpected message that our updated review had been accepted for publication.

Our updated review was published six years after we first submitted it. *Lancet* was 55 times quicker than Cochrane. We submitted our full review on 10 September 2001 and *Lancet* published it 40 days later, after comprehensive peer review.

This was the most high-profile conflict in The Cochrane Collaboration's history. It concerned one of the most controversial and hugely expensive interventions ever introduced in healthcare.

The overriding perspective for us was ethics. Women should not be denied information about the most important harm of screening, substantial overdiagnosis and overtreatment, which was a well-guarded secret before we stepped into the scene and published our findings in 2000 in *Lancet*.

The screening advocates kept quiet about overdiagnosis, as they were afraid it would deter women from attending screening. Such utilitarian ethics constitute unsolicited paternalism, which is only acceptable if we deal with incompetent patients, e.g. children or unconscious people. Women are not children, and the prevailing paternalistic attitude, which is still the norm, is unacceptable.

The affair demonstrated that Cochrane had a very weak leadership. It should have been easy to demand of the Cochrane editors that it publish the data on harms shortly after our *Lancet* paper with these data came out.

In 2011, Cochrane asked me to publish an article on Cochrane's website, "Mammography screening ten years on: reflections on a decade since the 2001 review." I ended the article this way: "It is getting more and more difficult to argue that it is reasonable to attend for breast screening."[105] Today, the article is gone. I find it is unprofessional to remove published articles, especially without informing the authors.

4 Editorial misconduct in the *European Journal of Cancer*

When you publish results that raise the question if a pivotal study is scientifically dishonest, you can come in deep trouble, and the journal that published your results might commit editorial misconduct to avoid trouble for itself. This chapter is about how threats of litigation can threaten academic freedom to the detriment of women who might not be told that scientific misconduct is suspected for a pivotal study that led to the introduction of mammography screening in many countries.

Is the Two-County trial scientifically dishonest?

Outside screening advocacy circles, we haven't met any researchers who knew something about the Two-County trial and weren't sceptical about it.

Nyström's 2002 meta-analysis, which was based on official mortality statistics, found only a 10% reduction in breast cancer mortality for the Östergötland part of the trial,[106] whereas Tabár and colleagues reported 24% when they decided on cause of death themselves without being blinded for screening status.[107] Tabár and colleagues reported 10 *fewer* deaths from breast cancer in the screened group despite the fact that the follow-up was slightly longer than in the meta-analysis and the age group was identical, and 23 *more* deaths in the control group.

When confronted with this large discrepancy, Tabár, Smith and Duffy gave a peculiar reply:[108] "It is asserted in the overview report that the endpoint committees in the Two-County trial were aware of patients' study groups. No evidence is presented for this assertion."

Surely, Tabár must have remembered what he and his co-investigators had done, and after some detective work, I found out that the cause-of-death assessments were *not* performed blindly. A local end-point committee determined the cause of death, which was confirmed by an investigator involved with the trial, other Swedish trialists, and the IARC Handbook of Breast Cancer.[109]

Three Norwegian researchers and I did a study that used the Swedish population-based registers for cancers and causes of death. We found that 192 breast cancer cases and 43 breast cancer deaths seemed to be missing in the 1985 publication of the Two-County trial, and similar discrepancies persisted in two trial updates. Our suspicion that some cancers and deaths were not included in the trial results was supported by other data.

We published our findings in March 2006 in the articles-in-press section of the *European Journal of Cancer's* website.[110]

Twenty days later, editor-in-chief John Smyth informed us that he had received "comments from a number of sources regarding some of the claims made in the article" and that he had removed our article pending further discussion and clarification. Smyth didn't forward the comments to us but asked for very minor clarifications and changes. We submitted a revised manuscript but then, to our great surprise, as our paper had already been published, the revised manuscript was sent out for peer review, and two months later Smyth informed us that his decision to withdraw our paper was final.

He referred to "the release of new information concerning the randomization process and the trials' opening and closing dates" and forwarded selected "Comments from the peer review process."

Selected comments? Again! That was what the Cochrane Breast Cancer Group had also done to us. We were now the victims of another Kafkaesque process where we were only allowed to see selected parts of the evidence. There was total confusion, as some of this "new information" contrasted not only with published data but also with randomisation dates we had received in earlier peer reviews.

Using any of the three different sets of randomisation dates in our analysis, we confirmed our original results. However, despite two appeals, Smyth did not offer us the opportunity to document our analyses. No matter what assumptions and which numbers from the various reports on the trial we used, we came to the same result, that cancers and deaths were missing.

Doing forensic analyses of the Two-County trial was frustrating because the trail always went cold. It was rather generous that the authors, which included Tabár, of the 1993 meta-analysis of the Swedish trials claimed that the cluster randomisation in the trial wasn't biased, with reference to an unpublished lecture.[111] Furthermore, a reference to the randomisation method in Nyström's thesis from 2000 led to an empty reference,[112] and when I asked Nyström about it, he sent an unpublished letter that didn't describe the method either.

Our paper was removed without warning. Four days after Smyth had informed us that he had withdrawn our paper, we observed that it was listed as withdrawn in PubMed, in violation of the *European Journal of Cancer's* own policy, which requires that, "In no instance should a journal remove an article from its website or archive."

I described our case in an anonymised fashion on the email list of the World Association of Medical Editors and asked for advice. Just an hour later, Richard Horton replied that *Lancet* would be keen to consider the case for publication, as "editorial misconduct needs to be as ruthlessly dealt with as any instance of research misconduct."

We described the affair in *Lancet* in November 2006[113] and published our research paper simultaneously in the *Danish Medical Bulletin*.[114]

A key player threatens legal action

A person close to Smyth informed me that Smyth or his journal, or both, were threatened by litigation, likely by László Tabár. But yet again, Peter Dean led the attack. He sent vitriolic emails around, which, typical of Dean, didn't contain any scientific substance or concrete criticism of our work. He copied one of them to 150 people. His letter to Elsevier, the owner of *Lancet*, was amusing in all its pejorative glory:

"patently shoddy scholarship and serious errors,"

we claimed that work published by others "has been fraudulently altered,"

"the claim amounts to scientific libel and defamation of character,"

"the claims are preposterous,"

"since they are now electronically published, they have an air of infallibility on which the authors will use to claim validity,"

"the accused scientists were never contacted in advance to offer an opportunity to set the record straight."

The argument that we should have shared our concerns with the trialists had no merit, as Tabár never provided meaningful answers when asked. Dean remarked that our paper seriously damaged the reputation of the journal and that he knew that a number of assump-

tions, estimations and approximations were incorrect and contrary to the published design of the trial. However, as always, he offered no evidence in support of his many opinions.

Dean responded in *Lancet* to our comment about editorial misconduct with arguments that were all false.[115] [116] He claimed he had no conflict of interest but had hidden his title as professor of radiology by giving his address as "Faculty of Medicine," and a PubMed search showed that he and Tabár had collaborated for decades - 30 years according to Dean himself.

Dean has a habit of harassing everyone who does not agree with him. He told Torben Schroeder, the editor of the *Danish Medical Bulletin*, that he hoped he would not be liable to litigation and that if he didn't act in ways Dean defined for him in his letter, "this would reflect even more poorly on the *Danish Medical Bulletin."*

Dean copied his letter to Schroeder to an impressive list of people that included the deans for the three Danish medical faculties, the chairman and the director of the Danish Medical Association, the legal editor of *Ugeskrift for Læger (Journal of the Danish Medical Association)*, the director of the Danish National Board of Health and four other key people working there, the director of the Danish Health Technology Assessment agency, the heads of the Danish screening units, and Elsebeth Lynge, who chaired the working group that wrote the Board of Health's misleading 1997 report that recommended breast screening be introduced in the whole of Denmark. Members of the royal family and our prime minister were not on Dean's list.

The *Scientist* described the affair, and Smyth said that "The EJC Editors acted professionally at all times and handled the manuscript fairly and in accordance with the standard editorial policies of the journal."[117] This is what moral philosopher Harry Frankfurt would call bullshit.[118]

In an email to the *Cancer Letter*, Tabár described our paper as "beset by elementary errors and fallacious assumptions."[119] As Tabár rarely responds to criticism of his trial, I have shown his full comments with our replies[120] in my book.[121] All of his pivotal statements are either false or misleading.

Four years later, in 2010, Tabár threatened legal action again, the day after we had published a comment on *BMJ's* website[122] where we noted that, "Assessment of cause of death was not blinded in this trial, and the investigators reported an effect of 24% in one of the counties when the official cause-of-death register only showed a 10% effect (11). We will probably never know what happened in the other county, as Tabár has denied other researchers - even the other Swedish mammography trialists (14) - access to his data."

Tabár argued that,

"These allegations concerning my scientific integrity amount to defamation of character. I am certain that the authors are aware of the attached publication by Holmberg et al. in the *Journal of Medical Screening*."

He claimed that this article clearly explained why the 2002 meta-analysis of the Swedish trials[123] reported other results than those reported by himself. He warned that investigators, and especially journals, should be cautious about implying scientific misconduct.

There was no defamation of character, and we did not imply scientific misconduct; we just stated the facts. Tabár must have felt badly hurt. He uttered something about our lack of civility and our caustic, slanderous remarks, and libelous allegations of which there were none.

I wrote to *BMJ* that I didn't know about this recent paper; that we referred truthfully to the historical facts we were familiar with; that there could therefore be no basis for a defamation trial; that I didn't think Tabar could prevail by accusing us of not knowing about everything he publishes; and that I didn't even think he would try. I also noted:

"He has threatened many people with litigation previously, and I can document some of these instances. He seems to do this in order to intimidate people and hoping to scare them to keep quiet next time. As far as I know, Tabár has never taken legal action, and I therefore think both *BMJ* and we can relax … Here is an example where people were much more direct, but which did not lead to litigation (from the draft of my book):

Kjell Asplund, chairman of the board of the Swedish Council for Technology Assessment in Health Care, had expressed serious criticism of the Two-County trial in the Swedish newspaper, *Svenska Dagbladet*, and the chairman of the Swedish Office for Scientific Integrity, Professor Lars Terenius, had said, also in *Svenska Dagbladet*, that although the study could not be called directly fraudulent, it was an evident case of scientific misconduct (Atterstam 21 July).[124] These two people were bombarded by letters from Tabár and others, demanding that they should retract these statements in the newspaper, which they didn't."

BMJ replied that, "our lawyers are advising that we don't fight the claim. So if we want to fight it hard we have to fight both our insurers and then Tabár. And our judgement is that the accusation that he didn't share his data isn't worth a fight to the death. That doesn't mean that we are going to cave in to all that he wants."

I also informed *BMJ* about an email I had received from Cornelia Baines:

"Given the way Tabár so frequently threatens to sue, I am not sure they will have the courage to go ahead. However, I am pleased that one journal told him to go ahead and sue and they would counter with a suit for his frivolous action. It worked … It would be a disaster for Tabár if he really sued. Better to keep the lid on so that all the worms don't come out!"

Tabár's American lawyer sent some silly demands to *BMJ* that they refused to accept. I told *BMJ* that Tabár's lawyer muddled the issues and that I had found many errors in his statements, which I explained over five pages.

I wrote to *BMJ* that even though Tabár had shared his data now, this did not compromise our statement that he had previously denied access to others and what we had written was well known and was described in the Swedish 2002 meta-analysis:[125]

"The Kopparberg part of the Two-County trial was not available for this overview. The unavailability of Kopparberg data was due to a decision not to continue with the collaboration with the Swedish collaborative group by the Kopparberg trialists shortly after the publication of the first overview (11). We regret this decision."

I suggested the editors invite Tabár to publish his views as a contribution to the scientific debate, but it took 2½ months and negotiations between the lawyers from either side before he accepted the offer.

The *BMJ* editors are obliged by their insurance to follow their lawyer's advice, and they deleted the two sentences Tabár didn't like: "We will probably never know what happened in the other county, as Tabár has denied other researchers - even the other Swedish mammography trialists (14) - access to his data."

I wonder why Tabár was so eager to have this removed, as he wrote essentially the same in his published reply:[126]

"Jørgensen and Gøtzsche have claimed in their recent Rapid Response on the *BMJ* website that 'Tabár has denied other researchers - even the other Swedish mammography trialists - access to his data' (1). This is untrue, as evidenced by my full co-operation with the

Swedish Cancer Society's Overview Committee (OVC) from 1989 through 1997 (2-6), and with the Swedish Cancer Society's Joint Review Committee (JRC) from 2006-2009 (7). It is to be welcomed that the *BMJ* removed this false claim from the Rapid Response website."

Tabár is a bully. He didn't explain that the *BMJ* did this after legal pressure exerted by himself and that they did not acknowledge they made any errors by publishing what Tabár called a "false claim."

Later, Stephen Duffy added insult to injury when he stated in *BMJ* that "one claim made by Jørgensen and Gøtzsche in the correspondence was withdrawn by the editors on legal advice."[127] Duffy didn't explain how foolish Tabár's hair-splitting was and he conveyed the impression that we had done something wrong, just as Tabár did.

We should not accept that threats of libel can be used to prevent inconvenient truths to be published. This is not in the best interest of science, and not in the best interest of the patients and citizens.

Our Norwegian collaborator Per-Henrik Zahl, of the Norwegian Institute for Public Health, and colleagues reported in 2001 that when they found that the tumour data in the Two-County trial were inconsistent, their requests for access to the data were refused.[128]

Karsten Juhl Jørgensen from my centre and I came to collaborate closely with Zahl. He is both a physician and a statistician, sharp and creative, but sometimes less good at explaining what he has done. So, we often spent some time to get our papers in shape so that the readers could understand them. It was fun.

After having seen Tabár's lengthy comment on *BMJ's* website, Cornelia Baines submitted a letter to *BMJ*. For legal reasons, *BMJ* didn't dare publish this part:

"Dr. Tabár tells us he has been very collaboratively inclined although according to his own information not between 1998 and 2005. However, I distinctly remember participating in a meeting convened by the US National Cancer Institute January 18 and 19, 1994: the NCI Working Group on Breast Cancer Screening Meta/Overview-analyses in Rockville, Maryland. Obviously, it had been hoped that the trialists would agree to submit their data so that analyses of combined raw data could be done by year rather than by quinquennieum. I so clearly remember Dr. Tabár disdaining to meld his data with data from other inferior trials. I so clearly remember the trialist beside me saying: If the women who participated in all the screening trials heard this they would be outraged."

What Baines was allowed to publish was this:[129]

"I remain skeptical about the amazing muddle of crucial numbers (participants and breast cancer deaths) in the Two-County trial that should not require interminable exegesis 24 years after the trial results were first published in 1985. And when it comes to validating causes of death, I just cannot be persuaded to lend more credence to decisions by selected 'specialists' compared to data from Cancer and Death Registries."

Window dressing to restore the Two-County trial's ill reputation

In contrast to Tabár's assertion, we were not aware of the paper by Holmberg and colleagues,[130] which had been published less than a year earlier. It was said to be "a complete audit of breast cancer cases and deaths" in the Two-County trial, but we were not impressed and regarded it as window dressing intended to get Tabár off the hook.

It was not an independent audit. The authors included Tabár and Duffy who have a lot to hide, and the Two-County trialists were not only directly involved with resolving disagreements between their own publications and those in the 2002 meta-analysis. They were also

members of a Joint Review Committee that determined the reasons for the disagreements and arrived at its own estimates of the effect of screening in the two counties.

There was no attempt at producing a new data set based on the clinical records that could have been assessed independently from what had taken place in the past: "where necessary, clinical records were retrieved."

There was no description of any attempt at blinding the provision of the data or the assessments, which could have ensured that no one knew whether a woman belonged to the screened group or to the control group when they decided on the cause of death. Assessment of cause of death can be very difficult, indeed sometimes impossible, and to do this in an unbiased fashion requires blinded recording of cause of death, blinded selection of data for review, and blinded review.

Karsten Juhl Jørgensen

Michael Baum

Per-Henrik Zahl

Breast surgeon Michael Baum, who opened the first mammography screening centre in the UK in 1988, recently wrote to me that cancer screening trials that do not report on all-cause mortality or do not have blinded, independent assessment of cause of death are unreliable. He mentioned the ProtecT trial for PSA screening for prostate cancer as an example.

Baum chaired the independent advisory committee and was a member of the independent blinded cause of death committee. They reviewed every death with all the data of the case and classified them in three boxes, undoubted prostate cancer, undoubted not prostate cancer or uncertain because of co-morbidities "competing" to the end. If that process had not been blinded, the slightest bias could have changed a negative to a positive result.

In contrast, the Holmberg study was astoundingly poor research that does not deserve to be called an audit. I am not surprised that the Joint Review Committee came up with very similar estimates to those published by Tabár originally.

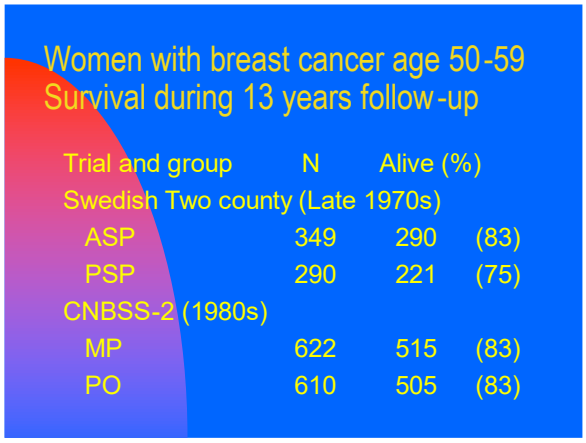
We were not the only ones who didn't trust Tabár's cause of death assessments. Pulitzer Prize winner John Crewdson from the *Chicago Tribune* contacted me in November 2000 and asked to have a meeting, which became several meetings.[131] He beleaguered Tabár for several days until he got away with data sheets that described causes of death, which he showed to me.

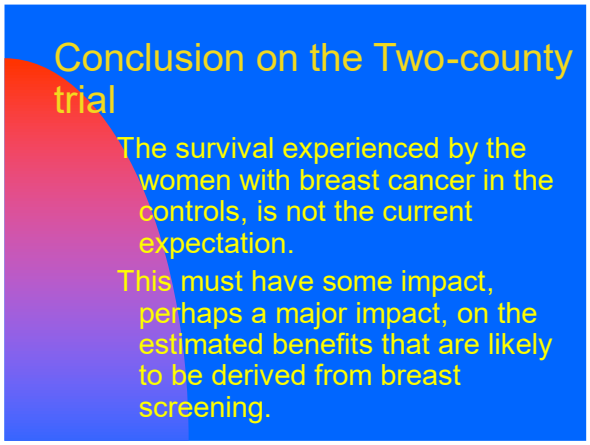
To put it mildly, the cause-of-death assessments were problematic, and Crewdson worked on them for quite a while. He never published anything, and several people have told me this was because Tabár had threatened the *Tribune* with litigation.

Crewdson published other observations, e.g. that 750 women disappeared from reports of the Kopparberg part of the trial after 1989.

Several investigators, including some from the Malmö screening trial, expressed concern to us about the data from the Two-County trial. Four years after randomisation, there was an abrupt increase in breast cancer deaths in the control group, whereas the trend in the screened group continued unchanged. One would have expected to see an unchanged trend in the control group and a decreasing mortality trend in the screened group.

Anthony Miller had visited Tabár in Sweden in the 1980s,[132] when they were still on speaking terms, and his visit had worried him greatly. He was convinced that the cause-of-death ascertainment was biased. I agree. Miller presented two interesting slides about this at the World Congress of Epidemiology in Montreal on August 18, 2002:





The women in the screened groups had the same 13-year survival in the Two-County and Canadian trials (83%) whereas the control group women had markedly lower survival in Sweden.

5 Beyond reason studies: dishonest researchers

> *This chapter is about dishonest researchers. When they take a strong lamp and don't like what they see, they shift to a lamp that is out of order and see something else. They do their best to fool the whole world with their misleading observations. When this is pointed out to them, they might lie about what they have done.*

Quite often, when large, randomised trials have not found an effect of an intervention some people strongly believe in, they pollute the world literature with an array of substandard studies that apparently show what they had hoped for.

The International Agency for Research on Cancer (IARC) is the cancer agency of the World Health Organization. It publishes many monographs and handbooks, and one of them states about breast cancer screening that:[133]

"Observational studies based on individual screening history, no matter how well designed and conducted, should not be regarded as providing evidence of an effect of screening."

Therefore, if researchers were honest, they would not claim an effect of mammography screening based on observational studies. But virtually all breast screening advocates are dishonest. This is the biggest problem with mammography screening. If people were honest, we would not have mammography screening. It is as simple as that.

Misleading observational studies claiming a large effect of screening

The prototype of a highly misleading observational study was published in *Cancer* in 2001, by László Tabár, Stephen Duffy and Robert Smith, and three others.[134] The title of the paper is "Beyond randomized controlled trials," but the study is so flawed that statistician Donald Berry told Robert Smith that they should have called it "Beyond reason."

Cancer is regarded as a prestigious journal, but Tabár's article was received on 29 December 2000 and was accepted six days later, which suggests it wasn't peer-reviewed, contrary to the journal's standards. Perhaps it helped that *Cancer* is owned by the American Cancer Society and that Smith was Director of Cancer Screening at the society.

In the Two-County area, breast cancer mortality during screening was compared with a previous time period before screening, which is an illegitimate comparison when the denominator is women with a breast cancer diagnosis. The authors included all the healthy, overdiagnosed women in the screened group who, by definition, cannot die from breast cancer because if they did, they would not be overdiagnosed.

Another huge bias is caused by the fact that those cancers that were detected in the period before screening were generally more advanced and therefore also more deadly than those detected during screening. Because aggressive cancers are asymptomatic for a shorter period, screening is more likely to detect slower growing cancers, which have a better prognosis (length bias). And when there is screening, the cancers are detected earlier, which falsely makes it look like people are surviving longer (lead-time bias).

The triumvirate found a 63% reduction in breast cancer mortality in those who attended screening. I pointed out some of the problems with their study,[135] but in their reply,[136] they compared women who attended screening with women who didn't, although it is clear from their own paper that they were aware that such comparisons are seriously misleading.

In a five-page accompanying editorial,[137] Tabár's study was praised as seminal, meticulous, a milestone, and a final critical test of the effect of screening, and the headline stated that screening was lifesaving. The stupidity came close to 100% when the editorialists believed that Tabár's estimates were "minimum figures."

The claim that screening reduced deaths from breast cancer by two thirds was repeated elsewhere, e.g. in *BMJ*[138] that noted that the case for breast cancer screening programmes was now beyond debate, with reference to a "meticulous report from Sweden."[139]

The triumvirate published a similar beyond reason study in *Cancer* in 2002,[140] based on Swedish women in seven counties. *Los Angeles Times* called it a "very impressive study" that "clinches the case for mammography," "effectively refutes" the claims that screening isn't beneficial and confirms "beyond any doubt" that a reduction in deaths can be obtained in large screening programmes.[141]

Five days later, I was interviewed for the *Chicago Tribune*:[142]

"Millions of women woke up one day last week to news that the last word had been written in the debate over mammography screening. Newspapers, TV and radio stations reported what many described as the definitive study, proving beyond doubt that getting routine mammograms sharply reduces a woman's chances of dying of breast cancer … Too bad it wasn't true."

We do randomised trials to study if our interventions have any effect. Then, when the effect is still uncertain after half a million women have been randomised and followed for many years, researchers with vested interests use flawed designs and claim that it has now been proven that mammography screening works. This is scientifically dishonest and absurd, and it is morally irresponsible.

The ultimate exaggeration: Screening may prevent all breast cancer deaths

In 2002, Tabár, Duffy, and Smith published a third beyond reason study, in *Journal of Medical Screening*, based on data from the Two-County trial.[143] They commented on this study in an invited debate they had with me in *Journal of Surgical Oncology*.[144] [145] [146] [147]

They claimed we had provided arithmetic inconsistencies in our research and gave five examples, which were groundless and that I rejected.

The worst mistake they made was that they considered it nonsensical to compare the invited and non-invited populations, but this is exactly what we do in randomised trials to avoid bias. They limited their analysis to women with a diagnosis of breast cancer and when they compared women invited to screening with women who had not been invited, they found a 19% reduction in all-cause mortality, and 13% in a more conservative analysis.[148] A year later, they repeated their misleading claim of a 13% decrease in all-cause mortality.[149]

They concluded in their trial report that, "Invitation to screening was associated with a reduction in deaths from all causes among breast cancer cases." This is a flawed comparison, but Tabár, Duffy, and Smith abused it to claim that there is no problem with assessing the cause of death in women with breast cancer.

In the discussion, they mentioned a "statistically significant 13% reduction in mortality in association with an invitation to screening." This is plain wrong. It was a 13% reduction among those with a diagnosis of breast cancer. Total mortality among those invited to screening was *not* reduced compared to those not invited, which the Two-County trial showed (the risk ratio for all-cause mortality after 7 years was 1.03 for the Kopparberg part of the trial and 0.99 for the Östergötland part).[150]

So, Tabár, Duffy, and Smith gave their readers the impression that screening can reduce total mortality by 13%, which is obviously impossible. Even if screening was 100% effective and prevented all deaths from breast cancer, this could not reduce total mortality by 13%.

In the discussion section of their trial report, Duffy, Tabár and Smith predicted that when a screening programme had been running for some time, one could expect a reduction of 3-4% in total mortality.[151] The lifetime risk of dying from breast cancer is 2.5-3%,[152] [153] and it was 3-4% in many countries before screening was introduced. One cannot, therefore, achieve a 3-4% reduction in total mortality with screening without avoiding all breast cancer deaths.

Tabár, Duffy and Smith produced the ultimate exaggeration, that screening for breast cancer saves everyone. If they continue their line of research for other diseases, they may find the recipe for eternal life.

They wrote in the invited debate that many scientists and clinicians have devoted "hundreds of hours to soberly and carefully refuting the irresponsible and reckless claims of Olsen and Gøtzsche, hours they otherwise might have devoted to their current work."

It is the other way around. I have used not hundreds of hours but years to refute "irresponsible and reckless claims" related to mammography screening and other interventions. Police work is time consuming, and much of my work has been devoted to debunking the false claims propagated by Tabár, Duffy and Smith.

The triumvirate published a fourth, even more exaggerating beyond reason study in *Lancet* in 2003, also based on the Two-County area.[154] They showed a 35% decrease in total mortality in women who had been diagnosed with breast cancer in the screening period compared with women with breast cancer diagnosed in a previous time period when there was no screening.

I noted that their paper was uninterpretable because of length and lead-time biases.[155]

In their reply, the triumvirate denied that their results could have been the product of lead-time and length biases and argued that they had observed a reduction in absolute mortality *in the population invited to screening*.[156]

As they were lying, because they reported total mortality *among women with a diagnosis of breast cancer*, not in the population, I sent a second letter to *Lancet* pointing this out. Nowhere in their paper did they report on total mortality in the population invited to screening. They reported on total mortality only in women with a diagnosis of breast cancer, which was clear from their abstract, the introduction, the methods section, the results section, and the discussion section.

Unfortunately, the editor didn't wish to publish my second letter but sent it to the authors and encouraged me to get an answer directly from Stephen Duffy, the first author on their reply. I asked Duffy where in his paper I could find the data he had described or whether his reply was erroneous. Duffy avoided answering my question and replied, "We published the absolute mortality reduction from breast tumours diagnosed in the periods studied and this is not affected by lead-time or length bias." I wrote back that I was right that Duffy's reply in *Lancet* was misleading since he didn't report on "absolute mortality in the population invited to screening." He now said that mortality was studied in those with a breast cancer diagnosis, which was correct, but in that case, he was wrong when claiming that this is not affected by lead-time or length bias.

Two months later, Tabár wrote a comment about their study in *Läkartidningen* where he noted that the mortality decrease had been observed among women with breast cancer.[157]

Thus, Tabár contradicted what he wrote in his reply in *Lancet.* The problem with lying is that sooner or later people usually contradict themselves.

Duffy, Tabár and Smith published at least six beyond reason studies and used them very effectively in their screening propaganda even though the fatal flaws in them are basic knowledge for cancer researchers and had been carefully explained to them on several occasions in correspondences.


László Tabár


Stephen Duffy


Robert Smith

It has always been controversial if women younger than 50 years of age should go to screening, and many countries do not offer screening to this age group even today.

But in 2011, Duffy, Tabár, Nyström and others published yet another beyond reason study. They reported in *Cancer* that screening in Sweden had reduced breast cancer mortality in young women aged 40–49 years by 26%.[158]

Their study was a total mess. They used unclear methods, with complex matching of screened and unscreened areas; added and subtracted person-years based on unverified lead times; and were selective regarding the biases they adjusted for. If, for example, they had adjusted for a pre-screening difference in breast cancer mortality, the effect would have been smaller.

Cancer rejected our letter to the editor with the argument that the authors had refused to respond to it. We appealed, saying that this only made it more important to publish our letter. Our appeal worked, but it took five months before our letter was accepted.[159]

We noted it is more reliable to count the number of deaths, and that the breast cancer mortality rate in Sweden in women aged 40–49 years had declined by 36% since 1989, although only half were offered screening, whereas the decline was only 16% in women aged 50–69 years who were all offered screening for over 20 years.[160]

Moreover, we referred to results from other European countries that also showed that the decline in breast cancer mortality was largest among young women who had not been invited to screening (see Chapter 7).

6 Difficult science about overdiagnosis and overtreatment

> *Mammography screening turns many healthy women into patients unnecessarily by detecting tumours that would never have harmed them or come to their attention in their remaining lifetime. This overdiagnosis and subsequent overtreatment harms many and even kills some women. Many articles have been published that purport to show that overdiagnosis is not a problem – but the fact is, it is very common indeed.*

Overdiagnosis is the detection of cancers that would never have gone on to cause symptoms or problems in someone's remaining lifetime. As it is not possible to distinguish between dangerous and harmless cancers, they are all treated as if they were dangerous. Because treatments for cancer may involve highly toxic chemotherapy, radiotherapy, and disfiguring surgery, many healthy women will be harmed.

"Carcinoma in situ" is something of a misnomer. It refers to cell changes that are not cancer. It is well known from autopsy studies that most cases of carcinoma in situ do not develop into invasive cancer,[161] but because they are treated as if they were cancer, they contribute importantly to overdiagnosis and overtreatment.

Overdiagnosis is the most important harm of screening, and it has been known for over 40 years that many screen-detected cancers would have regressed spontaneously if left alone.[162]

It is therefore strange that Ole Olsen and I were the first researchers to publish estimates of overdiagnosis with mammography screening, based on the randomised trials, apart from two earlier reports which are very difficult to find, as the titles and abstracts do not reveal that there are such data in the papers.[163] [164]

Our estimate of 31% overdiagnosis[165] (which means that when there is screening, we no longer have 100% diagnoses, but 131% diagnoses) was robust, but the screening advocates blurred the picture.

In 2005, statistician Sue Moss, primary author of the UK Age trial, published a review on overdiagnosis and overtreatment based on the randomised trials of mammography screening.[166] The paper was included in a series on overdiagnosis and overtreatment, edited by Nick Day, Stephen Duffy and Eugenio Paci, in *Breast Cancer Research*.

Moss made many important errors:

She didn't cite our 2001 *Lancet* review that provided a meta-analysis of overdiagnosis and had been extensively peer-reviewed.

She didn't give any data on overtreatment but stated that its extent was difficult to quantify.

She included diagnoses that had been made in the control group after they, too, had been invited to screening. This contaminated the data and made the effect of overdiagnosis in the screened group impossible to measure.

She included data from the New York trial, although many cancers in the control group should have been excluded because they had already been diagnosed before the women entered the trial.

She included cancers diagnosed many years after the trial ended, which dilutes the estimate of overdiagnosis because, in practice, the women are screened for much longer than in the trials.

She included the Edinburgh trial, which was so flawed that it was excluded from our reviews.

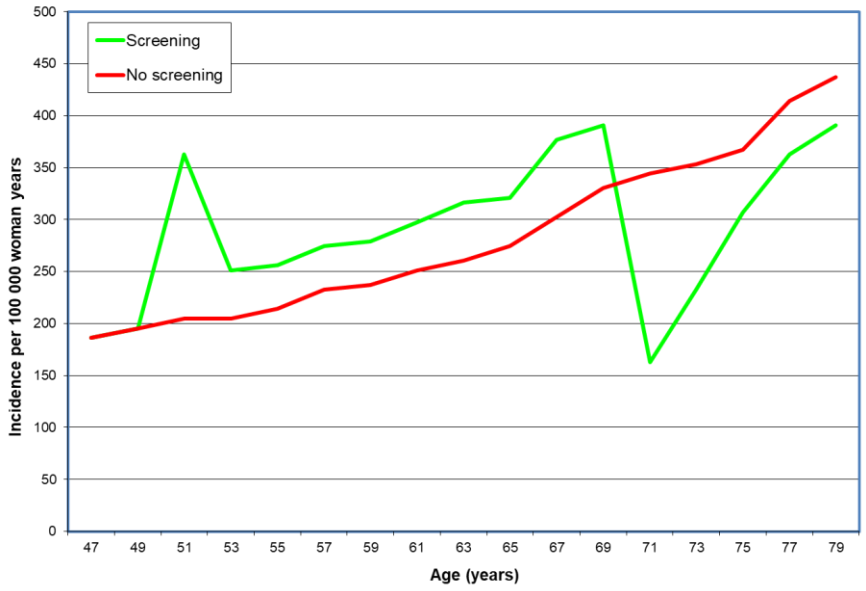
She didn't pool the data. This would have enabled an estimate of overdiagnosis and would have been well within her capability, as a statistician.

