

## SECONDARY PUBLICATION

## Benefits and harms of screening: Overdiagnosis and anticipatory medicine – A secondary publication

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### Abstract

The treatment of breast cancer has changed markedly since the publication of works that recommend screening for the early diagnosis of breast cancer. Retrospective reevaluations have revealed errors in screening; moreover, advances in oncological therapy and a better understanding of the disease have raised doubts toward the efficacy of these procedures, which might also cause side effects alongside the risk of overdiagnosis and overtreatment. On the other hand, the lack of information or even misinformation might cause confusion among the potential beneficiaries of these procedures, particularly the patients. These procedures are constantly being recommended by institutions, but the possible risks accompanied by these procedures are often not explained. It is easy to promote mammography screening if the majority believe that it reduces the risk of breast cancer and saves lives. Unfortunately, this is not the case. Many critics of screening are now demanding clear and precise explanations of the procedure and emphasizing on the importance of physical examination. Women must make informed decisions before screening by discussing their own risk profile, the possible benefits, and the eventual risks and harms of mammogram with their physicians. Women should be classified into two groups: those who would gain potential benefits from the procedure and those whose risks outweigh the benefits. A screening program that clearly does not offer more benefits than risks cannot be implemented by public health institutions. Providing complete and unbiased information, promoting appropriate care, as well as preventing overdiagnosis and overtreatment would be the best option.

**Keywords:** Screening; Breast cancer; Mammogram; Overdiagnosis; Anticipatory medicine

### 1. Introduction

Many researchers have criticized the efficiency of screening. They concur that trials advocating universal screening suffer from biased information on optimal results, use misleading advertising, and minimize or even conceal the negative physical and psychological effects caused by the application of screening in healthy people as well as the lack of information provided to the people.

First, we must differentiate a diagnostic and/or detection procedure from a screening procedure, as well as preventive medicine from anticipatory medicine (primary prevention).

In screening, the individuals included in the process are asymptomatic and have no medical history nor have that they undergone any examination before screening; otherwise, it would be considered a diagnostic procedure.

Regardless of the sensitivity and specificity of each screening procedure, not all of them present the same degree of inconvenience (damage and harm resulting from doing something). In some cases of screening, such as those for breast, colon, and prostate cancer, they are based on imaging test and/or endoscopy, in which risks may arise due to diagnostic errors and subsequent actions. There are other screenings, such as the screening for atheromatous cardiovascular disease, in which the procedure is totally predictive since it is not based on images, but rather the scores obtained through risk adjustment systems that make long-term predictions (up to 10 years), which might eventually lead to potentially harmful and unnecessary pharmacological treatments.

In 1975, Sackett published a paper in *The Lancet*<sup>[1]</sup> on the discussions and debates between the different roles of screening, case finding, diagnosis, and epidemiological surveys in disease detection. According to Sackett, discussions would improve when participants define the different purposes and characteristics of each procedure, recognize the ideological and intentional differences between the defenders and the critics, and value the quantitative and qualitative differences for decision-making in front of the individual patient or before the community.

While the advocates of screening, generally for irrefutable reasons, have claimed that with the existing evidence and given the current rate of disability and premature death, mass screening programs should be imposed for the detection of citizens with risk factors; methodologists have insisted that screening, like any other unproven health practice, could do more harm than good, and should meet scientific and ethical criteria before being implemented.

Sackett revealed the differences between the advice directed at an individual patient and that directed at a community. A higher level of evidence of efficacy is required to recommend treatment at the community level, especially when patients are solicited through screening. A community cannot be treated as a patient and *vice versa*.

Years later, in 2002, Sackett's displeasure toward the application of this type of medicine became more evident<sup>[2]</sup>. Sackett claimed that preventive medicine (referring to primary prevention, or as its critics call it, anticipatory medicine)

displays all three elements of arrogance. First, preventive medicine is "aggressive" in that asymptomatic individuals are often solicited and instructed on what they have to do to stay healthy; second, preventive medicine is "presumptuous" in that it assumes that its prescriptions always did more good than harm; third, preventive medicine is "despotic" in that it lashes out at anyone who dissents from its recommendations.

Considering the complications arising from overdiagnosis, and especially with overtreatment, Sackett argues that the pledge we must make when we solicit and exhort individuals to accept preventive interventions should be that they will be better off by adopting these measures. Consequently, the assumption that justifies the aggressive assertiveness with which we go after *naïve* healthy individuals must be based on the highest level of evidence. We must be certain that