A persistent criticism of using the randomised trials to estimate overdiagnosis has been that the period of follow-up was too short. However, the Malmö trial ran for nine years, which is longer than for any other trial, and there were 34% more mastectomies and lumpectomies in the screened group than in the control group by the time the trial ended.[167] After such a long time, by far most of this excess will have been a result of overdiagnosis, and not earlier detection of cancers that would have become evident about a year later (see Chapter 13 about lead time).

Observational studies are less reliable than randomised trials, but they are important for estimating overdiagnosis because screening in practice differs markedly from screening in the randomised trials.

If there was no overdiagnosis, the initial increase in total number of cancers and carcinoma in situ cases in the screened age groups would be fully balanced by a similar decrease in number of cancers and cell lesions as the group aged and was no longer offered screening, as these cancers would already have been detected.

In a much-cited *Lancet* letter from 1994,[168] Harry de Koning and colleagues from the Netherlands claimed exactly that. They asserted that the extra incidence found when screening began was due to early diagnosis and would be compensated for by a massive decline in incidence when women passed the upper age limit for screening because their cancers had already been detected. In support of this argument, the authors published a graph in *Lancet* as a visual representation of how this might look. It was, however, pure speculation (see figure). As noted by the U.S. National Cancer Institute, this decline in cancers in age groups no longer screened has never been observed.[169]



Expected breast cancer incidence with screening (green line) and without screening (red line). Wishful thinking, as the huge drop in elderly women has never been observed in practice (redrawn).

Our systematic review of overdiagnosis

Karsten Juhl Jørgensen from my centre and I compared trends in breast cancer incidence before and after screening in countries with organised screening programmes, taking account of changes in the background incidence and any compensatory drop in incidence of

breast cancer among older women.[170] Our method was simple and did not involve any assumptions, e.g. about the magnitude of lead-time bias. We included studies that had collected data on breast cancer incidence for at least seven years before screening and seven years after screening had been fully implemented to estimate the trend in breast cancer incidence, unaffected by the initial peak in prevalence when screening is introduced.

It was the first systematic review of observational studies of overdiagnosis ever performed. We published it in *BMJ* in 2009.

Our research was very labour intensive. Most of the data we found were useless. For example, data were missing for the pre-screening years; the data included the elderly that had never been invited to screening and in whom breast cancer is most common, which effectively concealed the increase in incidence resulting from screening; or the authors had combined both screened and non-screened geographical regions.

The deficiencies in the presentation of the data were so consistent and meaningless that we became convinced that the degree of overdiagnosis was being deliberately obscured. It was particularly suspicious that the data rarely included carcinoma in situ, as most of these cases are overdiagnosed. We observed that those who publish data on breast cancer incidence are, almost without exception, screening advocates.

Of the more than 300 articles we assembled, only five provided the type of data we needed. Three of the authors we contacted sent unpublished data or referred us to Internet resources for additional data, which enabled us to include data from the UK, Manitoba, New South Wales, Sweden, and parts of Norway.

We only retrieved the full data set from Manitoba. For the other areas, we adjusted our estimate of overdiagnosis by assuming that carcinoma in situ contributed 10% of the diagnoses in a population offered screening, in accordance with European data. We could not include the United States, as this country does not have an organised population screening programme and therefore has no well-defined pre- and post-screening periods.

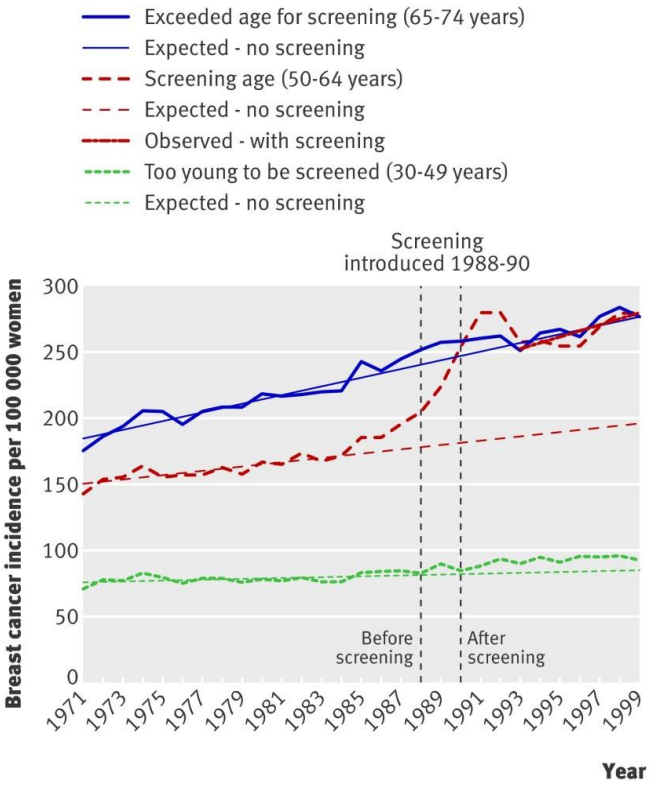
In some countries, there was a small drop in cancers among elderly women that we subtracted before we estimated overdiagnosis. Our results were remarkably consistent. The estimates varied from 44% to 57% overdiagnosis, with a mean of 52%, which was even higher than in the randomised trials.

This means that the harm done by screening is immense. One in three breast cancers detected in a population offered organised screening is overdiagnosed.

In the UK, the introduction of screening led to a marked increase in cancers in the screened age groups, with no compensatory drop in incidence among elderly women (see figure below; carcinoma in situ was not included). The incidence in women who were too young to be invited to screening increased somewhat over the expected rate, likely because of opportunistic screening – many younger women take up the opportunity to be screened if it is made available to them.

Robert Smith dismissed our findings saying they resulted from “poor methodology,”[171] but did not offer any explanation of the supposed shortcomings. The many letters that followed our article were also immaterial, as our methods were solid.

When our paper came out, a journalist asked representatives from the US breast cancer advocacy group, Susan G. Komen for the Cure, about our finding that screening needlessly turned many healthy women into cancer patients.[172] The CEO, Hala Moddelmog, replied: “I don’t think there’s evidence of overdiagnosis,” and Elizabeth Thompson, vice-president of health sciences, said: “We’re very concerned that insurance companies will stop funding mammograms when these kinds of studies come out.”



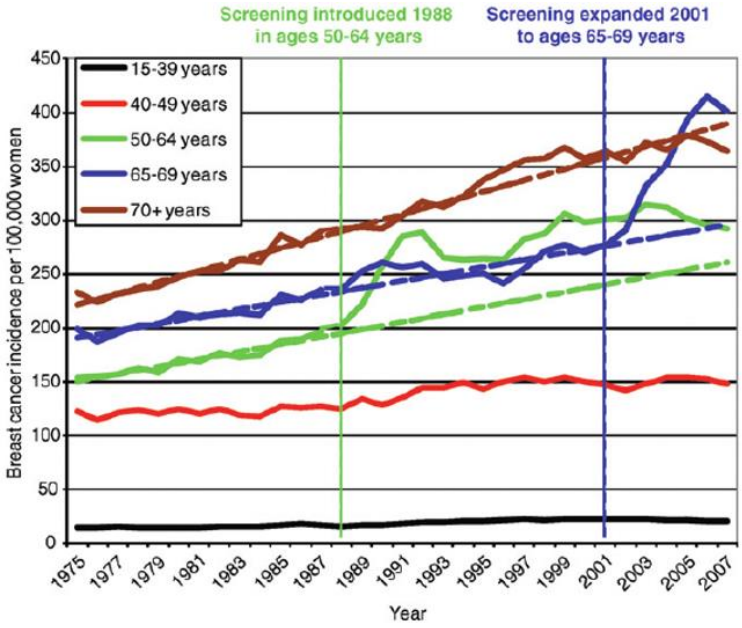
When the journalist then asked what they were telling women about the risks associated with mammograms, Thompson said, “We believe early detection saves lives, and we need to focus on getting out that message.”

It was disappointing to see a group which is supposed to have patients' interests at heart reject scientific evidence, while displaying unsolicited paternalism, and focussing on financial interests over health.

The official reaction in Australia was also one of denial. The Australian National Breast and Ovarian Cancer Centre quoted a position statement saying that the estimates of overdiagnosis from the randomised trials had a midpoint of 2-3%.[173] This was untruthful.

In our reply to the letters, we included more recent data from the UK and drew attention to the remarkable fact that when women in the age group 65–70 years were included in the programme in 2001–03, their level of cancer diagnoses increased dramatically (see figure below; dashed lines are incidences expected in non-screened populations).[174 175] This is despite the fact that they would have already been receiving screening when they were younger. This suggests that many cancers detected by screening would have regressed spontaneously.

In 2009, we also published a study of overdiagnosis in Denmark,[176] comparing areas with and without screening. We found 33% overdiagnosis. As expected, it was lower than in other countries. The Danish programme has low recall rates, e.g. in one of the two regions, only 1.3% per round were recalled. Furthermore, the attitude to the detection of microcalcifications is conservative (only 6% of all diagnoses are carcinoma in situ). And as the uptake of screening was only 63% in Copenhagen, this also reduces overdiagnosis. If there is no uptake of screening, there can of course be no overdiagnosis.



Making overdiagnosis disappear by using faulty statistical models

Screening advocates have consistently produced very low estimates of overdiagnosis, and Stephen Duffy is second to none in this discipline.

The manipulations always involve impermissible adjustments of the data. The most common approach is to use models and adjust the number of cancers detected at screening for a lead time that is far too long, which means that most or all overdiagnosis disappears.

Duffy published papers on overdiagnosis between 2003 and 2006 that purported to have found no overdiagnosis in the Two-County trial;[177] around 5% overdiagnosis in Florence;[178] 1% in the Two-County and Göteborg trials;[179] and 5% in Copenhagen.[180]

Duffy's methods are difficult to follow and even more difficult to swallow. Michael Baum has tried to find out where the estimates Duffy uses, e.g. for lead time, come from and if they are reliable. He went through the reference lists and found that the explanations given in the quoted papers were insufficient. He then retrieved references to the referenced papers and so forth, in backward cycles, but still couldn't make an informed judgement.

We have had the same experience, not only related to Duffy's studies but also when we tried to find crucial details about the Two-County trial.

There must have been grave errors in Duffy's assumptions, data, calculations, or in all three. If not, he would have found considerable overdiagnosis in his studies, which is evident if one disregards his models and looks at published graphs of breast cancer incidence in the countries and areas he has studied.[181 182 183]

In the study where Duffy reported 1% overdiagnosis in the Two-County and Göteborg trials, he used Markov chain Monte Carlo methods and a multistate model. With such methods, it is possible to get almost any result you want.

We have explained what the main problems are with Duffy's approach.[184] He doesn't review the literature systematically; his models involve assumptions that cannot be correct; he extrapolates far beyond the data; and he does subgroup analyses of attenders at screening even though it is well known that such analyses are seriously flawed. Those who turn up at screening are healthier than those who don't.

In 2014, Robert Smith argued at length about the need for lead-time adjustment.[185] We noted that it was wrong when Smith stated that the largest estimates of overdiagnosis are derived from studies that did not adjust for lead-time bias and underlying incidence trends.[186]

As just noted, we did this by studying to what extent the incidence of breast cancer declines in women who are no longer screened because of advanced age, relative to the expected incidence without screening, and we took this decline into account when estimating overdiagnosis, which is the correct way of adjusting for lead time. The studies Smith prefers reported 1-10% overdiagnosis, which is unsurprising, as the researchers used faulty models that removed most of the overdiagnosis by inappropriate adjustments.

Elsebeth Lynge, who was instrumental for introducing screening in Denmark, did studies of similarly poor quality. She claimed that "The experiences from Copenhagen and Fyn show that organised mammography screening can operate without overdiagnosis of breast cancer,"[187] which she must have known is impossible. She used Danish data for a study published in *Cancer*,[188] where the authors' analysis techniques made it virtually impossible to detect overdiagnosis.[189]

In 2011, my Norwegian colleagues and I used data from the Swedish Cancer Registry to study the natural history of screen-detected breast cancers.[190] We found that the four-year cumulative incidence of invasive breast cancer was about 50% higher in the screened group than in the control group, relative risk 1.49 (95% CI 1.41 to 1.58). After the first screening in the control group, the screened group still had a higher cumulative incidence of invasive breast cancer, relative risk 1.14 (1.10 to 1.18) after six years.

Because the cumulative incidence among controls did not reach that in the screened group, we concluded that many invasive breast cancers detected in the course of regular mammography screening can no longer be found at the end of six years. This suggests that the natural course of many screen-detected invasive breast cancers is to spontaneously regress. Even though mammograms given to the control group at the end of the trial may have overlooked some cancers, the difference of 14% in cancer incidence between the screening and control groups was much too large to be explained by oversight.

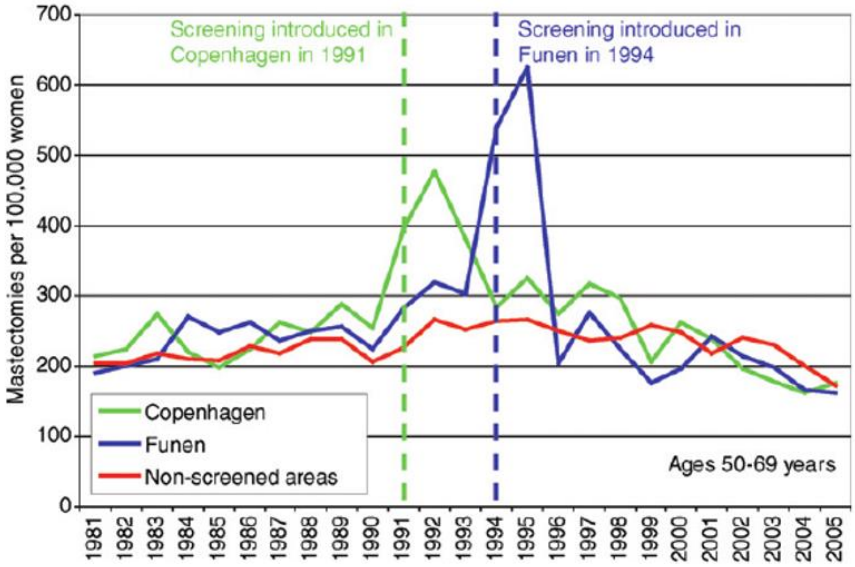
This study confirmed what my Norwegian colleagues had shown earlier, based on data from Norway. In that study, accumulated breast cancer incidence in a study group that was screened three times was 22% higher than it was in a control group that was screened only once at the end of a six-year period.[191]

A well-kept secret: Screening increases mastectomies

The fact that screening increases mastectomies has been flatly and aggressively denied by trialists, policymakers, websites supported by governmental institutions, advocacy groups, and by invitational letters sent to women invited to screening saying that early detection spares patients more aggressive treatments – in particular, mastectomy.[192]

Julietta Patnick, director of the cancer screening programmes in the UK, perpetuated this lie after our updated Cochrane review came out in 2006: "Women who were screened were also less likely to have a mastectomy than those who were not screened."[193]

It is easy to see that screening leads to more mastectomies, not only in the trials, but also in practice. Again, Denmark is ideal, as only 20% of the country had screening through-out 17 years (see figure below).[194]



When screening was introduced in Copenhagen and Fyn, there were huge increases in mastectomies, which were not followed by later declines. The declines in mastectomies were about the same in screened and non-screened areas.

We published this graph in 2011 and wrote numerous articles in medical journals and in newspapers, explaining that screening increases mastectomies.

However, in 2015, Danish screening advocates, including Elsebeth Lynge, published a "position paper" about breast cancer screening in Denmark.[195] In the abstract, they claimed that screening had not increased the number of mastectomies; that the use of breast conserving surgery had increased from around 25% in the 1990s to 69% in 2010; and that the absolute number of patients with a more advanced stage at diagnosis and the absolute number of patients undergoing mastectomy had decreased after the introduction of mammography screening.

We explained why these claims were all false or – in relation to the percentages - seriously misleading.[196] Imagine a town with a certain level of crime. You divide the crimes into serious ones and less serious ones. Over a period, the rate of serious crime increases by 20% and the rate of less serious crime increases by 40%. This is a development for the worse. But although *more* people are exposed to serious crime and *more* people are exposed to less serious crime, a trickster would say that, as there are now *relatively* fewer cases of serious crime, the situation has improved.

It is hard to produce data that suggest that screening doesn't increase mastectomies, and even harder to concoct data that suggest that screening leads to *fewer* mastectomies. But this is exactly what Tabár, Duffy and Smith have claimed.

They asserted there were *fewer* mastectomies in the Kopparberg part of the Two-County trial in the group invited to screening compared with the control group.[197] As always, some detective work was needed to demonstrate how they had cheated. It was scientifically dishonest that they didn't reveal that the numbers of mastectomies they used for the control group were derived after the whole control group had been offered screening. Before the control group was screened at the end of the trial, there were 17% more mastectomies in the screened group in Kopparberg.[198]

It is one thing to add mastectomies to the control group that don't belong there. A more subtle, but more commonly used, trick is to use percentages instead of numbers, which is what Lynge does. She used it in her position paper (see just above) and also in the Danish Board of Health's 1997 report that paved the way for screening. In it, she stated that 13% of the patients had a breast-conserving operation before screening was introduced in Copenhagen, and 45% had such an operation after screening was introduced.[199]

Such information is intended to fool people and it works, which is why so many screening advocates use it even though they know it is wrong.

In 2011, we confirmed with our Norwegian colleagues, using data from the Norwegian screening programme, that screening increases mastectomies.[200]

In the Malmö trial, an overdiagnosis rate of 10% was reported in women aged 55-69 at randomisation after they had been followed up for an additional 15 years after the 9-year randomised phase ended.[201] This estimate was unreliable for three reasons.

First, during the randomised phase of the trial, 24% of the women in the control group were screened.[202] If we adjust for this contamination, the overdiagnosis in the randomised phase, which was 32%,[203] increases to 40%.

Second, the authors claimed, without providing any supporting data, that control group women aged 55-69 years at randomisation were never screened at any point, even though it is highly likely that many of them would have had a screening mammogram after the trial ended, as they might have been led to believe that screening was effective. In Denmark, 44% of women who were within the screening age range but who lived in areas that did not provide screening, reported having previously had a mammogram.[204]

Third, the women were only screened for 9 years whereas in clinical practice they are screened for much longer, and overdiagnosis increases substantially at older ages. During the subsequent 15 years of follow-up, three times as many cancers were identified as during the 9 years randomised phase.

Overdiagnosis was mentioned in the 1986 Forrest report that led to the introduction of mammographic screening in the UK.[205] Results from only two trials were available. One was the New York trial, which found a similar number of breast cancers in the screened and control groups after seven years. The authors of the Forrest report therefore believed overdiagnosis was not a problem. However, as already noted, the reason that the New York trial did not find more cancers with screening was that many cancers in the control group had been diagnosed before randomisation and should have been excluded - as they were in the screened group.[206]

The huge effect in this trial, a 35% reduction in breast cancer mortality after seven years, is therefore spurious. With no difference in cancers, there should have been no effect.

The other trial was the Two-County Trial, which reported 30% more invasive cancers in the screened group than in the control group.[207] The trial investigators recommended performing further follow-up to determine whether this excess persisted, but they then made this impossible by inviting all the women in the control group to undergo screening after the randomised phase ended.

7 Taking on the screening establishment

This chapter documents that mammography screening has acquired religious status out of touch with reality and that the punishment is harsh if you dare touch the sacred cow.

Mammography screening has religious status

Faith is a great trust or confidence in something for which there is no proof, or an unshakeable belief in something even if there is proof against it.

In his book, "The God Delusion,"[208] biologist Richard Dawkins writes that Martin Luther was well aware that reason is religion's archenemy and had said, "Reason is the greatest enemy that faith has." In an interview on *BBC*, Dawkins warned about blind faith, saying, "Don't believe in anything for which there is no evidence."

After having studied mammography screening for 25 years, I have come to the conclusion that it has acquired religious status. The faith its proponents have in its great benefits, with little or no harm, is an unshakeable belief in screening despite proof that it has no benefits but serious harms. It does not save lives, and it does not save breasts, which are the two screening mantras.

In science, we are keen to listen to new research results and other points of view, as this makes us wiser. Members of religious sects don't listen to evidence that could shake their beliefs; they suppress it, distort it, or lie about it. And my opponents were quick to forget that I am a scientist; they made me a heretic as soon as I started to publish on mammography screening.

To say that screening doesn't work, or is harmful, or both, elicits strong anger among the faithful who obsessively guard the myths they have created. As Michael Baum said, "Anyone who dares challenge the sacred cow of screening has a terrible time."[209]

US statistician Donald Berry participated at the Global Summit on Mammography Screening in Milano in 2002, which he described as a screening lovefest in a letter to me:

"You two were chastised, as was I. I was shunned as though I was a leper. And after the meeting Peter Dean sent a message to half the Western world that was a vitriolic attack on me personally. There was no sense in which the meeting was objective. Or even honest. For example, Tabár presented an inane analysis of screening and breast cancer trends in Sweden, and no one said a word."

Berry replied to Dean, "I am impressed by the size of your 'cc' list. I want to thank you for not including my mother." As I was also cursed in Dean's letter,[210] we were both in danger of eternal punishment in Hell.

Daniel Kopans reported numbers from a mathematical simulation study suggesting that metastatic cancers could be reduced by 80% if women were screened every six months.[211]

Another participant, Cornelia Baines, published her experience from the summit.[212] She heard that *Lancet* had caused harm to womankind by publishing our research and noticed that after Tabár had presented his beyond reason study claiming a 63% effect of screening[213] no one spoke from the floor. By the time Baines caught on, the discussion had been closed. She asked several people why there had been no comments, and the answer was: "No one wants to fight with László."

The wrath that results when the Lord of Mammography Screening is challenged is well known and Tabár's strongest weapon is to threaten legal action, which is effective because screening has made him very rich. And even if you win, it could still cost you a lot of money.

The faithful routinely violate the ninth Commandment: "Thou shall not bear false witness against thy neighbour." When people lie profusely and constantly about you, and the liars outnumber the truth tellers by a wide margin, you will lose the battle in the public eye. It is essentially a battle between religion and science and the public prefers myths and fairy tales for dry science.

Untruthful statements and *ad hominem* attacks in Denmark

As already noted, I have been exposed to numerous untruthful statements, obfuscations, and *ad hominem* attacks in medical journals and the media and I shall give more examples.

In January 2001, two surgeons, Jens Peter Garne and Ib Hessov, considered it bad manners to contact the press before colleagues had seen our research and for our medical journal to write about it two days after it had been published, before it had been possible for decision-makers and experts to read and discuss it.

We had not contacted the press[214] and researchers have a duty to talk to the press when they have published research of general interest. Furthermore, the research data they alluded to, published in *Lancet* in 2000, had been freely available at the Danish Board of Health for six months before this and had been widely discussed in Denmark.

Garne and Hessov didn't make a similar comment when, in fact, the rules *had* been broken by one of their allies. Three weeks before Nyström and colleagues published their meta-analysis of the Swedish trials in *Lancet* in 2002, one of the authors discussed the effect on mortality in a Danish newspaper, and Elsebeth Lynge explained what it meant.[215] This was a violation of *Lancet's* embargo rules, and it effectively impeded a scientific debate about the research. The journalist asked me to comment, which I couldn't, as I didn't have access to the report.

Garne and Hessov claimed falsely that my statement in an interview that more women lose a breast when they attend screening originated from unpublished reports. We had published our data in *Lancet* a year earlier, and the Malmö trial had reported more mastectomies with screening 12 years earlier.

Garne and Hessov published an article a year later in our medical journal with the title, "WHO and *The Lancet*: yes to mammography screening."[216] But they deceived the readers again. They quoted a "solid editorial comment" in *Lancet* that seemed to be anonymous, as it had no authors. *Lancet's* editor, Richard Horton, often wrote anonymous editorials, but he had spent a lot of time examining our research before he published it in 2001 and he was convinced we were right. So, how could he write an editorial six months later saying there was no longer any doubt about the value of screening? This didn't make sense.

I therefore looked up the editorial. It was not anonymous. There were two authors, from the British Columbia Cancer Agency.[217] They did not express *Lancet's* views and they did not even say yes to screening; they doubted it. They noted that,

"The latest analysis does not tell us whether the massive effort to develop screening programmes in at least 22 countries and to encourage participation is worthwhile. That issue must be honestly confronted by those organisations and individuals with an interest in maintaining programmes for mammography screening."

But Garne and Hessov were not honest.

Garne and Hessov denied once again that screening increases mastectomies. Garne insinuated that we were unethical, as he wasn't aware of studies that documented that screening leads to more mastectomies.[218] However, we had already explained to him earlier that this was documented in the randomised trials.[219] We referred to this fact again; noted that carcinoma in situ is often treated with mastectomy;[220] and referred to a Dutch study that showed that screening had increased mastectomies more than tumourectomies.[221 222]

Repetition doesn't help when you are talking to dishonest people. Garne and Hessov wrote a sixth letter, "No evidence that mammographic screening results in overtreatment."[223] They argued that studies specifically designed to detect the "possible existence" of overdiagnosis didn't exist.

This was absurd. Their private logic means that if I performed a large asthma trial and found that 30 times as many patients died when they received a drug as when they received placebo, I should disregard this finding because the study was designed to look at asthma symptoms, not deaths.

Furthermore, the IARC book Garne and Hessov referred to in their letter claiming *Lancet* said yes to screening states that overdiagnosis is an obvious source of harm, and the book refers to both randomised trials and observational studies documenting substantial overdiagnosis. And yet, they claimed there is no evidence that mammographic screening results in overtreatment and calls it a scandal that we had said "without evidence" that two women lose a breast unnecessarily for every 1000 women who are screened.

After the Garne-Hessov attacks, you would think it couldn't be any worse, but in fact, the debate in Denmark took a vicious turn.

Two doctors from my own hospital, Ilse Vejborg, head of the mammography screening unit, and Niels Kroman, chief physician at the department of breast surgery, started a series of petty personal attacks in 2004.

First,[224] they compared our systematic review of the trials with Bjørn Lomborg's book, "The sceptical environmentalist," which is filled with selective quotations of data that speak against global warming and omits supportive data from the same sources.[225] The title of their newspaper article was, "Screening saves lives and breasts," which are both wrong.

Next, they cited a famous Danish comedy by Ludvig Holberg from 1723[226] but got most things wrong, including accusing us of circular reasoning when the comedy was an example of the logical fallacy that one cannot prove something based on two negatives.[227]

They accused me of having published deliberately misleading and even erroneous citations and noted that they had previously drawn attention to this "dishonest behaviour." They referred to two previous letters I had written but failed to explain what the alleged problems were, and there are no misleading or erroneous citations in these letters. They gave one example, which was wrong. They claimed that my statement that the US Preventive Services Task Force was sceptical towards mammography screening was "directly untrue." We replied that the Task Force had written: "What emerges as a more important concern, across all age groups, is whether the magnitude of benefit is sufficient to outweigh the harms."[228]

Vejborg and Kroman came back, with enhanced authority in the form of Chairman Peer Christiansen and Secretary General Henning Mouridsen from the Danish Breast Cancer Group and Chairman Henrik Flyger of the Danish Breast Surgery Society.[229] This addition of eminences didn't lift the level of the debate.

They claimed again that we had published "a number of untruthful statements" and that updated results from the trials in Malmö and Canada had shown an effect in line with other

trials, which was wrong. They argued that the US Preventive Services Task Force had found scientific evidence for introducing mammography screening, and that it was therefore "directly misleading" when I left an impression of the opposite. I hadn't. The Task Force noted that, "in absolute terms, the mortality benefit of mammography screening is small enough that biases in the trials could erase or create it."

Vejborg, Kroman and their allies remarked for the second time that we should not have quoted ourselves (our 2001 review of the trials in *Lancet*) because, "to prove a postulate by itself is not scientifically correct." This nonsense didn't apply to themselves, as they quoted their own research in their letter.

They even underlined how unacceptable it was that we had disregarded the rules for academic debate in our propaganda against screening. Words failed me at this point.

We were told that the extent of overdiagnosis we had reported was "totally undocumented" and that we had misunderstood the numbers on breast cancer mortality, both of which were false of course.

We responded to all this but despite the many falsehoods and defamatory personal attacks, we were not allowed to publish our reply in our medical journal, not even after we had appealed to the editor. He published a note that there had been so much debate about mammography screening that it should continue elsewhere, unless there were new decisive data. If so, he should not have published the Vejborg-Kroman nonsense.

What is most devastating about such debates is that it doesn't matter that you prove that your opponents are wrong. They just ignore it and repeat their mistakes.

In 2006, we published a paper in *BMJ* on the contents of invitations for publicly funded screening mammography.[230] It was widely commended internationally, and we won the first prize from the Society of Medical Writers for it without having participated in any competetion; we were just informed about it out of the blue.

However, in Denmark, all hell broke loose when we translated it and published it in our medical journal.[231] The same five people attacked us again. We were castigated in the title of their letter: "Mammography screening – ideology contra science,"[232] and we were told that it was not appropriate to conduct an ideologic discussion under the guise of science. We had a good laugh, as they were the ideologues.

We were told that when healthy people are invited to screening, it is important that they are informed soberly about both "advantages and drawbacks," and that what we had just published in *BMJ* was anything but sober. This remark was hypocritical. What we showed in our paper was that the women *were not* being informed about the most important harms of screening. We also showed, with verbatim quotations, that the Danish screening invitations were very far from being balanced and from providing a basis for informed consent.

Short of arguments, our opponents again resorted to personal attacks and blunt lies. They claimed that our paper in *BMJ* hadn't been peer reviewed and that it was wrong that carcinoma in situ was often treated by mastectomy and radiotherapy. We rejected their claims and noted that they paid no attention to the fact that two of the three Danish standard invitations contained nothing about harms, although this is a legal requirement, and that none of them mentioned overdiagnosis.[233]

The limitless stupidity continued. In 2008, Garne, Lynge, Kroman and the two heads of the Danish screening units, Ilse Vejborg and Walter Schwartz, still questioned whether screening leads to overdiagnosis and repeated that the source of this was ourselves – namely, our

Cochrane review.[234] They considered it "grotesque" that we said screening leads to more mastectomies.

We patiently rejected their views,[235] but our troubles continued. A week later, Garne and his backing group[236] complained that we had not taken lead time into account. We referred to our study showing there is something fundamentally wrong with the lead-time models some researchers have used to conclude that there is very little overdiagnosis,[237] and explained that we had instead looked at the incidence of cancers when the women are no longer screened,[238] which is a reliable method.

Was there a 25% effect of screening or no effect?

In 2005, we published a review in our medical journal[239] where we mentioned a flawed observational study from *BMJ* that had just been published. It claimed that screening had reduced breast cancer mortality in Copenhagen by 25%.[240] The senior author, Elsebeth Lynge, had used this result for a political purpose, declaring to the media that the importance of extending screening to the whole country could no longer be doubted.

Lynge and colleagues had compared Copenhagen, where screening was introduced in 1991, with non-screened areas in Denmark. There are four major problems with their study.[241]

First, they used a statistical model that was unusually complicated and difficult to understand. This is always suspicious, as the choice of model can have a substantial impact on the results. Two years later, Lynge reported results from several models, one of which showed an *increase* in breast cancer mortality in Copenhagen compared with non-screened areas.[242] The authors asserted that their original model should be preferred, but didn't explain why, and none of the models were validated.

Second, the full mortality reduction appeared already three years after screening started and didn't increase in the remaining observation period. When a model gives results that contrast markedly with what we know from the randomised trials, the model should be discarded.

Third, the study only included Copenhagen. This was curious, as the head of Fyn's screening programme was among the authors. Furthermore, Fyn introduced screening in 1993, has a population of similar size and has a higher proportion of "faithful users" than in Copenhagen (76% vs 53%).

Fourth, the study didn't describe breast cancer mortality rates in women who were too young or too old to have benefited from screening, although the absence of similar reductions in breast cancer mortality among these women would have strengthened the study's conclusions.

Our Norwegian colleagues and we published several rapid responses on BMJ's website[243] where we criticised Lynge's study and Stephen Duffy tried to rescue the drowning study:[244]

"With respect to criticisms of the Copenhagen mammography study, Dr Lynge's response is measured and correct. With its control for temporal and spatial effects, the Copenhagen study is a model of rigorous evaluation and honest interpretation."

Such undeserved praise – complete empty of scientific arguments – does not belong in a scientific journal.

Five years later, we published a much stronger study in *BMJ*, also using Danish data.[245] Our methods were simple and transparent; we did not use statistical modelling; we included

the whole country; we included age groups that could not have benefited from screening; and we added data from five additional years.

We did not find any effect of screening on breast cancer mortality. The decline in breast cancer mortality in women who could benefit from screening was 1% per year in the screening areas and 2% per year in the non-screening areas. The decline was 5% per year in women who were too young to benefit from screening in the screening areas, and 6% per year in the non-screening areas in the same time period.

Our results were very clear and very threatening to the screening advocates, and our paper was attacked by the whole choir with vested interests: Robert Smith, Stephen Duffy, Elsebeth Lynge, Daniel Kopans, Peter Dean, László Tabár and Lennart Nyström. They focused on very minor issues that were not important for our results.[246] This tactic has been called "weapons of mass distraction."

Lennart Nyström

Harry de Koning

Elsebeth Lynge

A comment from the Danish Breast Cancer Group (DBCG) was particularly miserable:

"DBCG, which represents all the professional expertise of breast cancer diagnosis and treatment in Denmark strongly take exception from the conclusions of the Cochrane Centre."

They also drew the "you are killing my patients" card, which was laughable considering that we had just shown that screening *does not* reduce breast cancer mortality.

The DBCG demonstrated its own incompetence by mentioning an analysis they had made showing that during the past 30 years, the five-year mortality had decreased from "barely 40% to barely 20%," without a word about length and lead-time biases. They even claimed that screening leads to less use of aggressive surgery, and, as is usual for screening advocates, they hid that the opposite is true by talking about proportions instead of number of operations.

The DBCG also noted that breast cancer mortality was higher in Denmark than in our Nordic neighbouring countries, which had screened for breast cancer for many years, and they therefore welcomed that now, at long last, we had nation-wide screening in Denmark.

Researchers from the Danish Cancer Society were more truthful when they compared Denmark and Sweden and noted that a 10% difference in survival among breast cancer patients had existed for the past 40 years, far longer than when screening was begun in either country.[247] Curiously, Henning Mouridsen contradicted himself, as he was a member of DBCG and co-authored both papers.

The heads of the two oldest screening units in Denmark, Walter Schwartz and Ilse Vejborg, declared that our paper would lead to loss of lives. Robert Smith and Stephen Duffy repeated their usual condemnations saying our paper had "multiple methodological failures," was based on "flawed methods" and contributed "nothing of substance."

Pretty interesting comment, considering that our paper was peer-reviewed twice and that *BMJ's* statistician took great care, as the editors wanted to be sure we were right before they published such a provocative finding.

The ultimate exaggeration: Screening without overdiagnosis

In 2003, Lynge told the media it is possible to screen without overdiagnosis, citing a paper she had published with Anne Helene Olsen.[248] We explained in our 2005 review that this claim was so heavily criticised that it should be regarded as academically non-approved.[249]

At Olsen's PhD defence, which I attended, one of the examiners, Noel Weiss, pointed out that Olsen could not exclude that there was overdiagnosis in Denmark and he noted that there were more cancers in the screened group. The other examiner, Niels Keiding, professor of biostatistics, said that, considering that Olsen was a statistician, it was curious that there were no numbers and no statistical analyses in her paper, but only some graphs. He also said that the data were too weak to support her strong conclusion about the lack of overdiagnosis. Both examiners asked Olsen for her opinion on this, but she didn't reply.

Olsen's tutor was Elsebeth Lynge, and her political manoeuvres worked. The minister of health asked the Board of Health to look at her Danish study claiming a 25% mortality reduction to judge whether screening should be extended to the whole country. The Board had published the 1997 report that recommended screening, and Lynge was behind both reports and was an advisor to the Board on screening. Therefore, the question from the ministry boils down to asking Lynge whether she believed in a study published by Lynge.

Other events showed that Lynge did not separate science from politics. The university selected her as chair for the evaluation committee when Karsten Juhl Jørgensen from my centre submitted his doctoral thesis on mammography screening in 2010. As all three members had conflicts of interest, we complained to the university about the composition of the committee, noting that Lynge had already denigrated Karsten's work in the media and that his work represented a serious criticism of her own papers.

This made no impression on Lynge who replied that she was not conflicted, as did the other examiners, which the university accepted. We therefore complained again, this time not only referring to the university's own rules ("No one can participate in the evaluation of a thesis in the presence of circumstances that may be suitable to raise doubt regarding the impartiality of that individual") but also to the law of public administration. We cut in stone what we meant:

"Mammography screening is a controversial intervention and a major international political topic of dissent involving huge economic interests and career investments … Any researcher will naturally wish to defend their own work against criticism, and in this case, we are concerned that the examiners could be tempted to 'find an excuse' for rejecting the submitted thesis, as such a move could be used as a very effective political tool in the ongoing dispute."

This time, the university accepted our appeal and appointed a new committee without conflicted members. Karsten became Doctor of Medical Science without further obstacles. The two examiners were very good, but a screening advocate, Jens Peter Garne, opposed *ex*

auditorio for 45 minutes, which was embarrassing, also for himself.[250] He showed a headline from a Danish newspaper, *500 breasts are removed every year without reason*,[251] and tried to hold Karsten responsible for what the journalists had written. The article noted that we had calculated that, because of screening, 500 women had the whole breast or part of the breast removed, which was correct.

To discuss a headline in a tabloid newspaper at an academic defence was pathetic, considering also that Karsten had eight papers for his thesis, five of which were in the *BMJ*. He obtained a 3-year postdoctoral grant from the Danish Research Council and was one of only five young elite researchers in healthcare that year.

In 2007, Karsten and I were awarded the first prize from the Society of Medical Writers, for our *BMJ* paper on the content of invitations to mammography screening.[252]

There are three other awards I have been particularly happy to receive in relation to my work on mammography screening, as they carry the names of great people: the Skrabanek Foundation Prize in Dublin in 2001; the Niels A Lassen Award in Copenhagen in 2001; and the Michael Berger Award in Düsseldorf in 2009.

Petr Skrabanek was a thinker. When he wrote a detailed and instructive review in the *Lancet* on breast screening in 1985,[253] a critic used not only the trick "if you can't beat them, lie about them," but also the "you're not one of us" trick. Skrabanek was accused of being an armchair scientist. He responded to the untruthful statements and added, "people who sit are not necessarily less often right than those who walk about: Einstein did no more than 'armchair' research."[254]

Niels A Lassen did research in physiology, but the chair of the award committee said the motivation for giving me the award was that, like Lassen, I challenged traditional beliefs and stuck to my findings under pressure, as long as I hadn't been proven wrong.

Rejection of an excellent PhD thesis: Flagrant abuse of power

The head of the Norwegian breast screening programme, Mette Kalager, was also sceptical when Lynge became one of the examiners on her PhD thesis, but she accepted it, which cost her dearly.

One of her three papers had demonstrated considerable overdiagnosis in Norway, but the examiners – of which only Lynge had expertise in mammography screening – rejected this paper for no good reason. Lynge even demanded that all discussion of overdiagnosis should be deleted from the thesis. This had nothing to do with science but everything to do with the politics of protecting mammography screening against criticism.

I had seen the paper as a peer reviewer. It was of much higher quality than Lynge's own papers, and it was outrageous that she rejected it. It was later published in a prestigious journal, *Annals of Internal Medicine*.[255]

This was a scandal and indisputable political censorship. Mette's main tutor, Professor Hans-Olov Adami from Harvard University and Karolinska Institutet, advised her to withdraw the paper in order not to cause additional delays. But he wrote a most damning letter to the Dean of the Medical Faculty at the University of Oslo noting that "The quality of the evaluation committee's comments is astoundingly low with limited scientific substance and indeed an element of vested interests and biased views."

Adami found that excluding Mette's paper on overdiagnosis was a lost opportunity to have a rich scholarly discussion about an issue of enormous relevance and methodologic complexity. Referring to Lynge's own paper on overdiagnosis, Adami noted diplomatically

that there was a need for methodologic improvements of the type Mette and colleagues had attempted.

One of Mette's papers was published in *New England Journal of Medicine*.[256] She found a 10% reduction in breast cancer mortality that was not statistically significant (p = 0.13). Furthermore, two thirds of this little decline was due to better organisation, treatment and breast cancer awareness. She told me it should not be a problem to get her thesis approved with only two papers because this journal is so prestigious. She therefore revised the thesis and resubmitted it.

To her great surprise, it was rejected in September 2011 by the same committee that had recommended her to withdraw the paper on overdiagnosis and resubmit the thesis, and yet again, for no good reason, and in a reject letter with little scientific substance.

Mette was convinced that what was happening was all wrong.[257] Unwilling to accept what she thought was a violation of academic freedom, she hired lawyers and engaged her union in her fight.

I became involved and sent a letter to Rector Ole Petter Ottersen and the Dean of the Medical Faculty, Frode Vartdal, noting that the circumstances surrounding Mette's thesis were so extraordinary that I needed to react. I accused the university of maladministration and Elsebeth Lynge of having abused her academic trust.

The university then raised doubts about Lynge's motives, and they ended up removing her. But officially, not because of this. The official excuse was that, with three women on the committee, there was gender inequality. People will go a long way to save face even if it makes them laughable.

It was agreed that a new committee was needed. Adami suggested me as chair, which the university rejected. They regarded me as conflicted because I disagreed scientifically with Lynge. This is an invalid argument. Scientists often disagree, with brings science forward. There are many obvious flaws in Lynge's research, and I had alerted other scientists to them in my scientific papers and in my book about mammography screening.[258] This was my obligation as a scientist, and it could in no way disqualify me as an examiner of a thesis. On top of this, Lynge was out of the picture.

Oslo University broke many other elementary rules in the way they handled the case, which I mentioned in an 11-page letter to the Rector and the Dean. Even Lynge's two co-assessors complained to the university about its unprofessional handling of it all,[259] which was a clear case of maladministration.

Rector's reply to me was arrogant. He did not respond to any of the questions and concerns I had raised but merely wrote that, "The handling of this case has been in agreement with current rules and academic principles." This was false, but the typical kind of bullshit top administrators use when they come in trouble. He also noted that I was not "part of the case."

I feel it is a moral imperative for me to help when good people I know come in trouble because of bad people, and Mette and Adami appreciated my assistance.

Many people were upset about the affair, and I was interviewed in several media, including the Oslo University newspaper, in the article, "Abused by the evaluation committee."[260]

A year later, Mette got her PhD, after 1.5 years of agony. In her third article, she showed that at least 33% of the improved survival was attributable to improved breast cancer management through multidisciplinary medical care.[261]

This story was a disgrace for academia in general and for Oslo University in particular. Mette abandoned her post as head of the Norwegian mammography screening programme, as her own research had confirmed that screening is harmful.

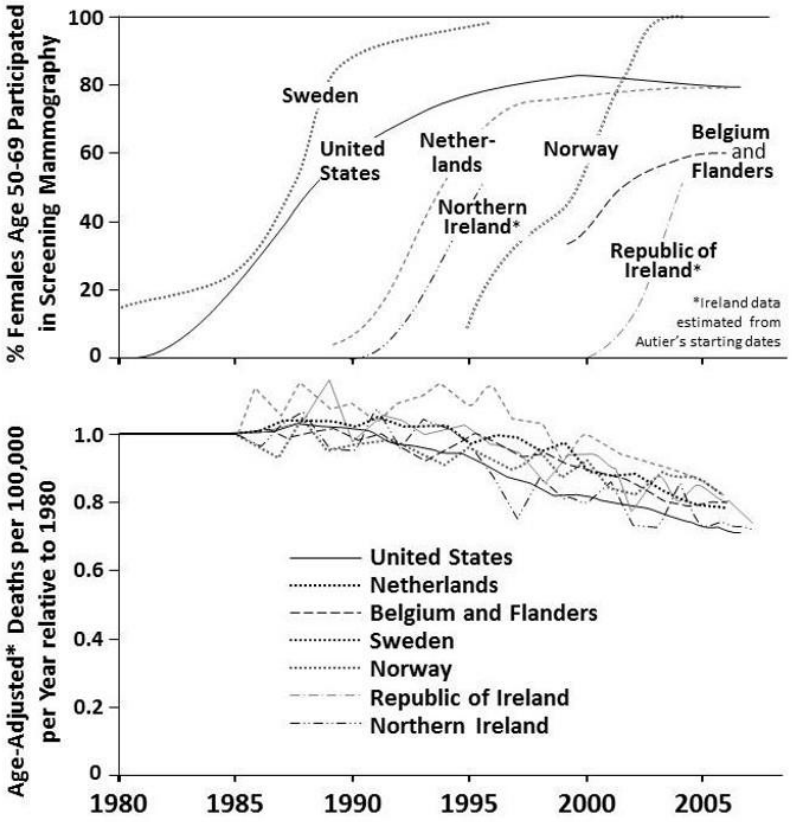
When she changed her mind about screening, the punishment from the screening community was harsh. People at the Norwegian Cancer Registry, where she worked, accused her of scientific misconduct, a groundless accusation, rejected by the Norwegian Ombudsman.

What is perhaps most amazing in all this is Lynge's double standards. Her own PhD student, Anne Helene Olsen, obtained her PhD despite the fact that her article, which claimed there was no overdiagnosis in Denmark, did not support this.

Critical e-letters: Published and disappeared when nobody was watching

In 2010, Philippe Autier and colleagues showed that, in 30 European countries, breast cancer mortality had decreased more (37%) in women below 50 years of age than in the age range most commonly invited to screening, 50–69 years (21%), and that the decreases had consistently started several years before screening could have had any effect.[262]

In 2011, Autier published another revealing study that compared three pairs of very similar neighbouring countries that had introduced screening 10-15 years apart. [263] There was no relation between start of screening and the reduction in breast cancer mortality. The fall in breast cancer mortality was about the same in all countries and started at the same time, around 1990. Furthermore, the decline was similar in the United States, where screening started as early as in Sweden (see figure).[264]



The reactions by screening advocates related to these findings were extraordinary in the United States. In 2010, the editor of *Radiology*, Herbert Kressel, invited us to write a paper in the "Controversies in Radiology" series and noted that Daniel Kopans had agreed to take the opposing view. We requested that none of the parties should be allowed to see the other's contribution before publication, which was granted.

We explained in great detail why screening cannot have more than a trivial effect, if any, whereas the harms are substantial.[265] Kopans had Duffy and Smith as co-authors, and they cherry-picked studies such as Tabár's "beyond reason" studies.[266] They claimed an over-diagnosis of only 1% and even put "overdiagnosis" in inverted commas in the title of their paper, as if it didn't exist.

They ignored serious errors that had been pointed out to them previously and they lied profusely about our research. We *did not* assume a stable underlying incidence, but took account of increasing trends; we *did not* base our estimate on a single year after screening, but on many years; we *did not* assume that all carcinoma in situ is overdiagnosed; we *did* take lead time into account (by adjusting for a fall in incidence in elderly, previously screened women when it occurred); we *did not* assume that all additional incidences after the initiation of screening were overdiagnosed, and our follow-up *was* long enough.

We submitted a letter to *Radiology* explaining the many errors Kopans, Duffy and Smith had made, but Kressel refused to publish it. We then sent a letter to the blog on the journal's website where it was published as an e-letter.[267]

Few people will find an e-letter, as they are not indexed on PubMed, and when I looked for it in 2023, it was gone. On *Radiology's* website,[268] there were 7307 e-letters, but when I searched on the title, or on our names, or on the number of the e-letter, 243781, there was no match.

I wrote to the journal and after some correspondence, they found it and provided a link,[269] which, however, is not to our e-letter but to the article by Kopans, Duffy and Smith. I therefore still consider our e-letter effectively buried by the journal.

Radiology prepared a press release about the two papers to which Kopans and we contributed. A few days before the papers came out, we were informed that the press release had been cancelled. We told the editor we were disappointed because a press release would draw attention to the papers, which was important for the screening debate. The editor seemed to agree, as he had found our paper thought-provoking, which would "certainly generate a good deal of conversation among our readers."

We asked for an explanation and urged the editor to reconsider his decision. We were then told that "because this was a two-sided news release, we needed to have full participation from the authors of both sides. We strive to provide fair and balanced news to the media and it was at the last minute that we found out not all of the authors agreed to participate and we needed to respect their wishes and cancel distribution."

I participated in a podcast recording with Smith and Kressel two weeks before our papers came out, and as both sides had shared their papers for the purpose of the podcast, our opponents knew what was coming. Our co-author, US radiologist John Keen, suspected there might have been political pressure from the American Cancer Society. The society must have been concerned about Autier's papers, which we had cited. Further, the Society would hardly be happy about publicising a paper where we looked a lot better than Kopans.

It would have been easy for *Radiology* to issue the press release. The editor could have allowed Kopans to withdraw his quotes stating that he refused to comment.

It is unfortunate that people or institutions with vested interests can suppress important press releases and it shows that they put their own interests above those of the women. For transparency, I have reproduced the missing press release in my 2012 book.[270]

Many US radiologists subscribe to the news service Aunt Minnie, which mentioned the papers and had quotes from Kopans.[271] The bloggers generally felt Kopans's arguments had no credibility. I described the untruthful statements he had made about our research on the Aunt Minnie website,[272] but in 2023, any trace of this was gone. There were 27 publications that mentioned my name, but our criticism of Kopans had been removed.

These experiences remind me of an episode in the "Yes Minister" *BBC* series: "It is only totalitarian governments that suppress facts. In this country we simply take a democratic decision not to publish them." Or we remove them when nobody watches.

8 What are women told and why is it misleading?

Hundreds of millions of women have been seduced into attending screening without knowing it doesn't work and could harm them. This disregard of the principles for informed consent and national laws is one of the biggest ethical scandals ever in healthcare.

Information on websites and in invitations: Misleading and insufficient

In 2004, Karsten Juhl Jørgensen and I published a study in *BMJ,* "Presentation on websites of possible benefits and harms from screening for breast cancer."[273] Curiously, even though most websites stated that the women's decision about participation should be based on informed consent, the information they offered was not sufficient to allow this.

The success of a screening programme depends on the participation rate, and we found that information from governmental institutions and professional advocacy groups was less about informing and more about persuading.

What was often missing was information on the harms of screening, and data on the risks from false positive and false negative results. Moreover, the information on harms was framed differently to that on benefits. Data on the impact of screening on breast cancer mortality was based on several years of screening, whereas the risk of being recalled because of a suspicion of cancer was related to a single screening session. Like was not being compared with like.

The benefit was given as a relative risk reduction three times as often as an absolute risk reduction. Showing benefits as a relative risk reduction makes an intervention seem more effective than it is. It was also common to scare women with impressive numbers of cancers detected in a year in a country. Furthermore, saying that false positive findings can sometimes cause "anxiety" is much more soothing than saying that 25% of screened women (50% in USA) will experience significant psychological distress for years after a false positive result.[274]

In 2001, a long-awaited revision of the UK leaflet on breast screening was launched. The prevailing paternalistic attitude to women, with little respect for their autonomy and for informed consent, had not changed, however, and was roundly criticised in *Lancet*.[275]

We therefore decided to study invitations to mammography screening, research which we published in *BMJ* in 2006.[276] They were disastrous. The 31 invitations we obtained from seven countries were less like invitations and more like an offer you cannot refuse, and they were even more persuasive and unbalanced than the websites. We examined 20 pamphlets, and 19 of them (95%) had suggestive headlines, such as, "Have a screening mammogram, it may save your life."

Refusing screening was difficult, e.g. "If you would like to avoid participation, we ask you to fill out a form. You obtain this form by calling the breast-diagnostic centre" and "If the time is very inconvenient, we ask you to contact the mammography screening centre as soon as possible."

This is inappropriate for a voluntary examination, as it gives the women the impression that it is their duty to accept it. In most "invitations," a time had already been allotted, which creates an obligation to attend. Reminder letters often contained strong appeals, e.g., "I am concerned that you have not yet responded to our recent invitation for a screening mammogram," which is not only overfamiliar; it also induces guilt.

In Sweden, women weren't informed about anything that could be relevant for their decision to participate in screening or not. None of the invitations mentioned the major harms of screening, or the uncertainties related to treatment of carcinoma in situ.

When our paper came out, Julietta Patnick, director of the UK cancer screening programmes, said to the *BBC*: "I would strongly encourage all women to make an informed choice to attend for screening when invited."[277] Intriguing. How can strong encouragement from an authority have anything to do with free, informed choice?

In 1987, when Michael Baum was professor of surgery at King's College in London, he was given the task of establishing the first mammographic screening unit in southeast England.[278] He took great pride in setting up the unit but became increasingly disturbed by the lack of true informed consent and by what he saw in practice.

The most dangerous cancers grew quickly and often surfaced between two screening sessions, and it became clear that it would be impossible to reach the target of a 25% reduction in breast cancer mortality.[279] Worst of all were the unexpected high numbers diagnosed with ductal carcinoma in situ, a condition they rarely saw before screening began. Many of these cases were multifocal and ended up with a mastectomy. As Baum noted, "how do you explain to a woman that she is 'lucky' that we caught it 'early,' yet ends up having a mastectomy?"

Things came to a head in December 1994. The deputy chief medical officer called an emergency meeting of the national steering committee to come up with a strategy to protect the programme in the face of the accumulation of adverse publications in the medical media. Baum argued passionately for a revision of the false promises in the leaflet that went out with the invitations so that the lay public would at least be able to make an informed choice, as in his mind it was a pretty close call to judge whether the benefits outweighed the harms.

He was a lone voice at the table and the chairman summed up the opinion of the gathering as follows; "Professor Baum, if we include all this new information in the leaflets then the women are unlikely to attend, and we will fail to reach our target of 70% uptake." To which Baum replied, "If that is indeed the view of this committee then I can no longer serve, as I believe that women have the right to self-determination. I hereby resign and intend to make my feelings felt by going public on the topic."

Baum noted that, "As a surgeon I have a legal and ethical commitment to describe to my patients the harms and the benefits of my interventions, but a double standard clearly exists among the screening community, who seem to be in denial."[280]

Machiavellian methods again: The updated Danish leaflet

Ten days after our review of invitations to screening had been published,[281] the director of the Danish Board of Health declared that their leaflet should be revised so that it would be correct and balanced. The Board held a meeting asking for suggestions for revisions. The invitees were mainly people with an interest in promoting breast screening, but there were four of us without such conflicts:

Margrethe Nielsen, co-author of the 2006 and 2009 Cochrane review; Ole Hartling, chairman of the Danish Council of Ethics; general practitioner John Brodersen, who had studied the psychosocial effects of false positive findings; and me.

We were worried about the vested interests and became convinced that the Board of Health's real agenda was to defend the status quo under the guise of having appeared forthcoming. We therefore asked for guidance before the meeting and suggested that the contents of the leaflet should be based on the best available evidence and that data for benefits and harms should be given as absolute numbers with the same denominator, for example per 1000 women. We received no reply.

Machiavellian methods came into force once again. After the meeting, the Board informed us that, as it had not been possible to achieve consensus, it would finalise the leaflet itself together with a "Committee for Health Information" we had never heard of.

We replied that we hoped we would get the opportunity to comment on the next draft, particularly as the current draft was far from being balanced. Furthermore, we questioned why there was such a large discrepancy between what we had agreed at the meeting – even with the screening advocates – and the content and wording of the draft. Finally, we noted that we assumed that the Board would use the best available evidence and would therefore take the comments we had offered in writing into consideration.

Again, we received no reply from the Board. The final version arrived six months later, and it was a disaster. The leaflet was not evidence-based; our suggestions had been completely ignored; and the leaflet reflected the views of the screening advocates.

We consulted an expert in health law, Mette Hartlev, who supported our view that the revised leaflet didn't comply with Danish law. The body responsible for enforcing Danish law in this area is … the Board of Health.

Interesting. The Board of Health is supposed to be the watchdog of the Board of Health, just like Elsebeth Lynge was supposed to evaluate the research by Elsebeth Lynge. It felt like living in a banana republic or Russia.

The leaflet didn't even live up to what was written in the Board's own report from 1997 that paved the way for screening: "The offer of participation in the programme should include very careful information to women mentioning advantages and disadvantages."[282]

There were 13 main problems with the leaflet,[283] [284] which looked like a sales brochure for a used car. It is difficult to imagine more flagrant disregard for conflicts of interest, sound science, informed consent, and women's needs.

The leaflet was also provincial. There were no references to the best available evidence; all six papers in the reference list were to Danish publications; the four most important ones had been written by people with a conflict of interest; and the claimed 25% positive effect of screening came from Lynge's flawed study from Copenhagen (see page 54).

There were questions in parliament to the minister, but to no avail. The minister replied that it was his perception that the Board had acted in an exemplary way, including describing openly the advantages and disadvantages of screening. Of course. And guess who had briefed the minister on what he should say? The Board of Health of course!

The four of us were so disappointed that we wrote a leaflet ourselves to provide the information women needed to make a rational decision. We tested draft versions among general practitioners in Denmark, Norway and Sweden and among laypeople, which led to considerable improvements. The leaflet started with a summary:

"It may be reasonable to attend for breast cancer screening with mammography, but it may also be reasonable not to attend, as screening has both benefits and harms. If 2000 women are screened regularly for 10 years, one will benefit from the screening, as she will avoid dying from breast cancer. At the same time, 10 healthy women will, as a consequence, become cancer patients and will be treated unnecessarily. These women will have either a

part of their breast or the whole breast removed, and they will often receive radiotherapy, and sometimes chemotherapy. Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether or not it was cancer, and even afterwards, can be severe."

We were much too kind, as it had never been demonstrated and was even unlikely that *anyone* would benefit from screening. We acquired funding from a small Danish cancer foundation (KræftFonden) that allowed us to print and distribute the leaflet to general practitioners and gynaecologists in Denmark in March 2008.

Maryann Napoli, from the US Center for Medical Consumers, called it "the first honest mammography information for women written by health professionals,"[285] and volunteers translated it into many languages. Our 2012 update exists in 17 languages, including Arabic, Russian and Chinese.[286]

We presented the leaflet on Praxis, a Danish prime-time television programme that devoted more than 20 minutes to the subject.[287] The journalists went to great lengths when preparing the programme and were persuaded by our scientific arguments. I had to explain repeatedly the background for our numbers and what the differences are between randomised trials and observational studies, and I felt at times I was being interrogated. Clearly, the journalists wanted to be certain they bet on the right horse when they went against the all-powerful Board of Health.

Breast screening: The facts - or maybe not

Our 2006 article on the content of invitations had included a box with recommended information, as advised by the *BMJ* editors. The UK leaflet had been updated again, after we published this box, but its contents remained essentially the same as the 2001 version and still violated accepted guidelines. For example, the guidelines from the UK General Medical Council state that, "You must tell patients if an investigation or treatment might result in a serious adverse outcome, even if the likelihood is very small."[288] The likelihood of being harmed through overdiagnosis as a result of screening is more than small; it is substantial.

The UK leaflet implied that screening leads to fewer mastectomies: "Around half the cancers that are found at screening are still small … This means that the whole breast does not have to be removed." Carcinoma in situ wasn't mentioned, although it constitutes about 20% of the diagnoses made at screening sessions and is often treated with mastectomy.

As our *BMJ* papers on websites and invitations didn't have much impact, if any, in Machiavellian power circles, we decided to write a paper about the shortcomings of the new UK leaflet. As the leaflet had the authoritative title, "Breast screening: the facts," we called our paper, "Breast screening: the facts - or maybe not."[289] Our own leaflet had become very popular, so we published it in the same article. *BMJ's* editor-in-chief, Fiona Godlee, called it one of her top 20 articles in the last 20 years.[290]

When our paper on the new UK leaflet came out, 23 people from the United Kingdom, the United States, Canada, Australia and France published a letter in *The Times* calling for action.[291] The signatories included a breast surgeon, epidemiologists, practising physicians, patients, and journalists, and the message was strong.

The letter noted that "there is evidence to show that up to half of all cancers and their precursor lesions that are found by screening, if left to their own devices, might not do any harm to the woman during her natural lifespan ... The most disturbing statistic is that none of the invitations for screening comes close to telling the truth. As a result, women are being

manipulated, albeit unintentionally, into attending. It is therefore imperative that the NHS BSP [National Health Service Breast Screening Programme] rewrites the information leaflets, for example by using the template provided by the Nordic Cochrane Centre, and leave it to the properly informed woman to accept the invitation or not."

However, patronising attitudes don't disappear easily. Peter Johnson, chief clinician at Cancer Research UK, said it was dangerous to scare people away from a programme that had brought substantial benefits.[292] I explained on *BBC* Radio 4's popular "Woman's Hour" programme that women couldn't make an informed choice because of the one-sided propaganda they received.[293] In the same programme, Stephen Duffy derided me and said that my numbers were "completely inaccurate" and talked about an "atmosphere of hysteria." If anyone was hysterical it seemed to be Duffy.

This time, the usual mantras from the screening advocates had little effect. Only two days later, an article in *The Times* announced that the NHS was tearing up its leaflet and writing a new one from scratch.[294]

But Julietta Patnick didn't intend to abandon her strong taste for unsolicited paternalism. She said that, according to research, "putting too much numerical information meant women just put the leaflet down." In actual fact, an abundance of research has shown that the great majority of cancer patients want as much information as possible, and it seems highly likely that healthy women who run a risk of being made cancer patients unnecessarily would also want information.

In "Behind the headlines," produced by the NHS Knowledge Service, Patnick said that – instead of one breast cancer death spared (which she erroneously equated with one life saved) per 10 women receiving unnecessary treatment, as had been stated in *The Times* – the ratio was much nearer to a one-to-one ratio.[295] In *New York Times*, she echoed Duffy and "dismissed the Cochrane figures as inaccurate."[296] We were perplexed by this. Our numbers were accurate and came from the randomised trials, and she was getting the ratio wrong by a factor of 10. Was this an honest mistake or a deliberate intention to mislead?

Sir Mike Richards, England's National Cancer Director, repeated the one-to-one ratio and said, "There are no doubts in my mind about the benefits." Richards toed the party line, which in the UK can earn you a knighthood. Dame Valerie Beral from the NHS Breast Screening Programme was Commander of the Order of the British Empire, and Patnick was Commander of the British Empire. As there is no longer any British Empire, should we interpret this as the Empire of Cancer Screening?

People in charge are unwilling to admit their mistakes. Per-Henrik Zahl noted in 2009 that even though it is very rare that women get a thrombosis when they take oral contraceptives, they are nevertheless informed about this risk.[297] In contrast, the risk of being harmed by overdiagnosis as a result of breast screening is very large, but Norwegian women are not informed about it.

Rita Steen from the Norwegian Cancer Registry responded to Zahl's comment with this remarkable statement:

"The reason that we now include this information is not that we think overdiagnosis is a large problem in the programme, but because the problem has received so much attention in the debate about mammography."

So, were it not for our research, Norwegian women would have been kept in the dark.

This lack of respect for women was also apparent in Denmark. In June 2009, we published a paper in our medical journal listing the major problems with the Danish Board of Health's

new leaflet,[298] which we sent to the Board together with our own leaflet and our criticism of the UK leaflet, suggesting that a revision of the Danish leaflet was necessary. Nothing happened.

In December 2010, shortly before Christmas when people had other things on their mind, the revised UK leaflet was published. This was the third version in just nine years, and it was still less than satisfactory. Spokespeople for the NHS's programme had stuck to the beliefs about benefit that prevailed 25 years ago and continued to question the issue of overdiagnosis.[299] The only hint at overdiagnosis in the leaflet was this ambiguous sentence: "Screening can find cancers which are treated but which may not otherwise have been found during your lifetime."

Some women would interpret this as, "Great! Screening finds cancers that are hard to find – that's why I go for screening."

I subjected this sentence to a test among fourth-year medical students. They were unprepared – just as women invited to screening are – as they had not been lectured about screening. Most of them couldn't tell what the sentence meant and most felt that laypeople would perceive the message as positive, e.g. a chance of cure.

It should be a criminal offence to misinform the public to this extent. We published our observations in the article, "The Breast Screening Programme and misinforming the public,"[300] but although we had carefully documented with Danish data that screening increases the incidence of mastectomies, Patnick continued misleading the media:

"We know that 97 per cent of women with screen-detected cancers are alive five years later compared to just over 80 per cent of women diagnosed without screening, and screening lowers a woman's risk of having a mastectomy."[301]

The lies never stopped; they were just repeated, totally unimpeded by any type of reliable evidence, and with complete disregard of emerging new data. Such things take mammography screening out of the realms of science and into dogma.

Distasteful personal attacks in Sweden

Our 2009 papers in the *BMJ* about overdiagnosis[302] and the UK screening leaflet[303] elicited strong reactions from screening advocates.

In Sweden, we were subjected to distasteful personal attacks, which began with the first title, "Scare campaign about mammography."[304] The authors, oncologist Sven Törnberg and Lennart Nyström, couldn't know what our motives were, and the fact was that women had been scared into getting screened.[305] We found it shocking, for a country that has guarded the rights and autonomy of its women in a tradition that goes back to the Vikings, that today's Swedish women should be deprived of access to the information they need to make their own decision.

Törnberg and Nyström manipulated the numbers and got them wrong. They used the relative risk to inflate the apparent benefit (a 30% reduction in breast cancer mortality) and the absolute risk for overdiagnosis so that it looked small (0.1%, which is wrong by a factor of 5 according to the trials).

They also spread doubt about what overdiagnosis is and asked how one can distinguish between a cancer that is overdiagnosed and one that is not. This is nonsense. Overdiagnosis is a statistical concept. It is not possible to make a distinction in an individual case, which is why all detected cancers are treated.

As always, when you show that your opponents are wrong, their style deteriorates. The title of their second letter was: "Is anxiety related to the investigation worse than premature death from breast cancer?"[306] We have never contrasted these effects, which would be silly.

Törnberg and Nyström's *ad hominem* attacks were likely the most unscrupulous and mendacious we had ever experienced, which says a good deal. They claimed we didn't find it problematic that women die prematurely from breast cancer. Of course, we do, but it is also a problem that many healthy women receive life-changing treatment for a disease they don't have.

Their paper ran to just over one page. I had not seen so many untrue statements in such a small space before. Here are seven accusations they made of us:

1. We are unscientific or have deliberately misled the readers with false numbers. (This is incorrect. We know how to do science and our numbers are scrupulously checked for accuracy).
2. We have clearly forgotten how we once calculated. (We don't forget what we do; we calculate in the same way every time; and document our calculations).
3. "In our extrapolations …" (There are no extrapolations anywhere).
4. Our goal is clearly not to be objective. (Wrong – it is to give the women honest information).
5. Clearly, our aim is to scare women into not attending screening, which we also admit in the rest of our article. (We have no such aim and have not admitted this).
6. We cling to our prior belief. (We do not – we have no prior belief; we are scientists and conclude based on evidence).
7. We have blamed all incidence increase on overdiagnosis and refuse to accept that there are several causes for incidence increases. (Yet our papers prove that this accusation is a blunt lie).

Törnberg and Nyström argued that our estimate of overdiagnosis is not "theoretically possible." More nonsense. We do not rely on theory, but on empirical data. Moreover, as in their first paper, they manipulated numbers again by estimating the number of overdiagnosed women for only one screening round, while noting the effect on mortality after several rounds. This is like complaining about paying too much income tax by totalling the tax over ten years, but the income over just one year.

We had not initially been aware of Törnberg and Nyström's first article, but after Swedish colleagues informed us about it, we submitted an unsolicited reply.

We wrote to the editor-in-chief, Jan Lind, asserting that if he allowed Törnberg and Nyström to reply, we should expect to get the opportunity of replying to their reply in the same issue, which we had been unable to do the first time, even though the first article contained *ad hominem* attacks.

As Lind didn't reply, we reminded him of our request. He still didn't reply but later sent us Törnberg and Nyström's second article "for information," noting it was the final comment and that no more debate would be accepted. As it contained lies and defamatory statements (see the seven examples just above), we believed Lind had committed editorial misconduct because we could not defend our reputation.

I appealed to Lind noting that I had raised issues about publication ethics and conflicts of interest in my capacity as editor on the list serve of the World Association of Medical Editors on several occasions due to my interest in these subjects. I also mentioned that there had been far too little debate about mammography screening in Sweden and quoted an email I had received:

"A big THANKS for your achievements in this matter, which for so long has been completely impossible to lift the tiniest bit here in Sweden."

I also quoted an email from a Norwegian colleague who wondered why Sweden was a country with so much (self)censorship and self-inflicted, oppressive political correctness?

My letter to Lind worked. He might have guessed we didn't intend to budge. Journals have owners, and editors are held accountable for their actions. The title of our reply addressed what Törnberg and Nyström had denied: "Overdiagnosis with mammography screening is a serious problem."[307]

One question remains. Why do Swedish screening advocates react so brutally? Is it because mammography screening is a national treasure and an object of national pride, something Sweden has given to the world, like Volvo, Saab and ABBA? I think so.

Inger Atterstam, a journalist from *Svenska Dagbladet*, described her experiences with freedom of speech in 2001.[308] For 20 years, it had not been possible to have a decent intellectual discussion about positive and negative aspects of mammography screening. Any criticism had been aggressively and emotionally condemned with accusations of the most awful motives and of irresponsible and unscientific behaviour. Despite this, there had been persistent rumours about mistakes and flaws in the trials, particularly in the Kopparberg part of the Two-County trial.

Atterstam had looked at the publications and was upset because of the many obvious violations of established scientific method. She wrote about it, but her articles were met with hysterical reactions that included personal accusations and persecution. She also remarked that there was a strange anti-intellectual lack of open discussion, and that screening had been presented to women as a solution to the whole breast cancer tragedy, which was very dishonest. The persistent mantra coming from the screening advocates was that she was harming patients.

Despite all the intimidation, she encountered gratitude for having the courage to speak up.

The Nestor of Swedish medicine, Professor Lars Werkö, also noted that it was difficult, if not impossible, to have a reasoned debate in Sweden about mammography screening and that the space for critical opinion was minimal.[309]

Screening advocates often give the impression of higher moral authority, because they act on behalf of women and for their benefit. A Swedish journalist hit the nail on the head when she said: "Women prefer people who speak the truth, even when the truth is uncomfortable. Just as men do."

Untruthful glorifications of own achievements in the UK

Reports from the UK breast screening programme were not truthful. They were glorifications of their own achievements that steamed with political correctness and spin. It had been expected that screening would have reduced breast cancer mortality by 25% in 2000.[310] [311] When this didn't happen, Yvette Cooper, under-secretary of state (Commons), saved face with a remarkable spin in her foreword to the NHS Breast Screening Programme report for 2000:[312]

"Breast cancer mortality in England and Wales decreased by 21.3% between 1990 to 1998, and it is estimated that 30% of this reduction was due to breast screening."

This was really smart PR for a failed programme. Decision-makers are busy and would likely not notice that what the programme had delivered was not 25% but 6% (30% of 21.3% is 6%).

In 2006, when our updated Cochrane review with data on overdiagnosis had come out, Michael Baum suggested that the National Institute for Health and Clinical Excellence (NICE) should evaluate the screening programme. A spokesman from the Department of Health responded that it would not be appropriate, because mammography screening was an accepted, evidence-based technology.[313]

We got it. The Department of Health will not allow NICE to touch the sacred cow.

The Annual Review from 2008 celebrated the programme's 20th birthday and was published by the Department of Health.[314] We dissected the review and exposed its innards in *Journal of the Royal Society of Medicine*. We were particularly critical of a programme that feels qualified to evaluate itself.[315]

Twenty years is a long time, and it would have been easy to demonstrate the expected 30% reduction in breast cancer mortality, which was the basis for the introduction of the screening programme, if it had happened. Instead, the 26-page review celebrated the anniversary, called it a "momentous occasion," exaggerated the benefit and glossed over the harms in a beautiful design that looked like a sales brochure for female sex hormones:

Even the title was incorrect. Mammography screening does not save lives, yet the brochure claimed the programme saves 1400 lives each year. This was referred to as a "key fact," but despite extensive detective work we were unable to find any documentation to support this. The reference offered in support of the claim was to another NHS report, which had claimed that screening reduces breast cancer mortality by about 35%.[316] It is not clear where this estimate came from, but it certainly is not supported by the data from the randomised trials.

Six years earlier, in 2002, the programme's website was more modest and noted that at least 300 lives are saved per year,[317] with reference to an observational study in England and Wales.[318] But the next sentence read: "That figure is set to rise to 1,250 by 2010." By whom? Julietta Patnick? There was no explanation how this miracle would be achieved.

Elsewhere in the material I downloaded from the programme's website in 2002, the prophecy of 1250 lives saved in 2010 had already come to pass – overnight, it seemed. Patnick declared, "We estimate that screening is now saving on average 1250 lives a year. On October 31st 2001, we will publish the NHS Breast Screening Programme's annual review."

So, in 2001, the programme announced it saved 1250 lives; in 2002, it was 300 and 1250; and in 2008, it was 1400. It is enough to make a mathematician seasick.

The opening statement of the 2008 review reads like marketing speak. The authors "look forward to the future developments that will deliver even greater benefits to thousands of women in the years to come." Oh dear, more seasickness ahead.

Overdiagnosis and overtreatment were not mentioned in this glossy report. We estimated that about 7000 unnecessary breast cancer diagnoses would be made per year in the UK in the invited age group.[319] The review converted this harm into something positive: "A huge number of breast cancers, over 100,000, have been detected since 1988, highlighting the importance of the screening programme in the early detection of breast cancer."

This is an example of "The popularity paradox." The more women that are diagnosed – regardless of whether they are overdiagnosed – the more efficient screening is described to be, and the more people will think screening saved their life.[320]

The other major harm of screening, the false positive findings, wasn't mentioned either. We calculated that about 70,000 women experience a false positive recall every year in the UK. As always, the report downplayed this risk by describing it for a single screening session and not as the accumulated risk over 20 years of screening, which is about 20% for screened women.[321]

Other essential information was also concealed. Biopsies can be either needle biopsies or surgical excisions, which have a much greater personal impact, but the review was not specific about this. After some detective work, we found out from another report that 3% of those recalled will have a surgical excision. This means that what the report euphemistically listed as 1676 "benign biopsies" were actually 1676 surgical excisions. It is hardly benign for a woman to undergo a surgical excision on a false suspicion of cancer.

This harm was further downplayed as affecting 0.1% of those screened per year. We calculated that the exaggerated mortality benefit mentioned in the review also amounted to 0.1% of those screened, but in this case over 10 years.

The number of needle biopsies wasn't presented either, but we calculated that 28,000 unnecessary needle biopsies are made per year that would not have occurred in the absence of screening.

The report presented no data on the numbers of mastectomies conducted. In fact, there were 36% more mastectomies for invasive cancer and 422% more for carcinoma in situ from 1990 to 2001 in the UK.[322]

The review also contained misleading survival statistics. A quote from Stephen Duffy is highlighted in the review, with no caveats: "The 10-year fatality of screen-detected tumours is 50% lower than that of symptomatic tumours."

That such information is highly misleading was recognised as early as in the 1986 Forrest report that led to screening in the UK.[323] The 2008 review was edited by the programme's director, Julietta Patnick. It is unforgivable that she and Duffy are so prepared to mislead the public.

The review is full of old-fashioned paternalism and a patronising attitude to women. For example, the stated aim is to increase participation in screening by continuing to support women to make the right choice for them. This statement goes directly against the decision

of the National Screening Committee that "the purpose of information about screening is to allow individuals to make an informed choice about whether to participate."[324]

The 2008 review sells screening with an old marketing trick, the loyal and satisfied customer. This is effective, as few would want to be a non-preferred customer. I once checked in at a Sheraton hotel and described myself as one of those customers the hotel would rather not like to see. Amazed, the clerk asked me what I meant by this. I pointed at a huge signboard that hung over the desk next to me that said, "Preferred customers," and I explained that since I was not a member of their executive club, I must be a non-preferred customer.

A happy and faithful customer said: "I know how important it is to have regular checks and to make sure you accept your invitations or make your appointment." She had even continued to request screening beyond the invited age range. We are told that "Women like Dorothy … have attended without fail for decades," which carries the implication that not accepting the invitation makes you a failure, a non-preferred customer. The omission of Dorothy's surname is another marketing trick that conveys a sense of familiarity and a sense of belonging to the regular customers' executive club.

We are also told that, "now a grandmother, Dorothy is passing on her knowledge and experience to her daughter and granddaughter to help them make decisions about screening when the time comes." The expression, "When the time comes" has the air of helping someone pick the right husband. It is nauseating.

Unlike Sheraton hotels, where the directors can be held accountable for shortcomings and omissions in their annual report to tax authorities and shareholders, it is unclear who is accountable for a grossly deceptive annual review of a public health programme where the costs are far greater than merely financial ones.

The media took an interest in our critique, which led to a considerable loss of trust in the programme. Glasgow general practitioner and journalist Margaret McCartney from the *Financial Times* felt we deserved a medal because we had published, unwaveringly over the years, what our research had shown.[325] She noted that breast screening seemed to contain an enormous amount of emotional investment, and that the only parallel she could think of was alternative medicine.

The 2009 review was equally dishonest as the 2008 report.[326] It said on the first page: "Recent statistics show that the number of women in the UK dying from breast cancer has fallen to its lowest level in almost 40 years ... a tribute to the continued progress made by the NHS Breast Cancer Screening Programme."

There is a reference to official mortality statistics. However, these statistics show no visible effect from the screening programme![327]

Nonetheless, the programme extended its invitations to women aged 47 to 49 and a named woman was a happy customer who had her cancer detected when she was 48. She will never know if she should be unhappy because her cancer was overdiagnosed.

The report quoted our two recent papers about the UK screening leaflet and overdiagnosis:[328] [329]

"The NHS Breast Screening Programme has strongly rebutted the claims made by Gøtzsche, believing his papers to be highly selective in the statistics used."

This empty jargon is typical for Stephen Duffy who is its likely source. The programme hasn't rebutted anything, and we did not "claim" substantial overdiagnosis; we demonstrated it. There was more:

"Survival rates for all screen-detected cancers are still 85% at 15 years and the screening programme has proved vital in saving thousands of women's lives."

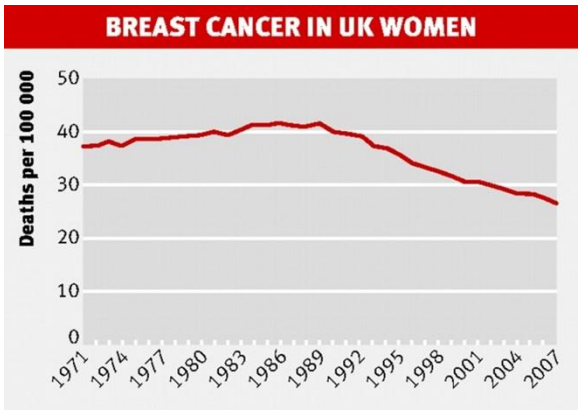
There is one interesting piece of information, though:

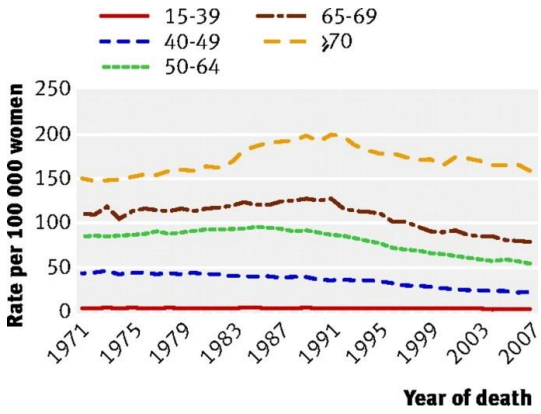
"Just over a quarter of women diagnosed with invasive breast cancer receive a mastectomy, while the figure is slightly higher for in situ and micro-invasive disease."

Considering an overdiagnosis of about 50% that also involves many invasive cancers, this comes close to an admission by the programme that screening leads to a substantial increase in mastectomies.

When *BMJ* news announced in 2009 that deaths from breast cancer had decreased,[330] Peter Johnson, Cancer Research UK's chief clinician, said that this had happened "despite breast cancer being diagnosed more often."

Thus, the spokesperson from the charity used all the overdiagnosed healthy women to the charity's advantage, as few readers would realise that his comparison was misleading. The good news was accompanied by a graph from the charity's website (see figure to the left).





However, the graph was also misleading. *BMJ* noted that there had been a decline in breast cancer mortality of 41% in women aged 40–49 years (who had not been invited to screening) as well as 41% in screened women aged 50–64 years. Even though the decline was the same, Johnson maintained that screening had contributed to the decline in breast cancer mortality.

This is hard to understand, so we checked the charity's website.[331] Just below the graph published in *BMJ*, there was a much more relevant graph, divided into age groups (see figure to the right).

This was revealing. The mortality rate in women at least 70 years old had continued to rise and didn't peak until 1991. This rise had concealed the fact that the decline in mortality in the most relevant age group, 50–64 years, had started three years before screening started. Given the natural history of cancer, any genuine effect of screening, if there were one, would not manifest itself until 6-7 years after screening was introduced. It seems the cancer society cherry-picked the graph and the years that were politically expedient.

The unethical UK AgeX trial

A trial extending the ages at which UK women are eligible for breast cancer screening - the AgeX trial - was registered in 2010. Its original recruitment target was 1.1 million women,

with follow-up until the late 2020s. In June 2011, the recruitment target was increased to “at least 3 million.” The trial randomises clusters (centres) to invite or not invite women for extra screening at ages 47-50 and 70-73.

In 2014, Margaret McCartney argued in *BMJ* that the trial is seriously unethical,[332] and I published a letter with Susan Bewley and others, also in *BMJ*, where we noted the trial’s deficiencies and called for it to be stopped.[333]

The chief investigator is Julietta Patnick, a historian who graduated in Ancient History and Classical Civilisation. She has virtually no experience with randomised trials; is not medically or scientifically qualified; and is professionally conflicted because of her roles running the national screening programme and chairing the trial steering committee. When challenged, she ignores questions about the trial or obfuscates.

The investigators’ submission to the research ethics committee had noted there was “limited evidence” on the value of extra screening. It was dismissive about the risk of over-diagnosis, and the harms were considered justified because the age range “is being extended anyway.”

It was quite explicit that there should be no informed consent, as an insistence on fully informed consent might jeopardize reaching the recruitment targets. The women were to receive the “new improved” national leaflet and would therefore not be fully informed about the harms of overdiagnosis. Trial participants are told that “the phasing-in of the age extension is randomised” so that “the net benefit can be scientifically evaluated.” This is not transparent information, and it is not balanced either. Perhaps there is net harm?

Participants should be told that the purpose of the research was to evaluate the benefits and the harms. Further, there is no assurance that the women realise they are participating in a randomised trial without being asked.

An official 2012 review of screening had stated that, “The impact of breast screening outside the ages of 50-69 years is very uncertain,”[334] but the women taking part in the trial are not told about this.

The seven-page study protocol, produced only after repeated freedom of information requests, contains two references and has no statistical analysis plan. The most important outcomes of all-cause mortality and morbidity (e.g. mastectomies) are not mentioned.

The governance and oversight are opaque. The research ethics committee has twice rejected proposed substantial amendments, and questions from outsiders about the lack of informed consent have been ignored.

This trial may be the largest human experiment ever without informed consent. I am not aware of any other intervention where the standards of science and ethics have sunk so quickly to the bottom as in mammography screening. It is frightening. And it becomes worse. Mandy Payne has added more recent information on the trial on the HealthSense website (previously called HealthWatch).[335]

Seven years into the trial, in September 2016, the target number of trial participants was quietly doubled again, to "at least six million." And the upper limit to the age range was extended from 73 to 79. The trial has been re-named and re-branded; there have been changes to the protocol, the research hypothesis, and to the primary and secondary outcomes.

The current version of the trial protocol says: "The total number of women entering the trial … is not a fixed sample size. If substantial uncertainty still persists, randomisation may well continue.”

I am convinced that if the investigators make total mortality their primary outcome, the trial will never stop, because breast screening is highly unlikely to save lives. The numbers of participants that would be needed to achieve sufficient statistical power to show any beneficial effect of screening on mortality, if it exists, would be astronomical. Even so, it is already the biggest trial ever undertaken.

Mandy Payne noted that the National Screening Committee criteria for appraising the viability, effectiveness and appropriateness of a screening programme include that,

"There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity."

As she argues, mortality means lives saved overall, not lives saved from a particular disease. It should include deaths that result from overdiagnosis and overtreatment.

Abuse of misleading survival statistics

Honest information for women is not on the agenda in Danish power circles either. In 2002, it was front page news that "Mammography saves women."[336] The five-year survival was 83% in a county with screening and 77% in two counties without. This information came from a PhD dissertation supported by the Danish Cancer Society, and the author said the numbers speak for themselves.

The results were also accepted without question by the top politician for health in the Danish counties, who advised that screening be introduced in the whole country, supported by the director for the Danish Cancer Society.

However, one of the examiners for the dissertation noted six days later that such comparisons are problematic, and I explained they are completely misleading.[337] As explained earlier, even if screening has no effect on mortality, five-year survival from time of diagnosis will always be better in a region with screening than in a region without, simply because the cancer is detected earlier than otherwise. The outcome is the same, but the patient is ill for longer. I also noted that the Danish Cancer Society should be concerned about its credibility.

They didn't heed my advice. In 2008, another Danish newspaper announced that "five-year survival has increased from 60% to 80% in 30 years."[338] Henning Mouridsen from the Danish Breast Cancer Group and Hans Storm from the Danish Cancer Society said that this was due to better treatments and screening. There was no explanation that five-year survival rates over a time span of 30 years are highly misleading.

Still in 2008, an article from the Danish Cancer Society touted that, mirabile dictu, after the government had donated a substantial amount of money for improved diagnosis and treatment of cancer, the survival had improved.[339] Although two of the three authors were statisticians and the third an epidemiologist, hence should have known better, they nevertheless interpreted this as evidence that the plan had worked. It barely stopped short of saying: Send more money.

I noted that the survival data were useless for saying anything about the effect of the donation and that they should have looked at annual number of cancer deaths instead.[340] The authors did not admit their error but replied that my attack on cancer researchers showed that behind my cool manner and my critical-scientific palisades, "other feelings were hidden, which evidently drove my commitment."[341] They were amateur psychiatrists, too.

The dishonesty persisted. In 2009, a newspaper reported that Denmark had the highest death rate in breast cancer among the OECD countries.[342] The Danish Cancer Society didn't miss the golden opportunity.

Chief physician Iben Holten said that the most important reason for this was that we are finding cancer too late, and chief statistician Susanne Møller added that Denmark had not had nationwide screening, in contrast to Sweden where the women are diagnosed earlier and therefore also have better survival rates. Two of the five regions in Denmark had still not started screening, and Holten was very sorry about this because, as she said, those cancers that were not found by screening have a far worse prognosis.

Senior statistician Gerda Engholm from the Danish Cancer Society said in 2013 in an interview that the lower survival rates for Danish women with breast cancer compared to other countries was largely because 80% of Danish women had not been offered mammography screening.

She argued that three years after the diagnosis was made, 89% of Danish women were alive, compared to 91-94% in Norway, Sweden, Canada and Australia.

I noted that she knew perfectly well that she was spreading misleading propaganda that was contrary to the facts,[343] as the mistake she made was so basic that it was known by everyone involved with cancer screening. Moreover, in the UK, which introduced screening in 1988, the three-year survival rate was only 87%, i.e. lower than in Denmark, but this information was not offered by Engholm.

What also makes Engholm's three-year survival comparisons suspect is that Danish screening officials have assumed that screening advances the time of diagnosis by three years. If this is true, no one diagnosed with breast cancer at screening would have died from breast cancer three years later, i.e. the three-year survival rate would be 100%.

I had pointed out these basic issues several times to the Cancer Society, also to Engholm, e.g. in our medical journal, when the Society had come up with its misleading propaganda, yet they continued to misinform the public. I therefore ended my article by asking:

"Does the Cancer Society have no shame?"

The marketing from the Danish Cancer Society is so effective that even top researchers that do not work with screening are led astray. In 2016, Bente Klarlund Pedersen wrote an article in a Danish newspaper with the title, "Screening for breast cancer saves lives and renders the treatment less aggressive."[344] She said that she went to screening because the lives saved are more important than those harmed by overtreatment, and noted that only 30% of Danish women had the disease in the first stage in contrast to 42-45% in other countries.

If you search for prevention of cancer (forebyg kræft) on the homepage of the Danish Cancer Society, the frontpage advises you to participate in screening, also for breast cancer. The page about screening for breast cancer touts:[345]

"With screening, most cancers are detected so early that the women can more often have a breast-conserving operation and thus avoid having the entire breast removed."

"Screening means that … fewer women die from breast cancer."

"Mammography screening can reduce mortality from breast cancer by more than 20 per cent."

"If the X-ray shows a lump or a change in the breast that makes the doctors suspect cancer, you will be recalled for a new examination … 2-5 percent of the women examined are recalled."

This information is highly misleading. The claimed benefits don't exist; the claimed reduction in breast cancer mortality is based on data for many years of screening whereas the recall rate is only based on a single screening session. Above all, no data are given on overdiagnosis, the most important harm of screening.

In 2014, the Danish screening programme was uncritically praised in a newspaper[346] and in other media, including in our medical journal, *Ugeskrift for Læger*. Those responsible for the programme, e.g. Ilse Vejborg, expressed great optimism based on the preliminary results, but the optimism was unfounded, as we explained.[347] There was unintended dark humour in the title of the newspaper article, which we used it in our own title: “Screening finds thousands of breast cancers,” adding: “but is it good or bad?”

We mentioned that Switzerland was the first country where an independent panel of researchers had recommended that screening for breast cancer should be abandoned, based on a comprehensive review of the scientific literature.[348] The panel's reasoning was that the beneficial effect is outweighed by the harmful effects, and that the balance between costs and beneficial effects was very unfavourable. Two of the panel members described their findings in *New England Journal of Medicine* under the heading, "Abolishing mammography screening programs?"[349] and an article in *Der Spiegel* asserted that leading German politicians believed that their newly started programme should be reconsidered.[350]

We noted that the US National Cancer Institute wrote in their review of breast cancer screening that "based on robust evidence" overdiagnosis exposes healthy women to "the immediate risk of treatment (surgical deformity or toxic effects of radiotherapy, hormone therapy or chemotherapy), late sequelae (lymphoedema), as well as sequelae of radiotherapy (cancer, scarring, or toxic effects on the heart).”[351] They also estimated that around half of the cancer cases found by screening are overdiagnosed.

However, the Danish dishonesty continued unabated. Henrik Støvring and Mette Lise Lousdal from the Department of Public Health, Aarhus University, commented in a newspaper article on a study they had published the same day in the *European Journal of Public Health*,[352] but their comment did not reflect their results.[353] There had been no benefit found from breast screening in Norway, yet they wrote that there had been a 30% reduction in the occurrence of the most advanced cases of breast cancer in the screened age group. That looked really good, but they omitted to mention that they found the same reduction in advanced cases in the 20-49 age group that had not been invited to screening. The decline in numbers of the most advanced cases was 33% among those who were invited to screening, but it was 38% for those who were not invited.

The expected reductions in breast cancer mortality never occurred

In Sweden, the expert on mammography at the Board of Health, Ingvar Andersson, the primary investigator for the Malmö trial, expressed disappointment in 1999 that, 14 years after screening started, it was still not possible to see any notable change in breast cancer mortality.[354] He felt it was necessary to wait another couple of years. Eleven years on, there was still no beneficial effect of screening in Sweden,[355] but this did not lead to official reactions or doubts.

In France, the mammography screening programme was reassessed in 2016, not only by specialists but also by a citizen group.[356] The steering committee noted an unexpected intense scientific controversy, centred on uncertainty about the benefit, and concerns about overdiagnosis and overtreatment. The national programme had not acknowledged this controversy, despite the extensive discussion in the scientific literature. The citizens concluded that they did not wish to keep the programme as it was, and in 2017, the Ministry of Health released a plan with broad ranging reforms.

In the Netherlands, there were also difficulties in showing any benefits of screening. In 1999, Harry de Koning and colleagues, using modelling, predicted that screening would reduce breast cancer mortality by 18% ten years after screening started.[357] Jan Hendriks, who developed the screening programme, remarked a year later that if the mortality from breast cancer had not been dramatically reduced by 2003, the nationwide screening programme should be stopped.[358]In 2003, when there was still no effect of screening,[359] de Koning conveniently added another five years.

We are still waiting for Godot. It calls to mind the religious fanatics who predict the world will be destroyed at a certain date, and when it doesn't, they come up with a new date.

In the United States, the American Cancer Society (ACS) is the primary promoter of breast cancer screening, and it benefits from a hard sell.[360] In 1996, the ACS set goals for cancer screening,[361] which remained the same in its 2009 Strategic Plan Progress Report.[362] Their aim was to reduce breast cancer mortality by 50%. In Norway, people from the Cancer Registry likewise predicted that screening would reduce breast cancer mortality by 50%.[363]

Pretty optimistic forecasts, given that screening hasn't reduced the occurrence of advanced cancers in either country.

In 1999, the ACS announced that early detection results in a cure "nearly one hundred percent of the time."[364] Upon being questioned about this figure by a reporter, a communications director replied, "When you make an advertisement, you just say what you can to get women in the door … You exaggerate a point," to which the reporter noted that on the other side of that door is a mammogram machine that generates an income. The ACS receives huge donations from the mammography industry.

The aggressiveness with which the ACS has marketed breast screening to US women is illustrated by this disrespectful advertisement that appeared in a cancer journal in 2000:[365]

Mammography screening is a lucrative business. When screening started in the UK, the National Health Service had never invested more in implementing a new type of clinical practice.[366] A recent analysis showed that in the USA, the total national cost of screening women in their 40s was $2 billion per year.[367]

The ACS issued new screening guidelines in 2015 and *Nature Reviews Clinical Oncology* asked us to comment on them.[368] We noted that the Society gave a false impression of consensus, not only between systematic reviews, but also between systematic reviews and observational studies, and of a certainty that didn't exist.

We pointed out that Norway and Denmark are the only countries in the world in which investigations of screening programmes have included a contemporary, same-age control group. The result? There had been no visible effect of screening.[369] [370]

A linked commentary celebrated the "progress towards consensus." But consensus is not a scientific discipline, it is politics. When the so-called consensus is not based on the most reliable evidence, it is not progress.

Australians were also deceived. Liz Wylie, medical director of BreastScreen WA, argued that "In Australia our mortality rates are falling even though the incidence of breast cancer is rising and that's because of early detection."[371]

Australian researchers wrote in their abstract that the incidence of large breast cancers (3 cm or larger) fell by 20% in those 50–69 years of age.[372] However, the accepted convention for staging tumours doesn't use 3 cm as cutoff, but 2 cm. Their own data showed that cancers size 2 cm or larger actually *increased*.

In Germany, the government passed a bill in 2006 penalising cancer patients financially if they failed to undergo regular cancer screening.[373] This law is so disrespectful of citizens who have made a rational decision not to be screened that jaws dropped in disbelief all over the world.

In 2010, I spoke at a pro and con session on mammography screening at a German cancer congress in Berlin with 10,000 participants. On my arrival, the chairman said that it had been difficult to persuade the organisers to invite me. People had been afraid that I would somehow leave the upcoming German screening programme in ruins. I was amused by this, as was the chairman, who said I didn't look dangerous to him.

I rarely went to conferences, and this one confirmed that I should continue to decline invitations. The level of the debate was so low that it was surreal.

The pro speaker was Karin Bock, responsible for the breast screening programme in south-west Germany. She made three errors in her talk that are typical of screening advocates:

She claimed that screening leads to less extensive surgery, as it finds tumours that are smaller than without screening.

She showed data indicating that *relatively* more cancers are found in early stages than without screening.

She noted that screening saves one life for every 200 women who are screened for 20 years. As I shall explain in Chapter 10, this is impossible.

After the meeting, someone handed me a mammography screening leaflet from the Ministry of Health[374] and said it was evidence-based. It said that screening leads to less surgery and that most experts agreed that for every death prevented, one woman was overdiagnosed. This is incorrect by a factor of 10.

The information offered to German women today, in 2024, is just as misleading as the information Kock gave at the meeting, namely that screening spares between 2 and 6 breast cancer deaths for every 1000 women screened for 20 years.[375]

The German leaflet from 2010 had only four references, and their choice demonstrated that it was not evidence-based: An unpublished German report about how it went when

screening was introduced in a selected part of the country; a paper in German that the authors called a "selective literature review;" an editorial in the *BMJ*; and an observational study from the Netherlands[376] published in a journal I had never heard of, *Seminars in Breast Diseases*. It was on the market for only ten years, and as Harry de Koning was one of the authors, I felt no need to read the study.

Following my presentation, a clinician said that screening didn't lead to more mastectomies because he didn't see them any longer. This is like saying there are no tigers in India because I didn't see any when I was there.

When I said the perceptions women had of screening were seriously distorted because of the pro-screening propaganda, I was told that *I made* propaganda because I talked about others making propaganda.

A clinician asked me if I wasn't happy that I had airbags in my car, as if this was the ultimate proof of the value of breast screening.

A rather vocal person argued repeatedly that overdiagnosis was only a hypothesis. It didn't impress him that I had just explained it is mathematically impossible to avoid overdiagnosis and that it had been empirically demonstrated, both in trials and in national screening programmes.

After all these years – with all our publications on screening and those of others that had explained the issues time and again – it escapes me how such well-educated people who work with cancer can be so oblivious to the evidence.

With all this systematic misinformation, it is not surprising that women's perceptions of the benefits and harms of mammography screening are so distorted.

A study of American and European women[377] found that 68% believed screening reduced their risk of getting breast cancer (which it doesn't, it just detects cancer), 62% believed that screening at least halved mortality (screening has no effect on mortality), and 75% believed that 10 years of screening saved 10 of 1000 participants (this is larger than the most optimistic estimate by a factor of 10, and it is 20 times the Cochrane estimate).

Other studies have shown that only 8% of women were aware that participation can harm healthy women and that 94% doubted there is such a thing as non-progressive breast cancer.[378] One-third thought screening detects more than 95% of breast cancers[379] (screening only detects between half and two-thirds of the cancers, and some of the most dangerous ones, the interval cancers, are detected between two screening rounds).

An earlier study from 1995 of American women aged 40 to 50 years found even bigger misconceptions.[380] The women overestimated by a factor of 20 their probability of dying from breast cancer within 10 years, and they overestimated the absolute risk reduction obtained with screening 100-fold.

In 2023, the US Preventive Services Task Force changed its recommendation for the starting age for mammography screening from 50 to 40 years. But there were grave problems. The Task Force had used complex statistical modelling, which is very sensitive to modelling assumptions, and they had used a 25% effect of screening on breast cancer mortality. As the authors of a critical comment in the *New England Journal of Medicine* noted,[381] the Cochrane review found a non-significant reduction in breast cancer mortality of only 13% for those aged 40-49 in the three trials that had a low risk of bias.

The women had been fooled again.

9 Screening advocates circle the wagons in *The Lancet*

The establishment reacted when the truth about screening had become impossible to ignore. They published a series of false statements to protect their interests.

In November 2011, a remarkable letter was published in *The Lancet*.[382] It has 41 authors, in alphabetical order, including Julietta Patnick, László Tabár and Peter Dean. Patnick was the corresponding author:

Although the wider scientific community has long embraced the benefits of population-based breast screening, there seems to be an active anti-screening campaign orchestrated in part by members of the Nordic Cochrane Centre. These contrary views are based on erroneous interpretation of data from cancer registries and peer-reviewed articles. Their specific aim seems to be to support a pre-existing opposition to all forms of screening (1).

These individuals, making claims of poor methods, selectively discount overwhelming scientific evidence from numerous randomised trials in different countries that organised screening reduces breast cancer mortality. They claim that the significant decrease in breast cancer mortality achieved by screening is due to improvements in treatment alone, discounting the benefits of early detection. If true, this would imply that breast cancer is an exception among adenocarcinomas in that early detection does not improve prognosis—a claim contrary to the evidence.

For women with breast cancer, early detection also results in improved quality of life from less extensive surgical treatment. Women with screen-detected breast cancer in the UK have half the mastectomy rate of women with symptomatic cancers - ie, 27% versus 53% (2).

Organised, high-quality breast screening is an important public health initiative by numerous governments worldwide. These policies are based on robust and extensive analysis of individualised patient data from scientific trials, with particular attention paid to the balance of potential benefits and harms (3). To imply that such an international action is mass misrepresentation, or that screening is done for the benefit of self-interested professionals, is as perverse as it is unjustified.

Comprehensive guidelines deal with the entire screening process (4). Organisations responsible for screening programmes regularly review published evidence on the effects of mammographic screening, and also contradictory interpretations.

We consider the interpretation by Jørgensen, Keen, and Gøtzsche (5) of the balance of benefits and harms to be scientifically unsound. Women would be better served by focusing efforts on how best, and not whether, to provide breast screening.

The signatories below, charged with provision and implementation of breast screening in many different countries, remain convinced that the scientific foundation for population-based, quality-assured, organised breast screening is one of the major accomplishments of the translation of clinical cancer research into public health practice. Early detection, in combination with appropriate treatment, significantly lowers breast cancer mortality and improves the life quality of patients with the disease.

This online publication has been corrected. The corrected version first appeared at thelancet.com on February 15, 2013.

The correction was about the authors' many conflicts of interest,[383] none of which were disclosed in the printed version of *Lancet*. It was not until February 2013, fifteen months after the original publication, that a new "appendix" detailing Bock and colleagues' numerous and significant conflicts of interest was added as an erratum.[384]

It is amazing that *Lancet* published this confession of faith by people who must have been worried that mammography screening, their livelihood, might be closed down.

Among the inaccuracies in this letter, Patnick et al. stated, with no reference, that screening results in improved quality of life. Under any reasonable assumptions about the magnitude of the benefits and harms, screening lessens the quality of life.[385]

An accompanying editorial showed that *Lancet's* editor, Richard Horton, who was so supportive when we challenged screening in *Lancet* in 2000 and 2001, had changed sides:[386]

"While potential advances in breast cancer prognostics and diagnostics are being investigated, an old controversy continues. A letter in today's issue defends the health benefits of population-based mammographic screening, which has come under recent attack by what the authors call an 'anti-screening campaign.'

Prospective randomised trials have shown that mammographic screening reduces breast cancer mortality. Breast screening programmes have been widely accepted as a proven, effective, population-based intervention. Yet an increasing number of researchers continue to raise concerns about overdiagnosis and the relative benefit versus harm.

This controversy has led England to set up an inquiry into the evidence supporting breast cancer screening. The results of this review, expected in early 2012, will be important, and not only for the UK. They must resolve distractions from the growing challenge of providing effective diagnosis and treatment for women with breast cancer."

Horton left no doubt that he believed screening worked and that the debate should now stop. His assertion that randomised trials "have shown that mammographic screening reduces breast cancer mortality" is misleading, and the massive harms screening causes are dismissed as "concerns about overdiagnosis and the relative benefit versus harm."

Letters to the editor were published five months later and they were interesting. Hazel Thornton wrote:[387]

"I was astonished to see the declaration at the foot of the letter from Karin Bock and colleagues (1) stating that the signatories have no conflicts of interest. How can this be the case for health professionals such as Julietta Patnick, for example? She, like others, is paid for running, recruiting, and promoting a public health screening programme. The UK programme requires an uptake of 70% to make it viable: incentive enough, I imagine, to persuade, coerce, and sell to potential participants.

This necessity to make the programme work has resulted in promotional activities. Citizens are invited to attend by means of persuasive literature (2), inadequate to enable informed consent, as is required by the UK General Medical Council (3). Robust public challenges to the unethical nature of this have been made (4), as have promises (not kept) to rectify. The programme's annual reviews further advertise the programme."

Susan Bewley wrote:[388]

"Merely lining up beside 'the wider scientific community' to claim that 'there seems to be an active anti-screening campaign orchestrated in part by members of the Nordic Cochrane Centre,' before stating that they 'remain convinced' that women's lives and health are saved, is an inadequate response to the concerns about lack of efficacy and harm that arise from the scientific evidence. The only orchestration of opinion seems to be from Julietta Patnick, the Director of NHS Cancer Screening Programmes."

Michael Baum wrote:[389]

"I was very cross to learn that the Nordic Cochrane Centre has been credited with orchestrating a campaign against breast cancer screening (1). I claim the distinction of first to recognise the false

promises of the UK's Breast Screening Programme. I was the first to note that women were not being offered true informed choice when summoned to attend for fear of missing the 70% uptake target (2).

The Nordic Cochrane Centre was a 'Johnny come lately' in my ensemble, although they provided compelling evidence in support of my concerns (3). Just when I thought the bandwagon had moved on, another group jumped aboard. In November, 2011, new guidelines on breast cancer screening were released by the Canadian Task Force on Preventive Health Care (4), which mentioned en passant that the overall risk of mastectomy is significantly increased in recipients of screening.

Although I would like to claim full credit for the orchestration of the screening sceptic's concerto, I have to confess that Maureen Roberts got there first. She was the director of the breast-screening unit in Edinburgh, UK, and died of breast cancer. Her last published paper was entitled 'Breast screening: time for a rethink?' (5). That was more than 20 years ago and still we are demanding one."

Jørgensen and I wrote:[390]

"The 41 authors of the Correspondence on the effect of population-based screening on breast cancer mortality (Nov 19, p 1775)(1) defend screening by reference to majority and authority. They look only for the benefits of screening and not its harms, and the only scientific claim - that women with screen-detected breast cancer have half the mastectomy rate of women with symptomatic cancers - is seriously misleading. Obviously, cancers detected between rounds are more aggressive than screen-detected ones. Breast screening increases the number of mastectomies and tumorectomies because of overdiagnosis (2,3). The independent authors of the new Canadian guidelines for breast screening acknowledge this (3).

Women must receive honest and balanced information about screening, and we refer to our leaflet, which volunteers have translated into 11 languages. If there is any effect of screening today, it must be marginal. Our Cochrane review of all the randomised trials shows this (4). Recent rigorous observational studies that we have summarised also show this (2). And a systematic review including data from several countries shows that screening has not decreased the incidence of advanced cancers (2); it therefore cannot work.

It is a medical triumph that women attend doctors much earlier when they notice something unusual, that centralisation of diagnosis and treatment has occurred, and that treatments are far better today than when the trials were done. However, what is most important now in fighting breast cancer is to reduce its occurrence. Since the overdiagnosis rate is about 50% (5), stopping the mammography screening programme would reduce the breast cancer incidence in the screened age group by a third ([150–100]/150)."

In contrast to the critical letters, the authors' reply is not indexed on PubMed. Three of the authors replied, with Patnick being the first author:[391]

"There is little new in these responses that the authors have not stated on numerous previous occasions.

We fail to understand how much clearer the interests of the 41 cosignatories could have been made than the text 'charged with provision and implementation of breast screening' in the body of the letter.

However one interprets them, the facts in the UK are that the mastectomy rate for women with screen-detected breast cancer is about half that of women whose breast cancer presents symptomatically. An attempt to explain this by quoting an over-diagnosis rate of 40–60% is convenient, but unrealistic and contrasts strikingly with a more balanced review finding of less than 10% (1). The Canadian review (2) indeed refers to a raised mastectomy rate from screening, but the sole reference quoted is that of Peter Gøtzsche. We regard the proposal to reduce the apparent incidence of breast cancer by failure of detection as unethical.

Demands are made for a rethink on breast screening. Previous rethinks in the form of the Canadian review and the earlier reviews by the US Preventive Services Task Force (3) and the International Agency for Research in Cancer (4) all found in favour of continuing to support breast screening.

A separate review (5) in the UK has now been announced and we should all await its findings without recourse to pre-emptive comments as to its membership.

We are all charged with provision and implementation of breast screening services."

Here is my take on this. The 41 authors' first reference is to my 1997 letter in *Lancet* about faecal-occult-blood screening for colorectal cancer.[392] They refer to this when they write that my "specific aim seems to be to support a pre-existing opposition to all forms of screening."

Other mammography screening advocates have also quoted this letter to demonstrate that I was against mammography screening to begin with.[393 394]

As explained in Chapter 2, I had no preconceived ideas about mammography screening and knew nothing about it when I was asked by the Danish Board of Health to review the randomised trials in 1999. This was in fact a perfect starting point for an unbiased assessment. Moreover, I have never been against "all forms of screening." I look at the evidence and if it tells me screening works and does not cause too much harm, e.g. screening for cervical cancer or postnatal screening for phenylketonuria, then I am in favour of it.

The letter I published in 1997 is this one:

Hardcastle (Nov 30, p 1472) (1) and Kronborg (Nov 30, p 1467) (2) and their colleagues report a beneficial effect of faecal-occult-blood screening for colorectal cancer which is the second commonest cause of death from malignant diseases in England and Wales (2). If the two studies are combined in a meta-analysis, the risk difference for prevention of death due to colorectal cancer is 0.001 (95% CI 0.002 to 0.000). Thus, for every 1000 patients screened, one death from colorectal cancer would be prevented (95% CI two deaths to no benefit). It is also interesting to look at the total number of deaths. The risk difference for the two studies is 0.0005 (95% CI 0.003 to 0.004). This means that with screening one would expect to kill one person for every 2000 persons screened (95% CI three persons saved to four persons killed per 1000 persons). The total number of deaths (by simply adding the numbers from the two studies) were 18 852 in the screening groups versus 18 818 in the control. It therefore seems that these patients die from something else if they do not die from colorectal cancer. This calls into question Lieberman and Sleisenger's (3) accompanying commentary in which they suggest that the cost per added year of life is US$10,000–20,000 and that the cost for each prevented death is $200,000.

The studies also raise a pertinent ethical issue: do we wish to turn the world's healthy citizens into fearful patients-to-be who, in the not too distant future, might be asked to deliver, for example, annual samples of faeces, urine, sputum, vaginal smear, and blood, and undergo X-ray and ultrasound examination with all it entails in terms of psychological morbidity and the potential for harm because of further testing and interventions due to false positive findings? If we compare with the considerable risks the citizens expose themselves to because of smoking and other unhealthy lifestyles, I believe that the answer should be no. Since the risks of false positives increase with the number of screening programmes introduced, it would be interesting and highly relevant to see a large, long-term randomised trial in which the experimental group is screened for a number of diseases and the control group for none.

There are two important messages in my letter. One is that total mortality is hugely important for cancer screening trials; in fact, it is the most important outcome because it is the only unbiased mortality outcome. I demonstrated (this was in 1997) that faecal-occult-blood screening for colorectal cancer didn't work because it killed as many patients as it saved.

The second important message is that, since there are many possibilities of screening for cancer, we should perform "a large, long-term randomised trial in which the experimental group is screened for a number of diseases and the control group for none." I warn against the uncritical adoption of screening for many different cancers because we do not know what the overall benefits and harms are.

Patnick et al.'s reply in *Lancet* is shocking in all its nudity. It repeats the original letter's claim that "the mastectomy rate for women with screen-detected breast cancer is about half that of women whose breast cancer presents symptomatically" and adds: "An attempt to explain this by quoting an over-diagnosis rate of 40–60% is convenient, but unrealistic and contrasts strikingly with a more balanced review finding of less than 10% (1)."

The Emperor's New Clothes

Patnick's misleading comparison has nothing to do with the level of overdiagnosis. Since overdiagnosis is unavoidable, this comparison will always be misleading. We noted in our letter that screening increases the total number of mastectomies.

Patnick also invented a strawman argument: "To imply that … screening is done for the benefit of self-interested professionals, is as perverse as it is unjustified." We have not expressed such an opinion, neither have others to my knowledge. But when a group of professionals band together to publicly dismiss concerns about screening, and are later compelled to disclose several pages of financial and professional conflicts of interest that would predispose them favourably towards screening, it does weaken the credibility of their argument.

Our 2011 paper in *Radiology* was not welcomed by screening advocates

Patnick's comments that my "contrary views are based on erroneous interpretation of data from cancer registries and peer-reviewed articles" and that "We consider the interpretation by Jørgensen, Keen, and Gøtzsche (5) of the balance of benefits and harms to be scientifically unsound," were not supported by any explanation about what we had done wrong or why our article (her reference 5), should be considered scientifically unsound.[395] It

came out two months before the *Lancet* letter in *Radiology*, which is owned and published by the Radiological Society of North America. Patnick et al. likely felt it was threatening for their interests.

In our *Radiology* paper, we asked if screening can be justified and documented in detail, with 55 references, that it leads to substantial overdiagnosis, an increase in mastectomies, and has a doubtful effect on mortality. I repeated many of the same issues four years later in *Journal of the Royal Society of Medicine* when I argued why screening should be stopped (there is free access to the article).[396]

In *Radiology*, we explained what was wrong with some very influential studies. As there were no letters to the editor afterwards, we might have shocked the radiological community to such a degree that they preferred to keep quiet, hoping our paper would be forgotten, rather than drawing attention to it in letters. Since our paper is important, I shall provide some extracts from it, with additional comments.

As already noted (see page 57), Kalager et al. published a paper in *New England Journal of Medicine* in 2010 with results from the Norwegian screening programme.[397] There was a 10% reduction in breast cancer mortality that was not statistically significant (p = 0.13) and they estimated that if there was any effect of screening, it would only be a 3% reduction.

Stephen Duffy and Robert Smith criticised Kalager's study saying the average follow-up of 2.2 years was too short, but this was the follow-up after diagnosis. The follow-up from the start of screening was 6.6 years,[398] which is when an effect was seen in the trials.

In 2013, Lynge and colleagues also published results from the Norwegian screening programme and found a similar result, a nonsignificant 11% reduction in breast cancer mortality. However, they published their findings in a specialty journal,[399] and their interpretation of them was entirely different.[400]

Lynge et al. wrote that prior mammography use in Norwegian women diluted the ''true'' effect of screening, which they claimed was a 25% reduction in breast cancer mortality, and said that their result ''corresponded very well'' with expectations. Interestingly, this ''true'' effect of 25% was the same as their previous estimate of a 25% effect in Copenhagen based on an observational study.[401] Lynge has amazing predictive powers. In a previous paper, from 2011, on mammography use in Norway, she *predicted* a 25% effect of screening in that country.[402]

Lynge noted that screening had not led to a reduction in advanced breast cancers in Norway but did not draw the logical conclusion that screening therefore cannot have reduced breast cancer mortality. She invented a 25% effect instead.

A 2005 study from the *New England Journal of Medicine* reported a 15% effect of screening on breast cancer mortality in USA over a 25-year time period,[403] but the authors overestimated the effect of screening substantially. They adjusted their statistical models for an increase in breast cancer incidence, but as this was caused partly by screening, it should not have been adjusted for.

After we published our 2010 study showing that screening had not decreased breast cancer mortality in Denmark,[404] Dean and Tabár asked: "Why does vehement opposition to screening come from Denmark, which has one of Europe's highest breast cancer mortality rates?"[405]

We explained in *Radiology*[406] that the difference between Sweden and Denmark had existed for decades before screening was introduced and that, in the screening period (1989–2006), in women aged 50–69 years, the reduction was 26% in Denmark versus 16% in

Sweden, although only 20% of Danish women were invited to screening versus all in Sweden (where more than 80% participated).

Despite the fact that Sweden has the longest running programme, the widest age range, and the shortest screening interval in Europe,[407] the reduction in breast cancer mortality is lower than the European median.[408]

We finished our *Radiology* paper by saying that if we wish to reduce the incidence of breast cancer, there is nothing so effective as to avoid screening mammograms. By avoiding the effect of overdiagnosis, this strategy reduces the risk of becoming a breast cancer patient by one third.[409]

We also noted that time had come to reassess whether universal mammographic screening should be recommended for any age group.

10 Extreme exaggerations

> *When you show that people are wrong, you embitter them, and their exaggerations might become extreme, beyond reason.*

As we have seen in abundance, people supporting screening tend to exaggerate its benefits and downplay its harms. We would therefore expect the benefit to harm ratio to be particularly misleading.

When you challenge misinformation about screening with solid science, you come in great trouble. Quite often, the misinformation then becomes even worse. Philosopher Arthur Schopenhauer mentions in his book, "The art of always being right,"[410] that being contradicted provokes people into exaggerating their statements beyond their proper limits.

The more evidence you present showing the faithful are wrong, the more bizarre and extreme their responses become, and the more bitterly will they defend them,[411] particularly when they have maintained their unsustainable beliefs for some time.

The UK debate became more embittered after we published our review of the contents of invitations for screening in *BMJ* in 2006.[412] This paper must have hit the self-esteem of the screening advocates particularly hard. Three years later, in 2009, the level of the debate sunk further after we published our criticism of the UK leaflet, also in *BMJ*.[413] There were many rapid responses on *BMJ's* website, and the exaggerations were monstrous.

Two epidemiologists, Nicholas Wald and Malcolm Law, claimed that over 20 years of screening, 12 women per 2000 would avoid dying from breast cancer.[414] We calculated that, if based on the randomised trials, their estimate meant that screening reduces breast cancer mortality by 90%.[415] They derived their estimate in a curious way that involved erroneous use of observational data and impermissible extrapolations.[416]

After Wald and Law's astonishing approach to science, Stephen Duffy joined the debate.[417] We wrote a lengthy reply, explaining all the serious errors he had made.[418] Since he disagreed substantially with our estimates of the benefits and the harms, we described which data sources and methods he had used compared to ours (see table).

Disagreement	Duffy's approach	Our approach	Advantage of our approach
Research design	Unsystematic reviews of randomised trials and observational studies	Systematic reviews of randomised trials and observational studies	Reliable, and therefore the recommended method
Statistical methods	Involves models and assumptions	Does not involve models and assumptions	Transparent easy to understand, and data massage is not possible
Statistical methods	Extrapolation far beyond what the data support	No undue extrapolations	Reliable, and therefore the recommended method
Statistical methods	Subgroup analyses of attenders	No subgroup analyses	Reliable, and therefore the recommended method

As always, it required detective work to find out what Duffy had done. He claimed that the estimate by Wald and Law was consistent with the randomised trial evidence but did not

explain how he arrived at this impossible conclusion. He just quoted a paper by himself, Tabár, Smith and others.

I looked it up and, as usual for this triumvirate, it was obfuscated. It referred to the number of breast cancer deaths in the Two-County trial but didn't state which publication they came from. Given the many papers on this trial and the varying numbers reported, it would be difficult and very labour intensive for most people to find the missing reference, but I found it by browsing all Tabár's articles in my archive.

I wasn't the least surprised to discover that the missing reference reported a 24% reduction in breast cancer mortality in Östergötland whereas researchers using the Swedish cause-of-death register only found a 10% reduction (see Chapter 4).

Whatever the true effect is in the Two-County trial, Duffy's claim that the estimate by Wald and Law was consistent with the randomised trial evidence was totally false.

Duffy wrote that our reply to Wald and Law contained "a number of inaccuracies" but the only other reference he cited in support of this was to an unsystematic review by the triumvirate. Their paper stated that in the Two-County trial, "Cause of death was determined on blind review," which is false in relation to the purported 24% reduction in Östergötland.

Duffy's claim that our estimate of a 15% reduction in breast cancer mortality had "no basis in empirical data" was also incorrect. We derived it from the randomised trials and published it in our Cochrane review.[419] We reported in this review that,

"Two trials with adequate randomisation did not show a significant reduction in breast cancer mortality, relative risk (RR) 0.93 (95% confidence interval 0.80 to 1.09) at 13 years; four trials with suboptimal randomisation showed a significant reduction in breast cancer mortality, RR 0.75 (0.67 to 0.83) (P = 0.02 for difference between the two estimates). RR for all six trials combined was 0.80 (0.73 to 0.88)."

We were forced by the Cochrane Breast Cancer Group to provide an estimate for all the trials combined (see Chapter 3), even though this was scientifically inappropriate and goes against clear recommendations in the Cochrane Handbook for Systematic Reviews.[420] Cochrane uses the GRADE system for assessing the reliability of randomised trials, and the GRADE handbook recommends that,[421] "If study methods provide a compelling explanation for differences in results between studies, then authors should consider focusing on effect estimates from studies with a lower risk of bias." This was the case in our Cochrane review where we split the trials according to whether they had been adequately randomised. Trials that are not adequately randomised should be viewed as a type of refined observational studies, which make the reported beneficial effects doubtful.

The most reliable estimate of the effect of screening was therefore a 7% reduction in breast cancer mortality, which was not statistically significant. It was uncertain if screening had any effect on breast cancer mortality, but it was clear that screening didn't lower mortality. We wrote in the Cochrane abstract:

"The two trials with adequate randomisation did not find an effect of screening on cancer mortality, including breast cancer, RR 1.02 (0.95 to 1.10) after 10 years, or on all-cause mortality, RR 1.00 (0.96 to 1.04) after 13 years. We found that breast cancer mortality was an unreliable outcome that was biased in favour of screening, mainly because of differential misclassification of cause of death."

Differential misclassification of cause of death was exactly what happened when the investigators in the Two-County trial were not blinded when they assessed the cause of death.

It was because of Cochrane's inappropriate censorship that we ended our abstract this way, which was a forced conclusion:

"Screening likely reduces breast cancer mortality. Based on all trials, the reduction is 20%, but as the effect is lower in the highest quality trials, a more reasonable estimate is a 15% relative risk reduction."

Duffy stated that the calculation by Wald and Law was "reasonable and simple" and "involves fewer assumptions" than ours. This was obviously false.

Duffy wrote that our assertion that Wald and Law's estimate entails a 90% reduction in breast cancer mortality with screening was clearly wildly inaccurate and was "presumably based on flawed logic."

In response to this, I explained how I had derived the 90% estimate:[422] [423]

"The first meta-analysis of the Swedish trials describes that after 9 years there were 2.6 and 3.3 deaths, respectively, per 1000 women, in the invited and control groups, and after 12 years, the numbers were 3.9 and 5.1 (13). Thus 2 breast cancer deaths per 2000 women were avoided after 10 years of screening, and not 6 as Duffy claims. There were 425 breast cancer deaths in the control groups of 125,866 women after a mean of 9 years of follow-up (13). If the effect of screening were a 90% reduction in breast cancer mortality, there would be 43 breast cancer deaths in a control group of the same size. The risk difference then becomes [425/125,866 – 43/125,866] 0.00338-0.00034 = 0.00304 , which gives a number needed to invite to screening of 328 [1/0.00304] to avoid one breast cancer death. This is very close to the 333 that Wald and Law reported (6 deaths avoided per 2000 in 10 years gives 333). Thus, if we were to try to generate the numbers provided by Wald and Law, but now based on the randomised trials, we would have to postulate that the effect were a 90% reduction in breast cancer mortality."

Duffy also accused us of a "highly selective interpretation of the published results on overdiagnosis," but it is not selective to perform a systematic review of the reliable studies,[424] disregarding Duffy's flawed studies on overdiagnosis. This, we call good science.

In our Cochrane review, we used the same simple algebra as for mortality when we reported that 30% overdiagnosis means that 10 women per 2000 are overdiagnosed.

Since randomised trials provide the most reliable evidence, I have no doubt that the reason why screening advocates use observational data and complicated statistical models when they study overdiagnosis is that they want to produce misleading results in favour of screening. Duffy doesn't even follow his own advice about models: "When there is disagreement between direct results from empirical data and modelled estimates derived by combining information from disparate sources, it would be wise to trust the former."[425]

We published our rebuttal of the claims made by Wald, Law and Duffy on 1 May 2009 on *BMJ's* website. Two months later,[426] *BMJ's* editor Fiona Godlee noted that general practitioner Iona Heath (President of the Royal College of General Practitioners 2009 to 2012), had turned down mammography screening because she thought the evidence was pretty clear that the potential harms of overdiagnosis outweighed the potential benefits.[427]

Heath worried, though, that her decision was based on information that her patients cannot easily find because the invitation leaflet doesn't mention harms. Godlee agreed that women should be made aware of the harm caused by overdiagnosis so they can make a more informed decision.

Godlee said that, in private emails, advocates of the NHS Breast Screening Programme had criticised the *BMJ* editors for not adequately presenting the facts in support of screen-

ing. She mentioned that *BMJ* would welcome a balanced article on this subject and that nearly two months on, after we had replied in extensive detail to the criticism Wald, Law and Duffy had raised that we had substantially underestimated the survival benefit of screening, we had not been challenged again.

20- and 25-fold exaggerations of the benefit to harm ratio

A month later, Wald, Law and Duffy joined forces and published a letter in *BMJ*, "Breast screening saves lives,"[428] where there was absolutely nothing about overdiagnosis, even though this was what Godlee had called for.

The exaggeration was now extreme. Wald, Law and Duffy wrote that over 20 years of screening, one woman per 100 screened will avoid dying from breast cancer. This is 20 times more optimistic than the estimate for 10 years of screening based on comprehensive systematic reviews of the trials, both by us[429] and the US Preventive Services Taskforce.[430]

If we assume the effect of screening is the same in the last 10 years as in the first 10 years of screening, it means that Wald and Law inflated their original estimate by 67%.

If Wald, Law and Duffy had been right about this huge effect, it would have been easy to see an effect of breast screening in UK mortality statistics in the relevant age groups, but as already noted, there was none (see page 72 and below).

Some doctors and scientists saw through Duffy's smoke and mirrors. One noted that "intelligent, unbiased analysis of the numerous existing studies ought to lead one to conclude that breast screening is of little or no value in reducing breast cancer mortality,"[431] and another asked: "Would we accept such extremely rosy extrapolations and assumptions from the pharmaceutical industry?"[432]

The criticisms did not perturb Wald, Law and Duffy who continued with their colossal exaggerations.[433] We calculated that their new, inflated estimate means that 2850 women would avoid dying from breast cancer every year in the UK.[434] This is twice as many as the 1400 lives the NHS Breast Screening Programme claimed were saved each year, which is already much too optimistic, apart from the fact that screening doesn't save lives.

There were other errors in their numbers,[435] and one of their statements was startling:

"The decline in breast cancer mortality over time has occurred despite a concurrent increase in incidence; it would have been greater had incidence remained the same."

This remark showed that Wald, Law and Duffy still denied that screening leads to overdiagnosis. Furthermore, they used a "generally accepted" 24% reduction in mortality from breast cancer and inflated this estimate, assuming it would have been 31% if all invited women had attended. This is like saying that if only everybody with meningitis had been treated earlier, more would have been saved, or if more people had stayed at home, fewer would have been killed in car crashes. Life is not like that, and the authors also ignored that attendees are healthier than non-attendees (self-selection bias).

Duffy consistently calls my calculations inaccurate, completely inaccurate, or even wildly inaccurate, which is empty rhetoric, as he has never demonstrated any errors in my research.

I thought it was a prerequisite for being a statistician that you can handle numbers and statistical methods, but this is not necessarily so. Duffy makes errors in numbers or methods, or both, in virtually every single article and letter he publishes about mammography screening. As an example, he used a wrong estimate (37% instead of 68% for the proportion of screening-detected cancers) when he arrived at a false statement about our

research.[436] His claim that only 37% of breast cancers are screen-detected was based on a 200-word conference abstract, but in the UK, 68% of cancers were screen-detected in 2006.[437]

And yet, Duffy is a professor of statistics.[438]

A year later, in 2010, came another extreme exaggeration, this time published by the triumvirate Duffy, Tabár and Smith, and others.[439] They estimated that up to 2.5 lives are saved for every overdiagnosed case, which is wrong by a factor of 25.[440]

The methods they used to arrive at their estimate were inappropriate. They cherry-picked the Two-County trial and used a 38% reduction in breast cancer mortality. This trial recruited women 40 years of age and over, but Duffy et al. only included the age group 50-69. I have tabulated all the numbers from the trial and have four sets of numbers of women for this age group, of which one set[441] is the same as Duffy et al. showed in a table:

	Invited	Not invited
Duffy et al.	46897	33074
Other data	47212	33268
Other data	46897	33074
Other data	47580	33642
Other data	47265	33448

As the other three sets of numbers are larger, Duffy et al. did not include all randomised women in their analysis, which is concerning.

They also used data from the UK Breast Screening Programme but misrepresented them. They considered the mortality stable in the unscreened age groups, but contradicted themselves, as they reported a significant 18% decline in breast cancer mortality in women below 50 years of age. The decline in the age group 50–69 years was 27%, but by some obscure method described in a footnote to a table, they nevertheless concluded that screening had reduced breast cancer mortality by 28% compared with other age groups.

This is pure hocus pocus, as I shall explain.

Duffy's lack of transparency in his research methods is startling, and the current result disagrees with official data. Cancer Research UK writes:

"Between 1989 and 2008 the breast cancer mortality rate fell by 44% in women aged 40–49 years; by 44% in women aged 50–64; by 37% in women aged 65–69; by 39% in women aged 15–39; and by 19% in women over 70."[442]

Thus, there is no sign of a screening effect, as women aged 40–49 years who were not invited to screening had the same decline in mortality as those aged 50–64 years.

In a figure, Duffy et al. lumped data for women under 50 years of age. As deaths from breast cancer before age 30 are very rare, and as there are many women and girls in this age group, the graph of incidence rates is close to the x-axis, which conceals the inconvenient truth that there was a huge decline in mortality in women aged 40–49 years.

Duffy et al. combined data from the age group 50–64 years with the age group 65–69 years, although screening of the latter group didn't start before 2001. This conceals another inconvenient truth: breast cancer mortality in the age group 50–64 years began to decline *before* the UK programme started in 1988.

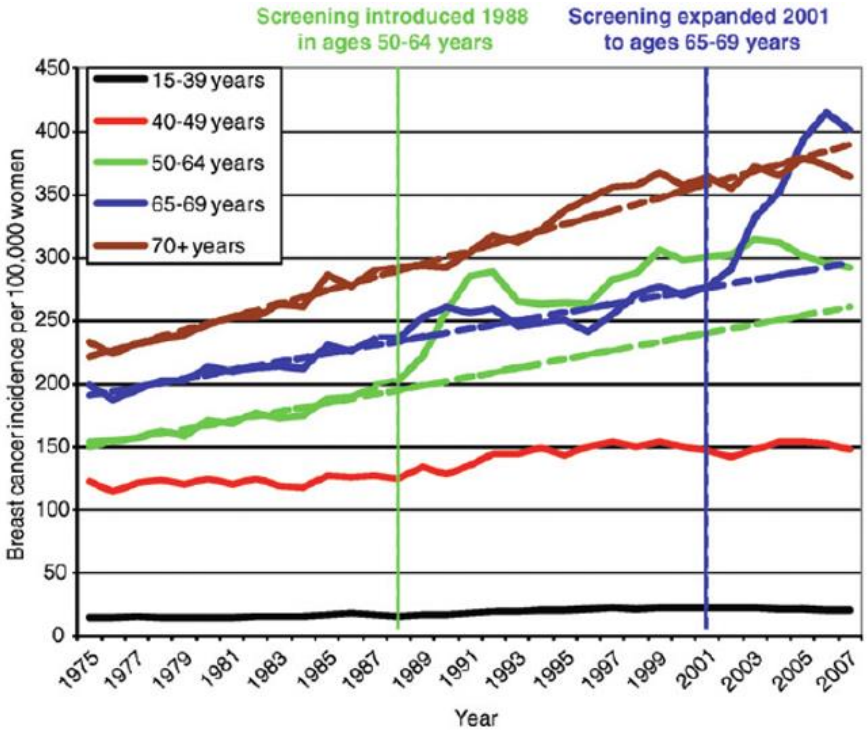
The methods Duffy et al. used for estimating overdiagnosis were also flawed.

First, they excluded carcinoma in situ, which is dishonest, as it wasn't stated in their paper. My co-worker Karsten Juhl Jørgensen asked Duffy on national British radio whether he only included invasive cancer,[443] which Duffy confirmed. It is a serious error to exclude carcinoma in situ and even worse to conceal it. It constitutes 21% of the diagnoses made through the screening programme, and they are more often treated by mastectomy than invasive breast cancer.[444]

Second, they used an unverified model with incorrect assumptions. It is wrong to assume that essentially all increase in incidence with screening represents earlier diagnosis. Most of this is overdiagnosis.

Third, they adjusted for a compensatory decline in breast cancer incidence in UK women no longer screened because of advanced age, which didn't exist for the years they examined.[445] This is clear if one looks at the freely available graphs at Cancer Research UK that show the incidence of invasive breast cancer.[446]

Fourth, as noted earlier (see page 45), more updated numbers show an abrupt increase when screening was extended to the age group 65-70 years in 2001, which by far exceeds any possible compensatory decline:



We estimated 57% overdiagnosis in England and Wales when we included carcinoma in situ.[447] With their faulty methods, Duffy et al. estimated 12% overdiagnosis.

In discussing our data, Duffy et al. said that the reason for our disagreement partly lay in the fact that they estimated the benefit "directly from empirical data" and avoided confusing invitation to screening with actually receiving screening. Thus, Duffy said again that data from randomised trials are not empirical data, which is absurd. Furthermore, it is immaterial for the ratio between benefits and harms whether one looks at those invited or those attending; they remain the same.

Duffy et al. also claimed erroneously that only 37% of breast cancers are screen-detected even though the correct number is 68% (see just above).

Moreover, they used strawman arguments. They concluded that our result on overdiagnosis implies that virtually all screen-detected cancers are overdiagnosed and call this an "absurd and frankly incredible conclusion." We have never said or implied anything that silly.

Finally, some of the authors, particularly Tabár and Smith, have competing interests, but none were declared in their paper, although the *Journal of Medical Screening* requests a statement from authors.

It would be hard to argue that what Duffy, Tabár and Smith did is not scientific misconduct. Was it fraud? Fraud is any activity that relies on deception in order to achieve a gain.[448] It becomes a crime when it is a "knowing misrepresentation of the truth or concealment of a material fact to induce another to act to his or her detriment" (Black's Law Dictionary).

I will leave it to the readers to decide if it is scientific misconduct, fraud, or a crime, or all three. If some people find it is neither, I would like to know why. Whatever we call it, I believe it is fair comment that to misrepresent facts about screening to this degree induces women to get screened, as they don't know what they are buying into. This is deception.

Vested interests at the *Journal of Medical Screening*

Duffy and colleagues published their article in *Journal of Medical Screening* owned by the Medical Screening Society, located at the Wolfson Institute of Preventive Medicine, the home institution of Duffy, Wald and Law.

Duffy serves on the editorial committee of the journal, together with the director of the UK Breast Screening Programme, Julietta Patnick. Nicholas Wald is president of the Society, director of the Wolfson Institute and editor of the journal. Malcolm Law is associate editor and a professor at the Institute.

An incestuous arrangement that guarantees a high level of agreement about how issues related to breast screening can best be distorted beyond belief, reason, and the raw data.

We demonstrated this kind of bias by comparing general medical journals with specialty journals in relation to how they cited the three versions of our Cochrane review and our comprehensive *Lancet* review from 2001 of the randomised screening trials.[449]

The methods we had used in our reviews were accepted more often in general medical journals than in specialty journals ($p = 0.001$), as were our results for overdiagnosis ($p = 0.05$). Specialty journals were also more likely to explicitly reject our estimated effect on breast cancer mortality ($p = 0.02$). We noted that several specialty journals are published by interest groups and that some authors have vested interests in mammography screening.

Jack Cuzick is also a director of the Wolfson Institute, and head of the Centre for Cancer Prevention. He is similarly off target as the others, which his review of my 2012 mammography screening book in *Lancet* demonstrates.[450] He seems to have an exceptional lack of understanding of basic methodological issues in relation to cancer screening.

The title of Cuzick's book review is telling: "Breast cancer screening - time to move forward." Please stop the debate and accept screening!

Cuzick argued that the long-term benefit of breast cancer screening is larger than in the trials, referring to a recent analysis of the Swedish Two-County study. He claimed that "the number of overdiagnosed cancers is similar to the number of deaths prevented," which is ten times more positive than our estimate in the Cochrane review.

Cuzick opined that our 2001 review in *Lancet* was a "context free" application of guidelines and that we focused only on the two trials with negative outcomes. The fact is that our review adhered to Cochrane guidelines and we showed and discussed the results of all the trials.

Cuzick claimed falsely that I should have misunderstood the paper by Duffy, Tabár and Smith where they reported a 13% reduction in all-cause mortality with screening.[451] I did not, and I showed that the triumvirate misrepresented their own research in this article (see page 39).

Cuzick's review was so flawed that I was allowed to rebut his criticism, which is exceptional.[452] I explained why it was wrong when Cuzick said that using total mortality after a breast cancer diagnosis avoids the need to ascertain cause of death, and when he argued that case-control data are far more informative than breast cancer mortality trends.

It is unbelievable that Cuzick, who is an epidemiologist, doesn't know that case-control studies are extremely misleading when used to estimate the benefits of cancer screening.[453]

In 2011, Dutch researchers and statistician Sue Moss from the Cancer Screening Evaluation Unit, Institute of Cancer Research, the UK, compared screening participants with non-participants and estimated a 65% reduction in breast cancer mortality in Nijmegen in the most recent time period they studied.[454] Seventeen years earlier, Dutch researchers and professor of statistics Nick Day from Cambridge, UK, used a similar design to claim a 52% reduction in breast cancer mortality in Nijmegen.[455] This large effect was implausible, and the authors reported that there was *no reduction* in the breast cancer mortality rate in Nijmegen at that time, when participants and non-participants were combined.

The Malmö trial investigators have demonstrated how large the bias can be.[456] They compared breast cancer mortality in participants and non-participants within the screening arm of their trial. After nine years, there was a non-significant 4% reduction in breast cancer mortality with screening when the data were analysed as they should be, coming from a randomised trial, but when the authors used the case-control design the two Dutch research groups had used, they found a significant 58% reduction. This impressive but spurious result was likely caused by selection bias, also called the healthy screenee bias.

We first published our critique of Duffy, Tabár and Smith's 25 times exaggeration paper on *BMJ's* website.[457] Two months later, we submitted a full paper to *Journal of Medical Screening*, mostly as an experiment to see what happened.

Nicholas Wald asked us to submit a letter to the editor instead and said that our criticism of the missing declarations of competing interests in Duffy's paper was unwarranted. I replied he might have his own conflict of interest and asked him to reconsider his decision.

Wald also informed us that he would send our letter for peer review. We wondered why he would do this, as none of the hundreds of letters to the editor we had published earlier that discussed a previous paper in a journal had ever been sent out for peer review. We furthermore noted that the authors we criticised would be asked to respond to our criticism, and that the very idea with letters was to allow people to publish their criticism, without any influence from peer reviewers who might be conflicted.

In his reply, Wald did not address the issues we raised but just said it was his decision.

We never saw any peer reviews but were informed two months later that our letter was accepted. As the word count for letters was limited, and we needed space to explain the many errors Duffy et al. had committed, we had deleted all descriptions of conflicts of interest apart from this one, which was published:[458]

"We also note that no conflicts of interest were declared. Tabár founded Mammography Education Inc, Arizona in 1980, which still exists (10) and in 1999, he declared an income of five million SEK in Sweden, which is an extraordinary amount according to Nordic standards. We believe that such an important conflict of interest should be declared."

In their reply,[459] Duffy, Tabár, Smith, and others continued to confuse their readers, as they had done in their paper. Their view on conflicts of interest was particularly bizarre and clashes with accepted international definitions:

"No communication from Professor Gøtzsche would be complete without the customary accusation of a conflict of interest. We do not propose to join in undignified finger-pointing. We would say that it is no secret that Professor Tabar makes his living by practising and teaching breast radiology. Indeed, it is a point of pride that he has trained 20,000 radiologists in breast imaging, students who in turn proved to be able to achieve substantial reductions in breast cancer mortality by early detection (7). He will continue to do so regardless of publication or otherwise of our research results. Thus it does not constitute a conflict of interest."

Difficulties with getting important papers published in the *BMJ*

We believe that what caused people to publish extreme exaggerations were three important papers we published in *BMJ* within just 14 months: Our criticism of the UK leaflet,[460] our systematic review on overdiagnosis in countries with organised screening programmes,[461] and our paper showing screening doesn't work in Denmark.[462]

These papers were very threatening to the screening advocates, and the two most recent ones were rejected by *BMJ* based on hostile peer reviews. They were accepted after we had appealed.

Our overdiagnosis review was seen by two peer reviewers who had huge conflicts of interest. One, Jacques Fracheboud, had published several dishonest studies with Harry de Koning, and in one of them, they quoted other researchers for an overdiagnosis of a few per cent while they manipulated their own data to avoid concluding that they showed considerable overdiagnosis.[463] The other one, My von Euler-Chelpin, belonged to the Danish research group that had claimed it is possible to screen without overdiagnosis.[464 465]

We told *BMJ* that we could provide an extensive rebuttal of the criticisms; that we felt we had been abused by the peer reviewers; and that a systematic review on overdiagnosis had never been published before, likely because all those with a conflict of interest preferred to continue claiming there wasn't any problem.

Our paper was sent for peer review again and this time, the selected peer reviewers, H. Gilbert Welch and Michael Baum, had the same interest as us, to get as close to the truth as possible.

Our paper about the lack of effect in Denmark was seen by two peer reviewers who had extensive knowledge of screening. *BMJ's* statistician Jon Deeks praised the "rigour with which the study was conducted." In line with this, the first reviewer, Cornelia Baines, wrote, "It is a pleasure to read this well-designed and appropriate analysis refuting a previously published and less than compelling report on breast screening benefits in Copenhagen." She noted that our methods were appropriate; that our rationale for critiquing the study by Olsen and Lynge[466] was persuasive; and that our paper was "fascinating and important."

In his usual style, the other reviewer, Stephen Duffy, wrote there were "a number of problems with the analysis and interpretation" and that "the authors' assertion that the

previous analysis by Olsen and colleagues has methodological weaknesses should not appear in the abstract and is in any case highly contentious."

To our big surprise, *BMJ* rejected our paper because they did not find it "clinically helpful for our general readers." This argument didn't hold because they had published the flawed paper by Lynge, which we criticised in our article.

We appealed and replied to Baines and Duffy and a new reviewer, Sophia Zackrisson, who provided reasonable comments. We noted that Duffy contradicted himself, misquoted and misrepresented our research, and maintained positions that were false or irrelevant. For example, he accepted that Olsen found that the full effect of screening in Copenhagen appeared after only 3 years,[467] which is impossible, whereas he claimed that our follow-up period of 13-16 years was too short to find an effect. Moreover, as we included women who were too young or too old to have benefited from screening and the whole country, our study had much more power than Olsen's study.

The *BMJ* finally reacted to all the nonsense propagated by dishonest researchers

Everything has its limits. After the endless debates with people like Duffy, Tabár, Smith, Wald and Law, and accusations from screening advocates that *BMJ* had taken sides, its editors had finally had enough. In 2010, they asked "a highly trusted observer of preventive health strategies," Klim McPherson, to take a look and come to a view.[468]

McPherson's paper was unusually frank.[469] He asked whether the time had come for a serious scientific rethink of the benefits of the screening programme, and he asked how a national programme of such importance could exist for so long with so many unanswered questions.

McPherson criticised Duffy's methods and results most devastatingly. He noted, for example, that Duffy's benefit to harm ratio was ten times more positive than that offered by the Malmö investigators (even though their estimate was also too positive).

Fiona Godlee drew her own conclusions.[470] She said that "those who argue that screening may be almost as harmful as it is beneficial come out on top."

Godlee chaired an Evidence Live conference in Oxford in 2013 where I lectured on mammography screening, and she told the audience she didn't go to screening because of my research. This lecture is publicly available.[471]

The press covered McPherson's revelations extensively. The *Independent* published an editorial, and in an interview, Godlee said:[472]

"The screening lobby thinks the *BMJ* has got a bee in its bonnet about screening. That is not the case – we follow the evidence. The Danish team [from the Nordic Cochrane Centre] do good work which is very thorough and of good quality. It is fair to say that we have not had the same quality of submissions from the other side. We would be delighted if someone came forward with a robust defence of the screening programme – I don't think they have done that."

But dishonesty has a life of its own, totally free from evidence, reality, and reason. Coming from this fantasy world, Professor Dame Valerie Beral, chair of the Department of Health's Advisory Committee on Breast Screening, told the *Independent* about the 1400 lives saved each year, which don't exist.[473] She also said: "What Klim McPherson and other critics have done is used old data from the US and Scandinavia, largely from the 1970s and 1980s," to which McPherson replied, "The idea that this is old data is neither here nor there: it is real data."

Beral added: “In the old days women had mastectomies for breast cancer – now they don’t [in cases where the tumour is small enough] so the harms have reduced … there are claims that cancer is over-diagnosed – but it’s a misnomer. We don’t know there are some cancers that won’t progress – it is an unanswerable question.”

I believe Beral lied deliberately. You cannot be chair of the Department of Health’s Advisory Committee on Breast Screening without knowing about the issues she denied existed.

There were other cracks in the mammography screening armour. In 2011, I published an invited paper in the *Canadian Medical Association Journal* with the title, “Time to stop mammography screening?”[474] It ended this way:

“If screening had been a drug, it would have been withdrawn from the market. Thus, which country will be first to stop mammography screening?”

As people still wouldn’t listen, I published a paper with an uncompromising title four years later, “Mammography screening is harmful and should be abandoned,” in *Journal of the Royal Society of Medicine*.”[475]

That didn’t wake people up either.

I shall now describe the ultimate exaggeration. I had often joked about when we would see a claim that screening reduces breast cancer mortality by 100% and eradicates the disease, but I did not expect it would ever happen, and there it was, in the *BMJ*.

In 2008, a headline in *BMJ’s* News section touted: “Survival of women treated for early breast cancer detected by screening is same as in general population, audit shows.”[476]

I was interviewed and noted it was not surprising that women who had a small breast cancer diagnosed at screening and who were judged to have “a good or excellent prognosis” actually had a good or excellent prognosis. This is a tautology. These data came from the Association of Breast Surgery and the NHS Breast Screening Programme.

But *BMJ* was not first. Tabár, Duffy and Smith claimed already in 2002 that screening can prevent all breast cancer deaths (see Chapter 5).

11 The UK "independent" review was window dressing

After 12 years of criticism that wouldn't go away, the UK establishment published a "Yes Minister" report that was a scientific disaster. The Lancet falsely called it independent and the best available systematic review. Unfortunately, this report had the effect that the much-needed debate died out.

In October 2011, Susan Bewley, professor of complex obstetrics, published an open letter in *BMJ* to England's National Cancer Director, Sir Mike Richards, calling for an independent review of the NHS Breast Screening Programme.[477]

Bewley had compared the NHS's and our leaflets and found that the former exaggerated benefits and did not spell out the harms. She also criticised Richards for having said that, "the large majority of experts in this country disagrees with the methodology used in the Cochrane Centre reviews of breast screening" and noted that simply disagreeing with the open, highly defensible, peer-reviewed Cochrane methodology was not enough. One needed to know what the vested interests were for the experts disagreeing, how they came to their conclusions, and why they disagreed.

Richards replied that an independent review of the randomised trials and the observational studies was under way and that the leaflet (even though it was only one year old) would be rewritten.[478]

The "independent" review was not independent

Richards noted that, "We are seeking independent advisers for this review who have never previously published on the topic of breast cancer screening." This was also disingenuous, as it ensured that those who knew most about mammography screening, including Karsten Juhl Jørgensen and me, would not become advisers.

BMJ published an editorial,[479] and there was a flood of well-argued rapid responses on *BMJ's* website. People generally didn't believe the review would be independent and there were good reasons for this distrust.

Richards was put in charge of the independent review by the Ministry of Health, together with Harpal Kumar, chief executive at Cancer Research UK. None of them were independent; they were powerful people favouring screening. Kumar had announced that, "Screening saves lives, so it's extremely worrying to see that the percentage of women going for breast screening is dropping."[480]

We noted that Richards's bias was apparent from his *BMJ* paper, where he had three references.[481] The first was the 2002 IARC working group report, which he cited for a 35% effect of breast screening among those attending screening, ignoring that such estimates are inflated, as those who turn up for screening are healthier than those who don't.

The second was the programme's 2006 report. Richards wrote that 400 women need to be screened regularly over a ten-year period to save one woman from dying of breast cancer. This estimate was wrong by a factor of five, according to the Nordic Cochrane Centre and the US Preventive Services Task Force, both of which are independent institutions.

Richards's third reference was a study performed by "eight leading international scientists," headed by Professor Stephen Duffy. Duffy is not a leading scientist. He gets numbers wrong all the time despite being a statistician and publishes dishonest research. Richards conveyed their estimate of 2-2.5 lives saved by screening for every one women overdiag-

nosed, which is wrong by a factor of 20-25. We therefore recommended Richards to change his advisers, as they so obviously provided him with wildly exaggerated estimates of the benefits of screening.

Like others, we suggested that a body such as the National Institute for Health and Clinical Excellence (NICE) should be in charge of the review, which would eliminate the risk of whitewash or hiding behind experts with vested interests.

The independent review's chair was Professor Sir Michael Marmot. He invited several people to inform a panel in London in March 2012, one by one, as if it were an oral exam. The expert witnesses who presented evidence to the panel and debated points relevant to the review were:[482]

Philippe Autier, Vice President, Population Research, International Prevention Research Institute (iPRI), Lyon, France.

Michael Baum, current Director of the Clinical Trials Group at University College London, Professor Emeritus of surgery and visiting Professor of medical humanities, University College London.

Dame Valerie Beral, Professor of Epidemiology and Director, Cancer Epidemiology Unit, University of Oxford.

Susan Bewley, Consultant Obstetrician and Honorary Senior Lecturer at King's College London.

Stephen Duffy, Professor of Cancer Screening, Wolfson Institute of Preventative Medicine, at Barts and the London School of Medicine and Dentistry, part of Queen Mary University London.

Harry de Koning, Professor of Screening Evaluation, Erasmus MC, Rotterdam, the Netherlands.

Ian Ellis, Professor of Cancer Pathology, University of Nottingham.

Peter C Gøtzsche, Director, Nordic Cochrane Centre, Copenhagen, Denmark.

Klim McPherson, Emeritus Fellow, Visiting Professor of Public Health Epidemiology, Oxford University.

Albert Mulley, Director, The Dartmouth Centre for Health Care Delivery Science and Professor of Medicine, Dartmouth Medical School, Dartmouth, USA.

Lennarth Nyström, Associate Professor, Department of Public Health and Clinical Medicine, Umeå University, Sweden.

Julietta Patnick, Director, NHS Cancer Screening Programmes and Visiting Professor, University of Oxford.

Sir Richard Peto, Professor of Medical Statistics & Epidemiology, Co-director of the Clinical Trial Service Unit, University of Oxford.

Paul Pharoah, Professor of Cancer Epidemiology, University of Cambridge.

Sir Nick Wald, Institute Director, Wolfson Institute of Preventive Medicine, Barts and the London Medical School.

Jane Wardle, Professor in Clinical Psychology and Director, Health Behaviour Unit, University College London.

Robin Wilson, Consultant Radiologist, The Royal Marsden, London.

The panel had been asked to read the Cochrane Review and several of my papers, and I sent a ten-page report and a pdf of my upcoming book[483] to the panel suggesting that, whenever they encountered a "funny" paper, they might wish to search for my criticism of it in my book, which could save them time.

Other expert witnesses also sent material and suggestions to the panel. Michael Baum noted that women get an invitation for screening with the appointment attached, which was unethical like unsolicited inducements to subscribe to *Readers Digest*. He proposed an information leaflet that allowed the women to judge when it would be convenient for them to attend if that was what they wanted.

Karsten Juhl Jørgensen wrote to me that if we stopped giving women a pre-allotted time, or even better, stopped sending them letters that they should go to screening, then screening would quickly die out and politicians would have saved their faces.

One of the organisers of the panel meeting, Martine Bomb, sent me an unpublished modelling study by Nick Ormiston-Smith, a statistical manager at Cancer Research UK, which was based on papers by Stephen Duffy and me. It showed the impact various assumptions had on the estimated level of "overdiagnosis." Yes, in inverted commas. Even in 2012, it was blasphemy to suggest that overdiagnosis existed.

I wrote to my colleagues that the paper was very confusing and that "the little I understand I don't agree with." Bomb then sent a new email saying a data error had been found and that the estimates from the Poisson regression modelling were wrong.

It was a weird experience to give testimony to the panel and being asked questions. My impression was that some of the panel members understood too little of basic methodological issues related to cancer screening.

After the panel meeting in London, there was total silence till the panel's report was published in *Lancet* in October 2012.[484] The authors were:

MG Marmot, chair, University College London, Dept. of Epidemiology and Public Health.
DG Altman, Centre for Statistics in Medicine, University of Oxford.
DA Cameron, Edinburgh Cancer Research Centre, University of Edinburgh.
JA Dewar, Dept. of Surgery and Oncology, Ninewells Medical School, Dundee.
SG Thompson, Dept. of Public Health and Primary Care, University of Cambridge.
Maggie Wilcox, lay member.

The whitewash

Although the report forced the UK establishment to even accept that overdiagnosis was a problem, it was a disastrous whitewash used to "carry on regardless." The Cancer Screening Empire had fought back, and we explained what was wrong with the report in *Lancet*.[485]

The panel had not paid any attention to important issues I submitted to it.

Its estimate of the ratio between women avoiding dying from breast cancer and overdiagnosed women was three times too positive.

The panel referred to the data from our Cochrane review but used the erroneous estimate of a 20% effect of screening, which the Cochrane Breast Cancer Group had forced us to accept and to write in the abstract (see page 17).

The panel ignored that we also wrote in the abstract that there were only two trials with adequate randomisation, and they did not show a significant reduction in breast cancer mortality (relative risk 0.93; 95% confidence interval 0.80 to 1.09 after 13 years).

The panel extrapolated the data far beyond the data range, which is impermissible. They assumed that the 20% effect would be the same today and would exist undiminished up to age 79 years, ten years after screening stopped, which are unreasonable assumptions, and concluded that screening prevents about 1300 breast cancer deaths every year in the UK.

This was just *too* politically expedient. As they say in *BBC's* "Yes Minister" series:

"The Prime Minister doesn't want the truth, he wants something he can tell Parliament."

The 1300 lives saved are very close to the claim from 2008 by the UK Breast Screening Programme of 1400 lives saved, which assumed, however, that the effect was 35%, not 20% (see just above),[486] and its claim of 1250 women saved (see page 70). With a British understatement: very weird, indeed.

There were other serious errors. Contrary to the opinion of the panel, the important advances in treatment that had occurred since the trials were done had reduced the effect of screening substantially. A woman who would have died without screening in the past might now live so much longer because of better treatment that she would die of a heart attack at an older age. Screening can have no effect for such women. We also noted in *Lancet* that breast cancer awareness had reduced the effect of screening.

The panel did not think that adjudication of the cause of death was a problem in the trials even though we had documented at length, in *Lancet*, in our Cochrane review and in our report to the panel, that it is a huge problem, which inevitably biases the trials in favour of screening even when blinded endpoint committees have been used.

The panel opined that all-cause mortality is not an appropriate outcome for trials of breast screening because the trials did not have sufficient power for this outcome, and *they didn't publish any information on all-cause mortality or all-cancer mortality*. Whether an outcome is appropriate or not has nothing to do with power. What matters is if the outcome is reliable, and since breast cancer mortality is not reliable, we need to look at other mortality outcomes. Furthermore, there *was* enough power to consider all-cause mortality, and not to do so was unethical and based on illegitimate assumptions.

We noted that screening did not reduce total mortality or mortality from cancer, including breast cancer (relative risk 1.02, 95% CI 0.95 to 1.10) and that some of the healthy overdiagnosed women will die from their treatment. For example, radiotherapy increases deaths from heart disease by 27%.[487]

The panel used an estimate of overdiagnosis of 19%, but the estimate in the Cochrane review was 30%,[488] and we found 52% overdiagnosis in a systematic review of countries with organised screening programmes.[489]

Lancet issued a misleading press release.[490] It mentioned the 20% reduction in breast cancer mortality and that among women aged 50-52 years who are invited to begin screening every year, just over 1% will have an overdiagnosed cancer in the next 20 years. This is highly misleading, as the overdiagnosis in the UK is about 50%.

The press release noted that, "According to Professor Marmot, the reduction in risk of death from breast cancer screening corresponds to one breast cancer death prevented for every 235 women invited to screening." This error was inexcusable. The 1993 meta-analysis of the Swedish trials reported a 29% reduction in breast cancer mortality after ten years, corresponding to one woman out of 1000 avoiding dying from breast cancer. Marmot's estimate was four times more positive than an estimate that was already too positive.[491]

The press release also mentioned:

"For each woman, the choice is clear. On the positive side, screening confers a reduction in the risk of mortality of breast cancer because of early detection and treatment. On the negative side, is the knowledge that she has perhaps a 1% chance of having a cancer diagnosed and treated that would never have caused problems if she had not been screened. Clear communication of these harms and benefits to women is essential, and the core of how a modern health system should function."

Michael Baum informed the organisers at Cancer Research UK (CRUK) that he had published a letter in *The Times* expressing his concerns on the absence of any information on all-cause mortality:

"To say that the trials were inadequately powered for this end point is a pathetic excuse. In the ProtecT trial of PSA screening for prostate cancer, cause specific and all-cause mortality are equal primary end points."

He also asked whose idea it was,

"to parade a group of women whose 'lives had been saved' by screening at the press conference? You should know of course that it is impossible to identify such women. They may be alive because they were overdiagnosed, they may yet die of the disease or maybe they … would be cured by treatment once the tumour progressed to a clinically detected size. If the CRUK aren't aware of this then they know nothing about screening and if they are aware then they are guilty of corporate scientific misconduct. Before I lodge a formal complaint which of these two categories does the CRUK fit into?"

Baum cannot remember if he ever got a reply.

An anonymous *Lancet* editorial,[492] most likely written, or at least approved, by Richard Horton, talked about closing a chapter; that the review "should begin to lay the benefits versus harm controversy to rest;" that "The Panel also considered how women feel about the available evidence: many women believe the balance of benefits to risks is worthwhile" (they cannot know this, as they have never been honestly informed); and that "Women need to have full and complete access to this latest evidence in order to make an informed choice about breast cancer screening" (which is impossible, given the report is so flawed).

The worst bit in the editorial was this, which contained no less than three errors in a short sentence:

"The Panel's report, the latest and best available systematic review, shows that the UK breast-screening programme extends lives and that, overall, the benefits outweigh the harms."

Lancet wanted us to believe that it had published the "best available systematic review," but that was the Cochrane review. Furthermore, the *Lancet* review was not even a systematic review, which another, more comprehensive report acknowledged: "This is a rigorous review of the evidence by an independent panel; it is not a formal systematic review."[493] And it is wrong that breast screening extends lives, as total mortality is unaffected by it. It is therefore also wrong to claim that the benefits outweigh the harms. Moreover, this is a value judgment, not a scientific conclusion.

Richard Horton was on the advisory board for the Nordic Cochrane Centre, and he asked me to remove him, arguing that "the position you have taken over this latest publication is damaging to women's health and deleterious to the reputation of the Cochrane Collaboration. I don't wish to be publicly associated with your view by being on your board."

I informed my closest colleagues about this, and Michael Baum replied:

"I'm sick of people telling me it's time to move on! Such a cliché. This isn't marriage guidance counselling. To move on means learning from the mistakes of the past, not burying them."

Karsten Juhl Jørgensen wrote to Baum and me that,

"Richard Horton appears to think that if Peter stops criticising breast screening, we will have 'world peace.' That would perhaps be the case if the opposition against breast screening was indeed an international conspiracy orchestrated by the Nordic Cochrane Centre. But this process is not in the hands of Peter - it is a wave of new research by various independent research groups that have in common the realisation that breast screening has been oversold ... a consensus report that does not duly recognise the new evidence will obviously not end the debate."

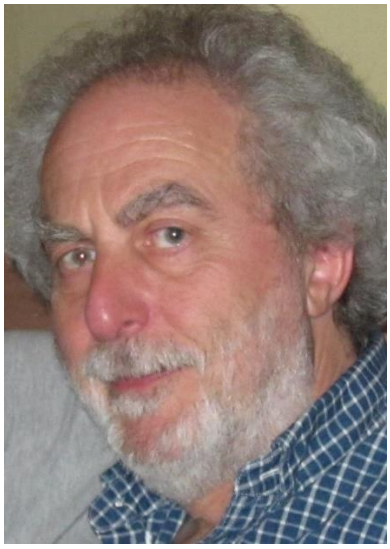
An Australian colleague noted that the panel's report could not settle anything and expressed surprise that it was so poor, "but it is probably the lowest common denominator of panel agreement in a difficult and controversial area."

Two years later, I met with one of the authors of the panel's report, Douglas Altman, at the Preventing Overdiagnosis conference in Oxford. I asked him why he accepted to be a co-author on a report that was so flawed, and he admitted he wasn't proud of it.

Doug died of colon cancer in 2018. He was a close friend and one of the world's finest biostatisticians. I have published more papers with him, over 50, than with anyone else, and his intellectual sharpness never failed. He agreed with my major criticisms of the disastrous Marmot report, above all with the lumping of reliable with unreliable studies.

What this illustrates is very depressing. It shows that psychological factors, e.g. group think and group pressure, may trump science, even for one of the most outstanding scientists in the world.

I was devastated. I had devoted so much time for 15 years to get the truth out about mammography screening. I realised it was impossible to win the battle because of the forces that did not want the truth to come out. If it did, it would mean the end of breast screening.


Douglas Altman


Mette Kalager


Cornelia Baines

12 Screening has not reduced the incidence of advanced tumours

The reactions to our paper in Annals of Internal Medicine that demonstrated considerable overdiagnosis in Denmark revealed just how entrenched the screening establishment is. There is none so blind as he who WILL NOT SEE.

In 2017, we published an important study in *Annals of Internal Medicine* that used data from Denmark spanning 30 years.[494] Our methods were strong because we compared screened and unscreened populations of the same age during the same time period, and we also included non-screened age groups.

No reduction in incidence of advanced tumours in Denmark

We found that screening had not reduced the incidence of advanced tumours (those larger than 20 mm), which means that screening could not have reduced breast cancer mortality.

In contrast, the incidence of nonadvanced tumours increased in the screening versus pre-screening periods, incidence rate ratio 1.49 (95% CI 1.43 to 1.54). When we accounted for regional differences in women younger than the screening age, we found 48% overdiagnosis. This means that one in every three invasive tumours and cases of ductal carcinoma in situ (DCIS) diagnosed in women offered screening represent overdiagnosis.

Our paper was highlighted by *Annals* as being one of the best they had published that year, and it was accompanied by an instructive editorial written by Otis W. Brawley, Chief Medical and Scientific Officer for the American Cancer Society (ACS), with the telling title, "Accepting the existence of breast cancer overdiagnosis."[495]

Before Brawley came to office, it was Robert Smith, Director of Cancer Screening, who was the official spokesperson for the Society in matters of cancer screening.

I have met both and they are as different as night and day. I have also read Brawley's autobiography, which is a moving and provocative read: "How we do harm: a doctor breaks ranks about being sick in America."[496]

This is what Brawley does. He wants to get the truth out, not least when doctors harm people, even if inconvenient for his closest colleagues. This is very unusual for someone in a leading position at a cancer charity. I believe this is why my brief encounter with Brawley at a US conference felt very warm. Brawley respected my research and found it important, in sharp contrast to his predecessor who always denigrated it.

Brawley mentioned in an interview that his father grew up under Jim Crow laws that prohibited educational opportunities for black children.[497] But his parents sent their children to private Catholic schools. Brawley was unusually bright, and he went to a prestigious Jesuit high school in Detroit. The Jesuits said they didn't teach people *what* to think but *how* to think and assess issues. This education underpinned much of the scepticism that fuelled Brawley's career.

Brawley mentioned that,

"My biggest frustration deals with a body of folks in modern medicine who fail to evolve. One of the most important philosophies in medicine is self-introspection - we need to constantly question ourselves and rethink the status quo. Much of our medical knowledge from 2000 is not valid in 2019. Cancer screening is the most obvious example of following dogma that doesn't produce better outcomes, but rather, for many tumor types, leads to unnecessary harm and a waste of our precious resources."

He added:

“During my almost 12 years at the ACS, I focused on putting science back into the process of prevention. Even to this day, there are a lot of people who don’t understand the nuances of screening, yet they want to give advice. I tried to make hard science replace emotion and personal opinion ... We need to take the emotional conflicts of interest out of policymaking and rely on science and what works.”

As I have explained above, Brawley’s description of people who are emotional, don’t understand the nuances of cancer screening, follow dogma, and lack the capacity for self-criticism fits perfectly well with Robert Smith and his two allies, Tabár and Duffy.

In another interview, Brawley commented on cancer screening guidelines and said:

"one can simplify a message so much that one is lying. Too much of that has happened in breast cancer over the past 30 years and that is why there is so much confusion."[498]

Brawley’s editorial in *Annals* is very good and measured. He mentions that discussions about breast cancer screening often deteriorate from constructive dialogue weighing facts to an emotional *ad hominem* argument, and that we owe it to the patients to be “evidence-based” rather than “faith-based.” He explains why so many people get it wrong:

Cancer overdiagnosis - the concept that some tissues fulfilling histologic criteria for cancer are of no threat and do not need to be cured - is very difficult for some to accept, especially among the most ardent supporters of breast cancer screening. The existence of overdiagnosis is perhaps easier to accept if one examines breast cancer diagnosis in its historical context. The biopsy definition of breast cancer was first provided by German pathologists in the mid-19th century. They developed biopsy techniques, used microscopes to describe the diagnostic criteria for invasive adenocarcinoma, and obtained tissue from autopsies of women who had clearly died of metastatic breast cancer.

Over the next century and a half, breast cancer imaging and diagnostics evolved. Because of these advances, it is currently possible to find and biopsy lesions (some as small as 5 mm) that were not detectable 30 years ago and fulfil the 19th-century definition of cancer.

If the lesion fits the profile of something that killed people in the past, the natural inclination today is to assume that the lesion will grow, spread, and eventually kill. However, some of these lesions may be genomically predetermined to grow no further and may even regress.

In many respects, considering all small breast lesions to be deadly and aggressive types of cancer is the pathologic equivalent of racial profiling.

Experienced clinicians have long observed that tumors, including those within the same pathologic grade, have various biological behaviors.

Overdiagnosis is increasingly recognized as commonplace among thyroid, prostate, and even lung carcinomas. Acknowledging the existence of breast cancer overdiagnosis challenges the value of screening: It means that the benefits of breast screening have been overstated, and that some women who have been “cured” were harmed because they received unnecessary treatment. Studies also show that breast cancer treatment is responsible for much of the decrease in breast cancer mortality.

In the future, it may be possible to identify women who are at very low risk and those at greater risk such that screening efforts can be refocused on individuals most likely to benefit.

Leading figures in the Danish Breast Cancer Group (DBCG) tried to sabotage our *Annals* study. At first, I wrote to the chair, Peer Christiansen, in 2011 that we were very surprised that he had said in an interview that,

"Screening has really improved cancer treatment. We see each year 200 fewer patients with tumours greater than 2 cm. This proves that we find and treat the cancer at an earlier stage. Screening leads to a much better survival prognosis."[499]

The headline for the newspaper article was, “Surgeons save breasts.”

Both statements are wrong. In my letter to Christiansen, I referred to Autier’s review of several countries, which found that screening doesn’t reduce the incidence of cancers larger than 2 cm,[500] but as I didn’t want to irritate Christiansen, who is a breast surgeon, I didn’t tell him that screening doesn’t save breasts but increases mastectomies. I asked what his documentation was for his statement about 200 fewer tumours greater than 2 cm every year.

I didn’t get a meaningful reply, and it wouldn’t have been possible, as what he claimed had not happened.

The information we needed for our study about cancers were kept in a database administered by DBCG but paid for by the regions. According to DBCG's statutes, its board must approve scientific projects and protocols.

We submitted our protocol and expected it to be rejected because the board members included staunch screening advocates, such as Niels Kroman, Ilse Vejborg, Henning Mouridsen and Peer Christiansen, and they were not fans of our research.

Mouridsen told us that our project's purpose was contained in an analysis DBCG was already engaged in and that, according to current practice, DBCG could therefore not deliver the data until DBCG's own analysis had been published.

We replied that we were disappointed and disagreed with the premises for the decision. Furthermore, we noted that, since their refusal had important principled implications for the terms of research in Denmark and the impartial assessment of the effects of established health interventions, we would move forward with our case.

We appealed to the chief of the joint secretariat for all Danish databases, Paul Bartels, and noted that we had discussed the matter with a person who had been a board member for several databases and believed that DBCG had abused its power in a case where it had a significant conflict of interest. We also noted that we considered complaining to the Parliamentary Ombudsman but encouraged Bartels to make it clear to the DBCG that their position could harm themselves.

Bartels reacted promptly, and Mouridsen had no other option than to give us the data we had requested.

Other studies also showed that screening doesn’t work

In December 2023, I looked up the citations to our *Annals* paper. There were 90, but none of them referred to the DBCG. I therefore wonder what type of research they told us they were already doing when they refused to give us access to their database in 2012, or if it was just something they had on their mind.

I went through the 90 citations and found nothing new. The important research on breast screening that we needed for informed decision making had already been done over a decade earlier and the results were clear. Only one question remained, which was stated succinctly by Hazel Thornton who was diagnosed with ductal carcinoma in situ at a screening session in 1991. In 2017, she wrote:”[501]

“How much longer do we have to go on waiting for those responsible to acknowledge that breast screening by mammography as now offered is not fit for purpose, is wasting valuable resources and harming more citizens than it helps?”

Alexandra Barratt and colleagues from Australia also quoted our *Annals* paper. They published a study in 2018 showing that screening was not associated with a lower incidence of late-stage breast cancers compared to the pre-screening era whereas the incidence of

localised and regional breast cancer doubled, and the incidence of carcinoma in situ increased over 100 times.[502]

Philippe Autier and colleagues published a study in *BMJ* in 2017 based on data from the Netherlands.[503] They compared screened age groups with non-screened age groups and found that there had been no decline in the incidence of stage 2-4 breast cancers and no effect of screening on breast cancer mortality. They reported an overdiagnosis of 32% after adjusting for clinical lead time according to our research,[504] i.e. assessing the possibility of a compensatory drop in women no longer screened because of advanced age.

They found that the decline in breast cancer mortality in the Netherlands had been largest in women too young to be invited to screening. This had also been the case in Denmark,[505] and was a general trend in 30 European countries.[506]

In the discussion section, Autier et al. noted that improved techniques, replacing film-based mammography by digital mammography had substantially increased the incidence of carcinoma in situ without decreasing rates of interval cancers, thereby increasing overdiagnosis, which had also been increased by extending the screening invitation to older women.

In an accompanying editorial to Autier's paper, Mette Kalager - in an unusually bold fashion - explained that there are two types of observational studies:

Those concluding that mammography screening is associated with little or no benefit but substantial overdiagnosis and those reporting larger benefits and only limited overdiagnosis.[507]

Curiously, there seems to be almost nothing in between these two types of studies. Mette hinted at what the problem is with poor studies by comparing Autier's study with another study from the Netherlands, also published in 2017, but in a specialty journal, *International Journal of Cancer*.[508]

These authors reported similar findings on breast cancer mortality but concluded that screening was associated with a statistically significant decline in mortality. This is difficult to understand, and Mette noted:

> The challenge in observational studies is how to interpret them, and the key is open and transparent reporting. Do the readers get all the data? Is the rationale behind the analyses clear and sound? Are sensitivity analyses performed (a sign of openness and curiosity)? And, finally, are the conclusions supported by the data?
>
> Autier and colleagues report stage specific incidence and mortality in different age groups. The analyses and presentation are transparent; the reader gets more than just a glimpse of the authors' observations. The previous study reports fewer details, so independent verification of the authors' conclusions is harder. Most striking, however, is that while the new study attributes most of the observed decrease in breast cancer related mortality to better treatment, the previous study attributes the decrease to screening despite a lack of data on cancer incidence or stage. Furthermore, the reduction observed after mammography was introduced also occurred among women who were not screened, and appeared only two years after screening started.
>
> Other evidence also points to treatment, rather than screening, as the main contributor to observed mortality reduction in these and other studies.

Mette very effectively hammered nails in the mammography screening coffin in her editorial. She noted that since there was no reduction in late-stage breast cancer in Autier's study, the authors concluded quite logically that any mortality reduction cannot be attributed to screening.

However, screening advocates continued telling the world the opposite, based on flawed studies. It is no surprise that Harry de Koning was last author on the untrustworthy study from the Netherlands or that Jaques Fracheboud was also an author.

It is no surprise either that the rapid responses by Harry de Koning, László Tabár, Peter Dean, Stephen Duffy and Elsebeth Lynge on *BMJ's* website were empty condemnations of a study whose results they didn't like. Their comments had no merit, as Autier explained.[509]

Jean V Doubovetzky and colleagues also cited our *Annals* paper. They reported that from 2000, four years before organised breast cancer screening was implemented in every part of France, to 2016, there was a steady increase in annual numbers of total mastectomies (15%, $p < 0.0002$) and in annual numbers of total and partial mastectomies (37%, $p < 0.000,000,1$). They noted that breast cancer screening increased the number of mutilating surgical procedures instead of decreasing it, as was expected and widely advertised to women.

Per-Henrik Zahl and colleagues also cited our paper. In a study of quality of life from 2020, they used a wide range of assumptions, spanning from 20% to 75% overdiagnosis, a reduction in breast cancer mortality from 10% to 30%, and a translation of a reduction in breast cancer mortality into a reduction in all-cause mortality from 20% to 80%.[510] Under any reasonable assumption, considering the most reliable evidence, the quality of life by going to screening was negative, i.e. screening was harmful.

An invited editorial in *Translational Cancer Research* from 2018 that quoted our paper is telling.[511] It was commissioned by the editorial office; it did not undergo peer review; and it is not listed on PubMed even though this database lists over 2,600 articles from the journal.

Elsebeth Lynge is the first author. She wrote that,

"In order to study overdiagnosis properly, data are needed for a screened cohort and an unscreened comparison cohort for a least 30 years. Such long-term data are not available."

This claim is not correct. With a lead time of one year or less,[512] [513] overdiagnosis can be studied reliably within a much shorter time span, for example the 17 years where Denmark only screened in 20% of the country.

Lynge claimed that "The most reliable data indicate overdiagnosis to account for 1-10% of all incident breast cancer cases," and she mentioned her own 2013 study from Denmark[514] saying that "overdiagnosis was estimated to be 2.3%."

Lynge got it horribly wrong, also in 2013. The results she reported back then in *BMJ* did not fit the observed data. We had access to the same dataset from the Danish Breast Cancer Group that they used, and we published a graph based on the data. We found a relative risk of overdiagnosis of 1.37 (95% CI 1.27 to 1.49).[515] When we compensated for a small, non-significant drop in incidence in previously screened women aged 70-79 years, we found an overdiagnosis of 30%, in good agreement with our previous estimate of 33% overdiagnosis in Denmark.[516]

Lynge compared her estimate of 2.3% overdiagnosis with our new study in *Annals* that found 48% overdiagnosis, which she condemned:

"This analysis was affected by serious methodological flaws. First, the use of absolute differences in changes over time despite different baseline levels; second, a focus on only non-advanced cancers, and third, an inadequate study design where part of the compensatory dip was calculated based on data from women never invited to screening."

To support her arguments, Lynge referred to a study she published in *European Journal of Cancer* in 2017 where she also criticised our *Annals* paper.[517] But her criticism was not valid. She used other methods than we did on our data and found other results, which are

post hoc observations with a high risk of bias. To reduce the risk of bias, you need to write a protocol before you collect the data, which is what we did.

Our methods are very solid and have been used by other researchers. We compared incidence rates and calculated the annual percentage changes before and after screening for each age group (35 to 49, 50 to 69, and 70 to 84 years) in screening and non-screening regions.

In our first approach, we calculated the incidence rates of advanced and nonadvanced tumours in the before and after periods for non-screening and screening areas among women aged 50 to 84 years. In our second approach, we analysed trends in advanced and nonadvanced tumours in the screening and non-screening areas among women younger (35 to 49 years) and older (70 to 84 years) than those included in the programme and compared these trends with those in women in the screening age range (50 to 69 years). This way, we accounted for regional differences unrelated to screening.

We reported that there was no compensatory decrease in the incidence of invasive cancer in women aged 70 to 84 years who were no longer offered screening. Therefore, we concluded that screening was not associated with a reduction in the incidence of advanced cancer and used the incidence increase for nonadvanced tumours in women aged 50 to 69 years to calculate overdiagnosis.

Including ductal carcinoma in situ, we found an overdiagnosis rate of 24% with the first approach and 48% with the second approach, which accounted for regional differences, and which we therefore considered more reliable.

Lynge dismissed our study entirely in her abstract:

"We found that both the use of absolute differences as opposed to ratios; the sole focus on nonadvanced tumours and the crude allocation of tumours and person-years by screening history for women aged 70-84 years, all contributed to the very high estimate of overdiagnosis. Screening affects cohorts of screened women. Danish registers allow very accurate mapping of the fate of every woman. We should be past the phase where studies of overdiagnosis are based on the fixed age groups from routine statistics."

In the main text, Lynge wrote about our two estimates of overdiagnosis:

"If true, breast cancer screening in Denmark causes considerable harm and would be unjustified as a public health policy."

This is the only time I have ever seen a screening advocate admit that if our estimates of overdiagnosis are correct, the screening programme would be unjustified.

Lynge also wrote: "The change in women below screening age is of course interesting but hardly tells about impact of screening."

This is not correct. When studying trends, it is relevant to see what happens in young women not invited to screening. We used this approach, in addition to comparing screened with non-screened areas, when we demonstrated that screening had not decreased breast cancer mortality in Denmark.[518]

Lynge did not suggest a level of overdiagnosis in her paper but wrote: "It is not possible to capture correctly the size of overdiagnosis with such crude data."

It seems Lynge had one valid point, though. She said it was incorrect that we disregarded advanced tumours because there was no compensatory decrease in their incidence in older women. Table 2 in our paper did in fact show that advanced tumours decreased more in screening than in non-screening areas, ratio of rate ratios 0.69 (95% CI 0.63 to 0.75).

I cannot tell why we overlooked this. But a correction would not have much effect on our estimates, which our other study of overdiagnosis in Denmark, with other methods,

demonstrated.[519] Our estimate of 35% overdiagnosis dropped to 33% after adjustment for a small compensatory drop in older, previously screened women, which was only present in one of the two screened regions.

Getting back to Lynge's editorial in *Translational Cancer Research*,[520] she mentioned that,

"A modelling study based on data from England & Wales and Norway indicated the inevitable overdiagnosis to be 2-4%."[521]

Lynge did not only get the title wrong, even though the study she quoted had been published two years previously (it is not ""Breast-cancer tumor size, overdiagnosis, and mammography screening effectiveness" but "Overdiagnosis in mammographic screening because of competing risk of death"), but she also ignored that the study is flawed.

There were many assumptions in this modelling study, e.g. "Postulated cohorts of screened and not screened women ages 50 to 51 were followed for a period corresponding to 10 biennial screening exams during 20 years, and a further 10 years, to ages 78 to 79." So, they did not follow cohorts of real women but constructed them.

Moreover, they used formulas "given by Duffy and Parmar, which assume an exponentially distributed lead-time," and these formulas were derived by using a multistate model for overdiagnosis and Markov Chain Monte Carlo methods on data from two randomised trials.[522] As already noted, such methods are very flexible and allow people to show almost anything they want. Moreover, the two trials Duffy used for his statistical explorations were the Two-County and the Göteborg trials, both of which are unreliable.[523] Duffy and his colleagues estimated the overdiagnosis "to be around 1%."

The final error in the modelling study was that they used an average lead time of 3.2 years, which is 3-5 times too long.[524] [525]

The flawed Euroscreen literature review

When Lynge wrote that, "The most plausible range of overdiagnosis overall was between 1% and 10% in European observational data," she referred to a 2012 literature review with herself, Duffy and de Koning among the authors, published in a supplement to *Journal of Medical Screening*.[526] This review was highly flawed but received a lot of media attention. We commented briefly on it in our *Annals* article:

"A literature review from the Euroscreen Working Group concluded that screening mammography had an overdiagnosis rate of 1% to 10%. However, the review included strong model assumptions about cancer growth patterns rather than observational data, excluded DCIS, and used calculations that included women in the denominator who were much older than those screened."

I published a detailed criticism of the Euroscreen review on *BMJ's* website in 2012.[527] The authors used inappropriate methods, including accepting results of case-control studies. I explained that the Malmö trial investigators found a 4% effect of screening when they analysed their data correctly and 58% when they analysed them as if they had come from a case-control study.[528]

Using flawed methods, the Euroscreen Working Group reported an effect of screening on breast cancer mortality of 38% or 48%. As these estimates corresponded well to the declines in breast cancer mortality we have seen in many countries, the Euroscreen Working Group seemed to say that there has been no effect of adjuvant therapy.

The authors performed a stunning act of hocus pocus that involved extrapolations far beyond the data and arrived at a benefit that was an overestimate of a factor of 16 compared to the estimate from the randomised trials.[529] [530]

I noted that Stephen Duffy, who was quoted in *BMJ's* news piece about the Euroscreen papers,[531] acknowledged that, "The key feature of a successful mammographic screening program is a reduction in the incidence rate of advanced tumors,"[532] and I added that Duffy owes us an explanation how screening can have a dramatic effect without reducing the rate of advanced tumours.

The Euroscreen Working Group noted that,

"In the absence of overdiagnosis, the initial increase in breast cancer occurrence in the screened group would be fully compensated by a similar decrease in cancers among older age groups no longer offered screening - the so-called 'compensatory drop.'"

Since our study of overdiagnosis in Denmark was the most ideal study that existed,[533] it is curious that the Euroscreen group dismissed it with the argument that our overdiagnosis estimate was "not adequately adjusted for breast cancer risk," which, moreover, isn't true.

In the *BMJ* interview, Duffy said "it is good news that lives saved by screening outweigh overdiagnosed cases by a factor of two to one." This is wrong by a factor of 20,[534] and screening doesn't save lives.

Eugenio Paci, another author on the Euroscreen review, said:

"We believe that not only should our conclusions be communicated to women offered breast screening in Europe but that, in addition, communication methods should be improved in order to raise women's awareness and to make information more accessible, relevant, and comprehensible."

I noted that the women in Europe should be spared these terribly false results and drew attention to our leaflet about mammography screening.[535]

Coming back to Lynge's editorial in *Translational Cancer Research*, she mentioned her own benefit-to-harm ratio, which was 2.6, close to Duffy's ratio of 2. The basis for this was a 2017 study from Denmark where she referred to a breast cancer mortality reduction of 23.4% and 2.3% overdiagnosis, which involved assumptions, as the women were followed until age 79,[536] even though this wasn't the case.

Lynge compared her own estimate with that in the Marmot review of the randomised trials, which was 0.33. That her estimate was eight times too positive compared to the Marmot review didn't make her consider if her own methods were reliable. She said, "Not surprisingly, the variation in these estimates derived [sic] from variation in the estimated overdiagnosis, which is the most difficult component for measure [sic]."

Three years later, Lynge published her benefit-to-harm ratio of 2.6 again.[537]

Lynge's non-peer reviewed editorial is a perfect illustration of what Mette hinted at in her *BMJ* editorial about the two Dutch studies that used the same data from Nijmegen:[538] Screening zealots should be disbelieved.

In a long review article, Philippe Autier and Mathieu Boniol described why the screening advocates should be distrusted.[539]

13 Why mammography screening doesn't work

This chapter is important because it explains why mammography screening cannot save lives, even though this is what we hear all the time from the authorities.

Breast cancer is a heterogeneous disease, with widely varying growth rates and metastatic potential. The growth rate is usually constant for long periods of time, and a large study estimated that 90% of the doubling times were between 69 and 1622 days.[540]

Tumour data suggest a marginal effect

However, spontaneous cell death is common and may increase with tumour size,[541] which means that the growth may decrease at some point or stop altogether. Cancers can also regress, which happens for many screen-detected breast cancers.

If we assume that the observed doubling times are constant until the tumour becomes detectable, it means that the average woman has harboured the cancer for 21 years before it becomes detectable at breast screening, at about 10 mm in size. It is therefore misleading to say that cancers are caught early with screening. They are caught very late.

To understand if screening can work and what a plausible effect could be, we can look at the tumour sizes in the randomised trials. There are data on average tumour size from four trials (see table, the sizes are in mm):[542] [543] [544] [545]

Trial	Invited group	Control group	Difference
Canadian trial	16	19	3
Malmö trial	14	19	5
Stockholm trial	14	19	5
Two-County trial	18	25	7
Mean of all trials	**16**	**21**	**5**

Using the formula for the volume of a sphere, we can see that a cancer of 16 mm will grow to 20 mm after one more cell division. The window of opportunity for mammography screening to work is therefore very small, only one cell division, after the malignant cells have already divided over 30 times.

For mammography screening to have more than a marginal effect, quite a few cancers would need to metastasise in this little time window. This isn't plausible, and it doesn't happen. Some cancers never metastasise, and some grow so slowly that it doesn't matter that they would ultimately have metastasised, as the women will die from other causes before the cancer ever becomes a problem.

Many cancers metastasise early, before they can be detected on a mammogram. A German study of 12,423 patients found a linear correlation between tumour size and the existence of one or more positive lymph nodes,[546] and I calculated that tumours with a diameter of 16 mm have metastasised in 35% of the cases. This is a conservative estimate, as many metastases are overlooked, e.g. a US study of 24,740 cases showed that nearly 25% of the node-negative patients eventually develop distant metastases.[547]

As screening is supposed to work by detecting cancers before they have metastasised, we can convert the tumour sizes into an expected effect of screening. The German study showed that tumours of sizes 16 and 21 mm are node-positive in 35% and 42% of cases, respectively, whereas the US study showed a difference of only 4% in node-positive tumours for a size difference of 5 mm. The weighted average of the two studies is 5%.

If we assume for simplicity that all patients with metastases will die from breast cancer, and those without won't, the expected effect of screening is a risk ratio of (42% - 5%)/42% = 0.88, or a 12% reduction in breast cancer mortality. This is close to what the most reliable trials have shown, a 10% reduction after 13 years.[548]

The true effect of screening is smaller than this, however. The tumour size difference of 5 mm is an overestimate because the tumours in the screened group include all the overdiagnosed tumours, which are smaller than other tumours, as they grow more slowly (length bias).

What is missing in the calculations is carcinoma in situ, which is mainly detected at screening. As these lesions are often multifocal, it is difficult to understand how they can be precursors to small single tumours, as is generally stated, unless we assume that the vast majority of these lesions regress.

The tumour data tell us that it is misleading to say to a woman that she has been cured from breast cancer. The cancer may come back at any time, e.g. after 5 or 20 years, and there is no upper limit as to when this could happen.

The data on tumour size show that most published estimates of lead time, generally between 2 and 5 years,[549 550] are wrong. There are only 2.3 times as many cells in a tumour of size 21 mm than in one of size 16 mm, which means that the average lead time for invasive cancer - the time screening brings the diagnosis forward - is only a little more than the doubling time. As the median doubling time in the US study was 260 days, lead time should be less than a year.

Observational data confirm that lead times of two or more years cannot be correct. With such long lead times, the large and persistent increase in breast cancer incidence rates that occur when screening is introduced must be followed by a huge incidence drop when women are no longer screened due to advanced age, but such a drop either doesn't occur or is very small.[551 552]

It is a dubious approach to adjust statistical analyses for lead-time estimates when studying overdiagnosis. Stephen Duffy and other screening advocates consistently do this, and by using too high estimates of lead time and obscure statistical models, they spuriously adjust away virtually all overdiagnosis (see Chapter 6).

We did some studies on lead time based on data recorded in the mammography screening programmes to find out what the average lead time is. In one study, we estimated the clinically relevant lead time for clinically relevant tumours based on the observed incidence reduction after attending the last screening round in Norway.[553] We compared this estimate with estimates based on models that do not take overdiagnosis into account, for varying levels of overdiagnosis, and found that clinical lead time was about one year. When overdiagnosed tumours were included, which is inappropriate, as harmless tumours, in principle, have an infinite lead time, the estimates increased to 4-9 years.

We explained in another article why it is wrong to use model-based estimates of lead time, which are theoretical constructs where the time when the tumour would have caused symptoms is not limited by the person's death.[554] We noted that the differences in the

estimates of overdiagnosis in the scientific literature were mainly caused by using different definitions and methods and not by variations in data.

Tumour data suggest the Two-County trial is unreliable

Tabár, Duffy and Day have asserted that the 30% reduction in breast cancer mortality they reported for the Two-County trial can be explained by their tumour data,[555] [556] but this is not the case.

Data from this trial presented in a graph showed that after 10 years, 6% of women with cancers between 10 and 14 mm in size had died, whereas 11% of those with cancers between 15 and 19 mm had died.[557] Thus, a difference in size of 5 mm corresponded to a difference in breast cancer deaths of 5%, which is in good agreement with the difference of 5% in tumours with metastases as calculated above. However, this did not correspond to a 30% reduction but only a 12% reduction in breast cancer mortality.

Other tumour data from the Two-County trial are also implausible (see the table):

Study	Tumour size	Metastases or deaths
German study	12	29% with metastases
	17	36% with metastases
	24.5	46% with metastases
Two-County trial	10-14	6% died from breast cancer
	15-19	11% died from breast cancer
	20-29	34% died from breast cancer

Considering the linear relationship between tumour size and the risk of metastasis, it is implausible that the death rate increases dramatically for the largest cancers. This big jump cannot be explained by random variation because there were 39 cancers at the first screen in the Two-County trial with a tumour size between 20 and 29 mm.

These and other data suggest that the reported data on tumour size and breast cancer deaths in the Two-County trial are unreliable.

Using other methods than mine, Per-Henrik Zahl and colleagues have also showed that a 30% reduction in breast cancer mortality is not possible, considering the tumour stages in the Two-County trial.[558] Their study was criticised by the chairman of the Swedish Cancer Foundation's Planning Group for Mammography Screening, Lars Erik Rutqvist who declared it "lacked scientific merit,"[559] but there was only empty rhetoric in this criticism.

The leader of the Norwegian screening programme at the time, Steinar Thoresen, was also disdainful. He remarked that Zahl's study should not have been accepted in a scientific journal; that he didn't know the motives of the Institute of Public Health (where two of the authors worked) for the "very unscientific battle it conducted against mammography screening;" and that he feared the Institute's credibility also in other areas would suffer.[560]

Thoresen also complained that the authors had not cited Tabár's first "beyond reason" study that claimed a screening effect of 63% based on flawed methods[561] (see Chapter 5).

Zahl calmly replied that the authors - in contrast to Thoresen - didn't have any economic interests in screening.[562] He sent me data from the Norwegian Cancer Registry that showed that the incidence increase after the prevalence round in Norway when screening started was for localised cancers while the rates of cancers with regional or distant metastases were unaffected by screening.

Similar findings were reported by researchers from the Norwegian Cancer Registry and the Institute for Population-Based Cancer Research.[563] However, they delivered the politically acceptable but scientifically wrong conclusion that their findings indicated that the programme worked as intended. Two years later, they showed that the total number of cancers that had metastasised *increased* when screening started and remained higher than before screening even eight years later.[564]

Even though it seemed to have been cut in stone that screening didn't work in Norway, the authors concluded otherwise: "Breast cancer diagnosed in the screening period had prognostically favorable tumor characteristics compared to breast cancer diagnosed in the prescreening period." They must have known that their statement was scientifically dishonest.

Everyone working with screening knows that overdiagnosed cancers have favourable tumour characteristics, and it is therefore deceptive to tell your readers about percentages. "Cosi fan tutte" was the title of one of Mozart's operas. They all do it – deceive people – and I shall explain again what is wrong with percentages.

If, for example, 60 of 100 cancers in a group without screening are advanced, and the only thing screening does is to overdiagnose another 30 localised cancers (which agrees fairly well with data from the Malmö trial),[565] then the percentage of advanced cancers is 60/(100 + 30) = 46% in the screened group and 60/100 = 60% in the control group. Thus, although the absolute rate of advanced cancers was not reduced with screening, there were *relatively* fewer advanced cancers with screening.

In 2002, Tabár, Duffy and Smith published a letter in *Lancet* where they noted that those trials that lowered the rate of node-positive cancers also lowered breast cancer deaths.[566] They showed the results in a table but did not perform a statistical analysis and they only included women in the age group 40-49 years.

This was curious, as the effect of screening has always been controversial in young women, and because their letter was a reply to Nyström's 2002 meta-analysis that included all ages.[567]

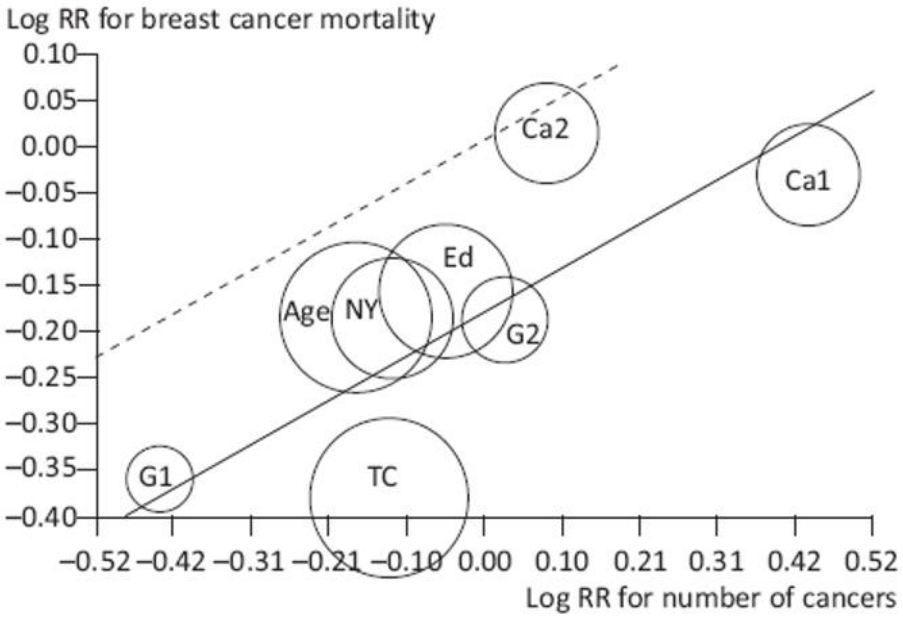
I have tabulated all the data on cancers and deaths from the trials and decided to investigate if I could reproduce their findings, using explicit methods and data for all the women that were included in the trials.[568]

Since the purpose of screening is to advance the time of diagnosis, thereby reducing the occurrence of cancers with metastases, trials that find many cancers, compared with the unscreened control group, will be expected to have the largest effect on breast cancer mortality. However, there was no such relation ($p = 0.19$ after 7 years and $p = 0.73$ after 13 years of follow-up).

In contrast, there was a significant relation in the expected direction for cancers in stage II and above ($p = 0.04$ after 7 years and $p = 0.006$ after 13 years of follow-up), and for node-positive cancers ($p = 0.008$ and $p = 0.04$).

This was reassuring but there was a problem, and it was not a small one. The linear relation between advanced cancers and breast cancer mortality was in the wrong place (see the figure on the next page). A screening effectiveness of zero means that the rate of node-positive cancers is the same in the screened group as in the control group, but this corresponded to a significant 16% reduction in breast cancer mortality (95% CI 9% to 23% reduction; when

log relative risk (RR) = 0.00 for number of cancers, then log RR for breast cancer mortality was −0.18, and RR for breast cancer mortality was 0.84).



The figure shows the relation between detection of node-positive breast cancer and the risk of dying from breast cancer in the randomised trials after 13 years of follow-up. Fewer node-positive cancers in the screened group are associated with fewer breast cancer deaths (lower left corner). Circle areas are proportional to the weights in the regression analysis. The hatched line represents an unbiased regression line that goes through (0,0) and has the same slope as the calculated regression line.

What this figure shows is bias, not a true effect of screening. Further analyses demonstrated that assessment of cause of death and of the number of cancers in advanced stages were both biased. Since the size of the bias, 16%, was similar to the estimated effect of screening, this result suggests that screening is ineffective.

In the United States, the age-adjusted incidence of breast cancer was rather constant before screening. When screening spread in the 1980s, there was a sharp rise in cases of carcinoma in situ. This would be expected to be followed by a decrease in the incidence of early-stage invasive breast cancer later, but this also increased,[569] and the incidence of cancers with metastases changed very little.[570 571]

Other studies of tumour data

Also in the Netherlands, screening did not reduce the incidence of cancers with metastases, but Harry de Koning and colleagues claimed the opposite in the title of their study:

"Decreased rates of advanced breast cancer due to mammography screening in the Netherlands."[572]

They split cancers with metastases in two groups, above and below 2 cm in size, which makes no sense as they had all metastasised. They were therefore all advanced cancers, and the 2 cm criterion is used to distinguish between advanced and non-advanced cancers when it is not known if they have metastasised.

What immediately catches the eye in their paper is a graph with metastasised cancers bigger than 2 cm that appear to go down over time. The inappropriate split of the data is misused in the abstract, which only mentions these cancers and notes that their incidence declined significantly. When I added the data from the graphs, I found that there was *no reduction* in incidence of cancers with metastases. In fact, the combined incidence was identical for the first year reported in the paper, 1989, and for the last year, 1997.

The authors concluded, "It is evident that breast cancer screening contributes to a reduction in advanced breast cancers and breast cancer mortality." This is not what their study showed, and there wasn't even data on breast cancer mortality in the paper.

The discussion section was also deceptive: "It is important to realise that the initial increase does not signify overdiagnosis, but that it is the result of the necessary downstaging of breast cancer diagnoses, if screening will be effective. Several authors concluded that overdiagnosis might be limited to a few percent."

There was no downstaging to cancers that had not metastasised and the overdiagnosis is far bigger than a few per cent.

What the study really showed was that screening doesn't work and causes a huge amount of overdiagnosis, as the incidence of localised cancers doubled, with no sign of a decrease later. Thus, de Koning's paper was seriously dishonest.

A 2012 study by Mette Kalager et al. from Norway didn't find a decline either in advanced cancers caused by screening.[573] They found the same decline of 24% in stage III and IV disease in screened and non-screened groups, which were women in the same age group and time period. Their study took advantage of the staggered introduction of breast screening in Norway in creating a reliable control group, and the decline was therefore caused by factors other than screening, most likely increased breast cancer awareness.

Another 2012 study from Norway, by Solveig Hofvind from the Cancer Registry of Norway and colleagues, was flawed, as the authors compared attendees with non-attendees within the screened areas.[574]

They reported that the incidences of stages III and IV cancer were two and three times lower, respectively, among participants compared to non-participants ($p < 0.001$ for both). As those who attend are very different from those who don't attend, their study cannot say anything about whether a screening programme leads to more favourable prognostic features in the detected cancers.

We alerted people to the flaws in this and other studies on *BMJ's* website.[575] Quite often, claims of a decline in advanced cancers had been made in studies with no control group.

A systematic review by Philippe Autier and colleagues from 2010 that included several countries and regions from the United States, Europe and Australia found that, on average, the rates of advanced cancers, defined as those larger than 20 mm, were not affected by screening.[576]

What does all this mean? We should never forget that the little effect screening might have had in the old screening trials, was offset by increased mortality from other causes in the screened groups, as there was no reduction in total cancer mortality and no reduction in total mortality.[577]

Michael Baum alerted people to this fact in a 2013 article in *BMJ* with the declarative title, "Harms from breast cancer screening outweigh benefits if death caused by treatment is included."[578]

He noted that, for the type of radiotherapy used when the trials were performed, the risk ratio was 1.78 for lung cancer death and 1.27 for death from a heart attack. Allowing for better treatments since the trials were performed, Baum found that 3-4 women per 10,000 screened avoid dying from breast cancer (assuming 15-20% effect of screening on breast cancer mortality) and that 3-9 per 10,000 screened will die from lung cancer or a heart attack because of radiotherapy.

Cochrane advises against preprints, is highly ineffective, and protects its "brand"

I updated our Cochrane review in January 2023 because many more deaths had been published since our 2013 update. One month later, my co-author, Karsten Juhl Jørgensen, had independently assessed the new data and agreed with what I found. The updated mortality data show even more clearly than before that mammography screening does not save lives. I published these data in May 2023 on my website in the public interest.[579]

The current requirements for Cochrane reviews are so extensive that it took six months for Karsten to fulfil them. We submitted the update in August 2023 and were told by Colleen Ovelman, who has the pompous title of "Executive Editor and Acting Head of Editorial Evidence Production & Methods Directorate, Cochrane Central Editorial Service," that they hoped to be able to send comments to us in November.

When we had not received any comments from the editors despite our reminders, I asked about the process in late December and was told that, "We have had some unforeseen circumstances that delayed the processing of your review."

Although we had not included any new trials, it took six months before we got any feedback. The peer reviews we received - from 11 people, 8 of whom were from Cochrane - were excessive, with 91 separate points we should respond to[580] (7,290 words, or the size of two normal scientific articles).

The many comments we received on the very minor, fourth update of a well-known and highly cited Cochrane review that had been around for 23 years illustrates that Cochrane had become a highly bureaucratic and ineffective organisation, which is why its major funder cut all the funding to the UK based Cochrane groups in 2023.[581]

We replied to the 91 comments and sent a revision of the review to Cochrane in March. The document was now 12,559 words. We had concerns about some of the comments, and the most important ones were these:

Cochrane comment: "There is no presentation of the result of data on all the eligible trials as a group."

Our reply: "We did not present a summary estimate for the low- and high risk of bias trials combined. This is in accordance with accepted standards when differences in risk of bias between trials can explain the heterogeneity. Here, there were substantial differences between the most (> 40% reduction) and least (no benefit) trials, and confidence intervals did not overlap. In such cases, one should trust the low risk of bias trials and a summary estimate that includes both low and high risk of bias trials would provide a misleading effect estimate."

Cochrane comment: "Measuring overdiagnosis is controversial, lacking agreement on how to estimate this theoretical construct … Please only include outcomes which have been clearly defined and transparently measured in the results sections of the discussion and summary sections of the review."

Our reply: “Our analysis of the increase in breast cancer diagnoses and the interpretation that this constitutes overdiagnosis is the same as in the review from the UK Independent Panel (Marmot et al.)[582] … Overdiagnosis in breast screening has taken a long time to become commonly accepted as the most important harm. Any systematic review that does not aim to quantify overdiagnosis would be deficient and would fail to allow an informed choice.”

Cochrane comment: “Authors should use language that accurately reflects the certainty of results. For example, statements such as ‘The most reliable trials did not support that breast screening reduce breast cancer mortality for any age group.’ should be rewritten to read ‘The most reliable trials indicated low certainty evidence that breast screening may make little to no difference to breast cancer mortality for any age group.’” Another Cochrane comment was very similar, but suggested we should write “uncertain evidence” instead of “low certainty evidence.”

We replied to these two comments that we found the suggested sentence very complex and not suitable for a plain language summary intended for others than those who work with the GRADE system on a daily basis: “Essentially, the meaning of the two texts is the same: the burden of proof for this intervention has not been lifted.”

Cochrane comment: “as stated in section 15.6.4 in the Cochrane Handbook, ‘If the confidence interval for the estimate of the difference in the effects of the interventions overlaps with no effect, the analysis is compatible with both a true beneficial effect and a true harmful effect. If one of the possibilities is mentioned in the conclusion, the other possibility should be mentioned as well’. Therefore, statements such as ‘did not show a benefit in terms of a reduction in breast cancer mortality’ should be amended to read ‘may show little or no difference in terms of a reduction in breast cancer mortality’ ... Similar edits should be made throughout this section.”

Our reply: “We find the recommended wording unclear and unnecessarily confusing. The question is if the trials can lift the burden of proof that an intervention is beneficial and in this case they cannot … Furthermore, it is subjective whether a difference is ‘little’ or not, which we therefore prefer to avoid.”

We felt we had responded adequately to the comments and expected the update to be approved quickly.

Ten weeks later, we had become a little impatient and inquired about the progress with our review. We noted that, a couple of days earlier, the Canadian Task Force on Preventive Health Care had published new draft recommendations on mammography screening,[583] which would obviously cause controversy and protests, and an update of our review was therefore highly timely.

Liz Bickerdike, Senior Managing Editor at Cochrane, apologised for the delays: “Unfortunately, one of the sign-off editors is unavailable which has led to some delays in assessing your revised draft review. I appreciate delays are frustrating. Please be assured that we are working to address this as quickly as we can. I expect to be in touch regarding an editorial decision by the end of the month.”

We replied that, “given the rapidly evolving situation in this area where two major guideline groups (the U.S. Preventive Services Task Force and the Canadian Task Force on Preventive Health Care) have sent out conflicting recommendations within the past month, we believe it is very important for an informed debate that our update is made available to the public and to decision makers. As it seems unlikely that our updated Cochrane review

will see publication this side of summer vacations in the northern hemisphere, we will upload it to medRxiv.org …"

Bickerdike was unhappy with this: "Cochrane does not currently have a specific preprint policy, and as such, we advise authors not to upload preprints of unpublished reviews to online preprint servers. Should you choose to upload the draft please note that it cannot represent an affiliation to Cochrane and cannot be described as a Cochrane Review."

This raised three interesting questions. If an editor is unavailable in a big, professional organisation, shouldn't there then be another editor who can sign off on a very important review? And, as far as I know, all prestigious medical journals accept publication of preprints, so why not Cochrane, which is supposed to provide up-to-date information of importance for decision making in healthcare? Finally, why the obsession with the "Cochrane brand?" As my co-author is employed at Cochrane Denmark, he cannot possibly avoid representing his affiliation to Cochrane in a preprint. And we cannot avoid that our preprint is of a Cochrane review, which everyone can see it is.

We responded that several other updates of a Cochrane review had been prepublished and uploaded our review as a preprint[584] in the public interest, which Cochrane should be concerned about but isn't.

This much appreciated outside Cochrane. During the first two days, over 50,000 people saw my tweet about the updated review.

We thought there couldn't be much more to discuss, but we had underestimated the Cochrane bureaucracy and censorship yet again. Three months later, we received 34 pages of comments, divided on 38 points and were told a major revision was needed, and that, if it was not accepted, the update would not be published, with no appeal. This was highly frustrating, also because some of the reviewers did not understand the basic issues.

I will report on the final outcome of this Cochrane Odyssey on scientificfreedom.dk/the-news/ (search for "breast cancer").

It seems that Cochrane has not learnt from past mistakes. As already noted, when I first published the review in 2001, the Cochrane Breast Cancer Group would not allow us to publish the harms of screening even though they were included in the protocol for the review, the group had approved and published. We therefore had to publish our full review in *The Lancet* to ensure the harms became known.[585] It took five years, with complaints to the Cochrane Steering Group, before the harms data became included in the Cochrane review.[586] FIVE YEARS!

In 2001, the editors of the Cochrane Breast Cancer Group insisted that "the review in *The Cochrane Library* is stronger" whereas I noted that the version we published in *The Lancet* "lives up to Cochrane standards better."[587] Our *Lancet* review was much more of a Cochrane review than the Cochrane review. It was the same, but also included the harms of screening, and it did not lump unreliable studies with reliable studies, which the Cochrane editors had forced us to do, even though it is misleading, and which we didn't do in our submitted 2023 update of the review.

Lancet's editor, Richard Horton, wrote that, "if a difference remains, let the scientists doing the review publish what they wish to say – it is, after all, their work. The editors can present their own view as a supplementary discussion or comment. That way, the debate proceeds properly, each side is given its voice, accusations of censorship are avoided, and the public sees science as a truly collaborative process, in which differences of opinion are not only respected, but also welcomed."[588]

I wish medical journals would heed this advice, which they, including *Lancet* itself, unfortunately often don't do.

When I showed the draft of this article to a colleague who is very familiar with Cochrane, she responded: "Seems like Cochrane is up to its old tricks … obfuscate and delay."

Time will show how the editors will handle our important objections to some of their proposals, and how long it will take before our updated review appears in *The Cochrane Library*. I find it particularly odd that Cochrane staff asked us to communicate that when the confidence interval includes 1, the intervention could be both beneficial and harmful, but then advised us to write: "may show little or no difference in terms of a reduction in breast cancer mortality." This wording excludes the possibility that screening could increase breast cancer mortality, and "little" is subjective and should not be used. How little should little be in order to be little, and how far can the confidence interval be from 1 before little becomes not little?

The three trials with adequate randomisation did not find an effect of screening on cancer mortality, including breast cancer, risk ratio 1.00 (95% CI 0.96 to 1.04) or on all-cause mortality, risk ratio 1.01 (0.99 to 1.04). The updated mortality data confirmed what we showed 24 years ago in *Lancet*,[589] that mammography screening doesn't save lives.

There are several reasons why I think the situation isn't any better today.

First, the women didn't receive much adjuvant therapy in the old trials. Only 0.04% in Kopparberg got hormonal treatment, even though tamoxifen is very effective, and only 0.4% in Malmö and Kopparberg received chemotherapy.[590]

Second, the detection methods have improved and overdiagnosis has therefore increased, as evidenced by data from New South Wales,[591] and this increases mortality from the harms of radiotherapy and chemotherapy.

Third, greater breast cancer awareness has played a role. In Denmark, the average size of the tumours was 33 mm in 1978-79, which decreased to 24 mm in 1988-89.[592] This change occurred before screening started, and it was beneficial, as it did not lead to overdiagnosis.[593] The difference of 9 mm is much greater than the average difference between the screened and the control groups in the trials, which was only 5 mm. This suggests that breast cancer awareness has been more important than screening for the decrease in breast cancer mortality we have seen in many countries.

Fourth, the decrease in breast cancer mortality has consistently been larger in young age groups that were not screened than in the screened age groups (see pages 55 and 58).

I cannot possibly come to any other conclusion than that screening doesn't work. The theoretical rationale for screening seems to be wrong, too.[594]

Problems with reading mammograms

In the screening debates, there has been surprisingly little discussion of the problems with reading mammograms.

In the randomised trials, those who read the films were highly motivated, as they hoped to show screening worked. In everyday practice, it is difficult to attract top-level doctors to something as boring as looking at mammograms, day in and day out. Even dedicated people will have difficulty maintaining concentration and carefulness when by far most of the readings are negative, and it is regarded as one of the most difficult tasks in radiology to spot cancers on mammograms. There is a scarcity of doctors for the job, and the quicker the reader is, the more money will be earned, and the more women can get screened.

These facts invite big trouble. Radiologists miss many breast cancers and the level of agreement when two or more observers evaluate the same mammograms independently is poor.[595 596 597 598]

US surveys have shown that average doctors missed more than 25% of the cancers, and some clinics missed nearly 40%.[599] But essentially nothing happens when doctors perform very poorly; they just go on missing cancers. More than 40% of US clinics had been cited for violating one or more federal rules every year.

Recall rates for further investigations because of a suspicion of breast cancer are about twice as high in the United States as in the UK, although cancer rates are similar.[600] Open surgical biopsies that don't result in a cancer diagnosis are also twice as high. Another study found that the recall rate in 31 US practices varied from 2% to 13%, which suggest serious problems with reading the mammograms.[601]

Regular self-examination doesn't work either

In 2003, we published a review of trials of regular self-examination, once a month.[602] There was no effect on breast cancer mortality whereas it doubled the number of biopsies. It is therefore harmful.

Women should consult a doctor if they find something unusual in their breasts but should not screen them.

14 Concluding remarks

> *The primary goal for all cancers is to reduce their occurrence. The best thing you can do if you are a woman in the screened age group is not to attend screening. This will lower your risk of becoming a breast cancer patient by one third and your risk of losing a breast by one fourth.*

In 2016, I got the HealthWatch[603] Award for my detective work in healthcare and was invited to London to give a talk. It started this way:[604]

"People ask me, why do you look for controversies? And I tell them, I don't, they come to me. My work is something like that of a medical detective. People come to me if they feel something is wrong in healthcare. When I start looking into these issues, I usually dig very deep. I find skeletons, and when I expose these skeletons, the people who buried them can get very angry."

Scientists should be driven by facts, logic, and uncompromising honesty, and they should strive to get as close to the truth as they can. However, during my long research career, my opponents, usually males, have often been driven by emotions, career aspirations, strong beliefs, money, and fame, with no interest whatsoever in moving science forward through a rational debate, as this could threaten their positions, self-esteem, and income.

As you have seen in this book, when it comes to mammography screening, the extent to which screening advocates are ready to violate basic scientific principles to arrive at politically acceptable but wrong results in their research is astounding. The saying that, "There is none so blind as he who *will* not see,"[605] often crossed my mind when I read research articles and letters to the editor in this area.

In 2009 to 2011, our research showed that mammography screening cannot be justified[606] considering its lack of effect on breast cancer mortality[607] and substantial overdiagnosis rate.[608] [609] We also demonstrated that invitations to screening were untruthful to such a degree that informed consent wasn't possible.[610]

When I published my evidence-based book about mammography screening in February 2012,[611] I therefore thought we were close to a tipping point where screening would be abandoned because it would be impossible for the politicians to continue defending it.

But I underestimated how much power conflicted people have in healthcare and how important it is for politicians to save face.

I published 36 papers on mammography screening in peer reviewed journals including three of "the big five" (*BMJ*, *Lancet* and *Annals of Internal Medicine*) and 139 other articles, but my main reward has been a lot of trouble and enemies, and that the dishonest research by screening advocates became even more deceptive and untruthful.

The debate stopped after the 2012 UK "Yes Minister" report

After my dreadful experience with the flawed "Yes Minister" 2012 Marmot report,[612] which came out nine months after my book had documented how unreliable most of the research is, I gave up and did not publish much about mammography screening after this.

The heated debate about breast screening I had started in 2000 lasted 12 years. But even though the Marmot report largely stopped it, a lot of bitterness and disappointment was left behind among people whose capacity for logical thinking was still intact, and it won't go away.

When the Two-County trial was published in 1985, Swedish researchers remarked it was necessary to look also at total mortality and they called for a debate.[613] The Project Group for the trial and the Swedish National Board of Health, which had supported the trial, replied that an account of total mortality would be irrelevant and without basis in scientific practice and that it was an absurd idea that screening could have increased mortality.[614]

Eleven years after these surprising remarks from the highest authority on health in the country, the Swedish trialists, including Tabár, the primary investigator for the Two-County trial, admitted that "the total cumulative mortality would seem to be the most objective measure."[615]

As noted earlier, it is disingenuous to suggest that total mortality is irrelevant, as screening inevitably increases mortality because of the extra deaths caused by radiotherapy and chemotherapy when used for overdiagnosed, healthy women.[616]

In 2004, Michael Baum noted that, "the bland assumption that the process of diagnosis and treatment of screen-detected lesions in the population at large, some of which might never have expressed a malignant potential in the woman's natural lifetime, is totally free of risk to life, is breathtaking in its arrogance.[617]

We knew from the beginning that total mortality was important and therefore reported it in our assessment of the trials to the Danish Board of Health in 1999 and in our first review of the screening trials in *Lancet* in 2000.[618]

From 2001,[619] [620] we also reported on total cancer mortality. This is one of our most important findings, as a reduction is expected if screening is effective. It has been ignored in the scientific literature, likely because it is threatening for the screening advocates.

Screening doesn't reduce total cancer mortality including breast cancer, risk ratio 1.02 (95% CI 0.95 to 1.10) after 10 years in the trials with adequate randomisation.[621] I explained this in some detail in 2004[622] and in our updated Cochrane reviews. The risk ratio for total cancer mortality in screened women would be 0.95 compared with controls if a 29% reduction in breast cancer mortality had occurred as was claimed. But what was reported in the same trials was a risk ratio for total cancer mortality of 1.00, which is significantly higher than expected (p = 0.02).

We report in our Cochrane review that data from the Two-County trial illustrate the misclassification directly. Among women with a diagnosis of breast cancer, mortality for other cancers was significantly higher in the screened group and mortality from all other causes also tended to be higher. The increase in mortality for causes other than breast cancer amounts to 38% of the reported decrease in breast cancer mortality in the Kopparberg part of the trial and 56% in the Östergötland part.

Thus, the implicit premise for using breast cancer mortality as outcome in screening trials - that an effect of screening translates into a proportional effect on all-cause mortality - is obviously invalid. The use of blinded end-point committees or official cause-of-death registers cannot avoid this bias.

The authors of the Marmot review did not report on total mortality or total cancer mortality, and they distorted the evidence by extrapolating the data far beyond the data range, which is impermissible. They also ignored that there were only two trials with adequate randomisation and ignored the many biases in the remaining trials. We had written about this in our Cochrane review three years earlier:[623]

"The largest effects on breast cancer mortality were reported in trials that had long intervals between screenings (Two-County trial), invited a large fraction of the women to only two or three screenings (Two-County and Stockholm trials), started systematic screen-

ing of the control group after three to five years (Two-County, Göteborg and Stockholm trials), had only one-view mammography rather than two views (Two-County trial), and that had poor equipment for mammography (New York trial); and the cancers found with mammography were considerably smaller in the Canadian trial than in the Two-County trial.[624] This suggests that differences in reported effects are related to the risk of bias in the trials rather than to the quality of the mammograms or the screening programmes."

The idea of parading a group of women whose "lives had been saved" by screening at the Marmot press conference (see page 102) reminds me of the propaganda for depression pills.

In a radio debate I had with MIND's National Chairman in Denmark, Knud Kristensen, he argued that some of their patients had said that depression pills had saved their life.[625] I responded that it was an unfair argument because all those the pills had killed couldn't raise from their graves and say the pills killed them. It is the same with mammography screening; it kills some women who are healthy but were overdiagnosed.

We ended our letter in *Lancet* where we criticised the Marmot review with a question: "Is it acceptable that a public health initiative each year converts thousands of healthy women into cancer patients unnecessarily, which is fatal for some of them?"[626]

Even with an optimistic view of screening, the effect is barely visible

If we assume, contrary to the evidence, but for the sake of the argument, that the claimed effect of screening on breast cancer mortality in the randomised trials can be translated into a similar effect on total mortality, then a woman's life will be extended by one day, on average, after ten years of screening.[627]

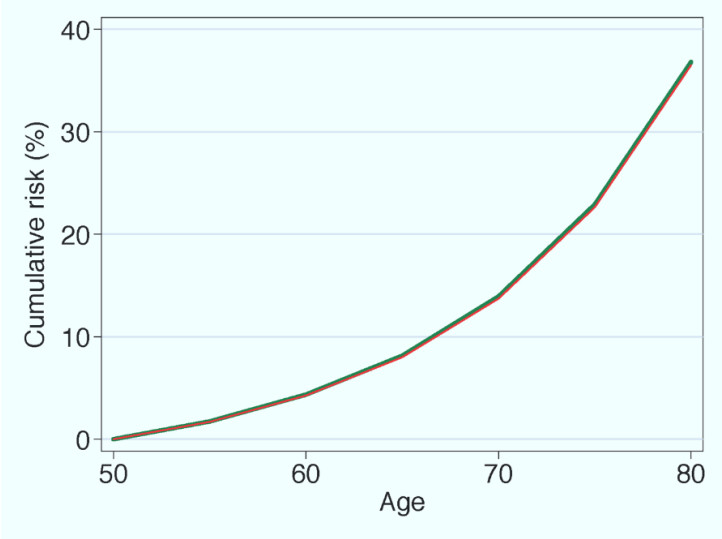
From this, we need to subtract the time it takes to travel and attend the screening sessions and the time used by staff members and other people, e.g. general practitioners. This is probably more than one day in 10 years, and the overall effect is therefore negative. Even if we assume that screening reduces breast cancer mortality by 30%, the life extension would only be two days.

The Marmot review claimed, assuming a 20% reduction in breast cancer mortality, that screening leads to a life extension of 27 days.[628] Obviously, this exaggeration of a factor of about 25 is only possible through impermissible extrapolations with untenable assumptions.

For comparison, women with node-positive breast cancer obtain a life extension of six months, on average, when they are treated with tamoxifen for 10 years,[629] which, in addition, is very cheap.

Donald Berry has compared the claimed effect of screening with mishaps in life and noted that the same increment in expected additional life could be obtained by losing an ounce of body weight or wearing a helmet for ten hours of bicycling.[630]

If we assume that screening reduces breast cancer mortality by 20% and that this translates into a reduction in total mortality, then the curves for the cumulative risk of dying look like this:



Courtesy of Professor Paul Pharoah, University of Cambridge

The green line is the cumulative risk of dying without screening; the red line is the risk of dying with screening (deaths caused by overdiagnosis have not been included).

It would have been difficult to sell screening to politicians by presenting such curves, and they are even too positive, as the two lines should have been identical.

What we have heard virtually nothing about is how often women suffer from chronic pain after surgery. Two to three years after breast cancer treatment, 47% of the women reported pain, usually several times a week, and only half of those with pain reported it was mild.[631] The pain was equally common after breast-conserving surgery as after a mastectomy, and it was more common when the women had received radiotherapy. Thus, half of all women – including all the overdiagnosed, healthy women – will suffer from chronic pain, some for the rest of their lives.

We have also heard far too little about what it means to be overdiagnosed. A patient with carcinoma in situ wrote in 2009 in the *Sunday Times*:[632]

"I expect that I have been classified as a screening success. Yet, everything about my experience tells me the opposite. Screening has caused me considerable and lasting harm … Two wide excisions, one partial mutilation (sorry, mastectomy), one reconstruction, five weeks' radiotherapy, chronic infection, four bouts of cellulitis (a bacterial skin infection), several general anaesthetics, and more than a year off work."

In the same article, the UK Department of Health noted it didn't agree with our numbers and said, "The majority of international experts on breast screening would agree with us." As our numbers come from the trials, it is not a question of agreeing or disagreeing, it's a question of facts. And who are the "experts"? No doubt most of them are conflicted.

Eight days earlier, a *Lancet* editorial, "The trouble with screening," described our information leaflet and our numbers, without any reservations about them, and quoted us for saying that the responsibility for the information provided should be kept separate from that for the screening programme.[633]

Getting a cancer diagnosis – or just being told that it could be cancer and that additional investigations are needed – can impact importantly on people's lives. Suicides have been reported, and in one case the woman wrote her suicide note on her recall letter.[634] The

strongest increase in suicide rate among cancer patients is seen in the first year after diagnosis where there is a 16-fold increase.[635]

In absolute numbers, this is a small problem, but when a cancer diagnosis can increase suicide rates, it may also increase mortality from other forms of self-destructive behaviour, which are quantitatively far more important. A woman who thinks she will die from breast cancer may not be particularly motivated to give up smoking or drinking.

It is strange that so much money is wasted on something that doesn't work and causes massive harm.

In the most recent trial, the UK age trial, which randomised women aged 39-41 years, the ten-year risk of dying from breast cancer in the control group was only 0.2%.[636] A woman's risk of dying from breast cancer in her lifetime is less than 3% whereas her risk of dying from cardiovascular disease is ten times bigger. Thus, instead of screening for breast cancer, we should focus on preventing cardiovascular disease for which many effective interventions exist.

Since the 1990s, we have had a Breast Cancer Awareness Month every October where people adopt the pink colour and display a pink ribbon. There are also "Running for the cure" events that attract thousands of people.

It is fine to run because it lowers the risk of dying from a heart attack but you should not only run once a year to support cancer charities (see figure on next page), you should run several times a week to support yourself.

You should distrust what authorities say about screening

As I have shown throughout this book, there are good reasons to distrust politicians, boards of health, people responsible for screening programmes, invitations to get screened, people earning a living from screening, cancer charities and, more broadly, most people publishing research on screening.

Screening advocates deliberately spread misinformation and sometimes lie about the facts. They know that the politicians cannot judge who is right and who is wrong and therefore tend to rely on authority rather than on sound science.

These authorities have done science and the women a great disservice by systematically deceiving the public, although they constantly remind us that what they do, they do on behalf of the women.

Scientific debates are frustrating when your opponents have disregard for the evidence. You often get nowhere even when you demonstrate that those you criticise have used wrong numbers, performed erroneous calculations, or manipulated the data beyond belief.

The opposite problem occurs when dishonest researchers criticise well-done studies whose results they don't like and use a myriad of tricks, emphasising trivial or irrelevant issues, magnifying dots to make them look like hand grenades, inventing problems that don't exist, claiming non-existing numerical errors, misrepresenting the methods and - if all else fails - lying.

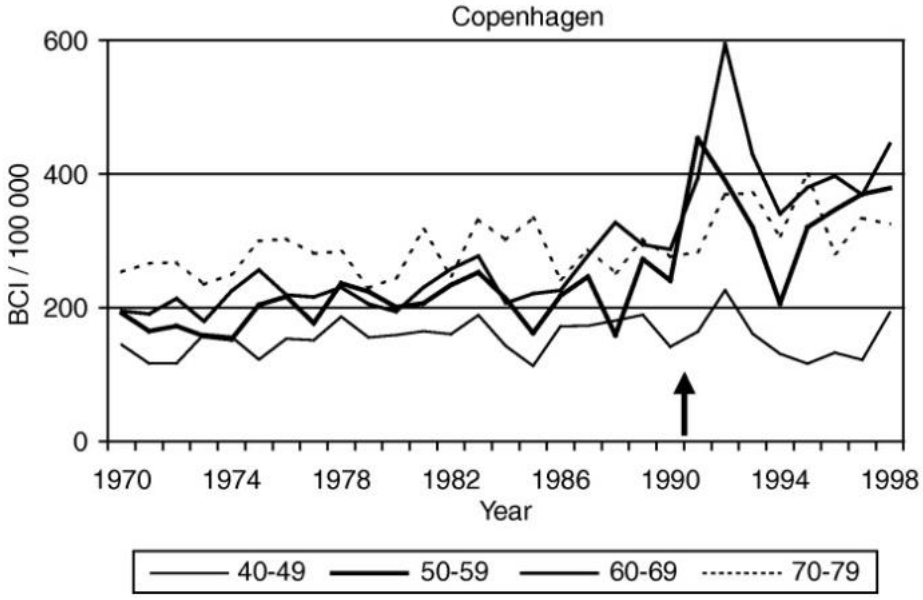
On numerous occasions, my opponents have accused me of having made errors in my calculations, but they mostly gave themselves a free ride by not saying what they were.

The fraudsters' tactics are often so skilfully deceptive that neither the editors nor the readers have the necessary expertise to see through the smoke, particularly when the tricksters hide what they have done in an impenetrable cloud of mumbo jumbo and statistical models with no documentation that the assumptions they use are correct.

I have provided numerous examples of this dishonesty in my book. Unfortunately, human psychology is such that people have greater respect for what they don't understand than for what they understand. This is one of the reasons why the tricksters often win debates with genuine researchers.

The screening advocates' approach to science is not hypothesis testing in the Popperian sense, running a risk of falsifying their theory. It is to torture their data till they confess. This type of "research" involves an element of circular reasoning because they start out with a strong belief and then manipulate the data to support that belief. What they do is not even induction as described by David Hume, which means making generalisations based on observations, because they ignore what they see, which we call wilful blindness.

As an example, a paper that looked at trends in breast cancer incidence and mortality in the Nordic capitals related to mammography screening didn't mention overdiagnosis with a single word even though the authors, which included Lynge and Nyström, presented this graph from Copenhagen (the arrow marks the start of screening):[637]



The Two-County trial has been by far the most influential trial in starting and maintaining screening programmes despite mounting criticisms, unanswered questions, and demonstra-

tions that the data on numbers of randomised women, numbers of cancers in various stages, and breast cancer mortality are so implausible and inconsistent that people have suspected scientific misconduct.[638] [639] It is beyond doubt that some of the numbers that have been published are false.

Money drives the misinformation

The fierce *ad hominem* attacks I have been exposed to have exclusively involved males, the only exception being Ilse Vejborg from Rigshospitalet, but she was always in aggressive male company when she charged. Perhaps it reflects the eternal problem of males being unable to control their testosterone-enhanced aggressiveness when challenged; some end up in jail and others become professors.

Money is the main reason why women are being misled about breast cancer screening. I once asked a famous Danish tumour biologist, Keld Danø, during a coffee break at an international meeting, whether he agreed with me that it was impossible to lower breast cancer mortality by 30% with screening, based on our knowledge of tumour biology.

He agreed. I then asked why people like him didn't participate in the scientific debate. He didn't reply and it is not difficult to imagine why. It is not wise to point out that your colleagues are wrong when you are on the receiving end of major funds from a cancer charity. It has long been suspected, although difficult to prove, that donations from such charities tend to favour those in the funding committee or their friends, and those who share their beliefs.[640]

It is not easy to get funding if you have views or results that are not mainstream. It is much easier to produce untrustworthy results people like to see, which is what Elsebeth Lynge has done. She opened a centre for epidemiology and cancer screening at the University of Copenhagen and has received millions in support from the Danish Cancer Society.

Several colleagues doing independent research on cancer screening have told me they have been threatened by key people with influence in funding committees at cancer charities. They have also said they have modified their papers out of fear of losing funding.

The research I undertook with Karsten Juhl Jørgensen was unfunded. We tried to get funds but didn't succeed, and I therefore paid his salary out of my budget. The only funding, I ever received for my research on mammography screening, was the support in 1999 from the Danish Board of Health to do our Cochrane review.

Elsebeth Lynge wrote, with reference to our *Annals* study, that if our estimates of overdiagnosis were true, "breast cancer screening in Denmark causes considerable harm and would be unjustified as a public health policy" (see Chapter 12).[641] Since our estimates *are* true,[642] screening in Denmark should be stopped.

Mette Kalager wrote in 2012: "I do not currently recommend screening mammography for average-risk women of any age."[643]

In 2004, Smith, Duffy and Tabár published a paper with the title, "The randomized trials of breast cancer screening: what have we learned?"[644] Nothing. These people have learned absolutely nothing because they prefer to ignore what they see.

Tabár declared in an interview in 2007 that mammography was the best thing that had happened for women during the last 3000 years, and he added,

"There are still people who don't like mammography. Presumably they don't like women."[645]

I see it a little differently. What we have learned is that mammography screening is the worst mass seduction of women the world has ever seen. Hundreds of millions of women have been seduced into attending screening without knowing it doesn't work and could harm them. This disregard of the principles for informed consent and national laws may be the biggest ethical scandal ever in healthcare.

This violation of women's human rights is the main reason why I have done so much research on mammography screening; why I wrote my 2012 book; and why I have now updated it.

My advice to women

Let me end this book on a positive note. The primary goal for all cancers is to reduce their occurrence, which is why we recommend people to stop smoking. It is much easier to reduce the risk of breast cancer than to reduce the risk of lung cancer. If women don't go to screening, they will reduce their risk of becoming a breast cancer patient by one third and their risk of losing a breast by one fourth.[646] [647]

About the author

I graduated as a Master of Science in biology and chemistry in 1974 and as a physician in 1984. I am a specialist in internal medicine, worked with clinical trials and regulatory affairs in the drug industry 1975-1983, and at hospitals in Copenhagen 1984-95.

I co-founded the Cochrane Collaboration and established the Nordic Cochrane Centre in 1993, became professor of Clinical Research Design and Analysis in 2010 at the University of Copenhagen, co-founded Council for Evidence-based Psychiatry in the UK in 2014 and the International Institute for Psychiatric Drug Withdrawal in Sweden in 2016, and founded the Institute for Scientific Freedom in 2019.

I am officially retired but continue my scientific work and I also work as an independent consultant, for example in lawsuits.

My greatest contribution to public health was when I opened the archives in the European Medicines Agency in 2010 and got access to the clinical study reports of drugs after a three-year long battle that involved a complaint to the European Ombudsman. The agency was solely concerned with protecting the drug industry's interests while ignoring those of the patients.

I have published over 100 papers in "the big five" (*BMJ*, *Lancet*, *JAMA*, *Annals of Internal Medicine* and *New England Journal of Medicine*) and my scientific works have been cited over 150,000 times. My H-index is 91 according to Web of Science (June 2023), which means that 91 of my papers have been cited at least 91 times. I am author of several books, including:

Critical psychiatry textbook (2022).
The Chinese virus: Killed millions and scientific freedom (2022).
Mental health survival kit and withdrawal from psychiatric drugs: a user's guide (2022, in 7 languages).
The decline and fall of the Cochrane empire (2022)
Vaccines: truth, lies and controversy (2021, in 7 languages).
Survival in an overmedicated world: Find the evidence yourself (2019, in 7 languages).
Death of a whistleblower and Cochrane's moral collapse (2019).
Deadly psychiatry and organised denial (2015, in 9 languages).
Deadly medicines and organised crime: How big pharma has corrupted health care (2013, in 18 languages). Winner, British Medical Association's Annual Book Award, Basis of Medicine, in 2014.
Mammography screening: truth, lies and controversy (2012). Winner of the Prescrire Prize in 2012.
Rational diagnosis and treatment: evidence-based clinical decision-making (2007).

I have given numerous interviews, one of which - about organised crime in the drug industry - has been seen by half a million on YouTube. I was in The Daily Show in New York on 16 Sept 2014 where I played the role of Deep Throat revealing secrets about big pharma.

A documentary film about my reform work in psychiatry, Diagnosing Psychiatry, appeared in 2017, and another one, with the working title, "The honest professor and the fall of the Cochrane empire," about my life and the moral collapse of the Cochrane Collaboration, is in production. Donations to the film can be given here. I also produce podcasts, in collaboration with filmmaker Janus Bang.

I have an interest in statistics and research methodology and have co-authored guidelines for good reporting: CONSORT for randomised trials, STROBE for observational studies, PRISMA for systematic reviews and meta-analyses, and SPIRIT for trial protocols. I was an editor in the Cochrane Methodology Review Group 1997-2014.

I am Protector for the Hearing Voices Network in Denmark.

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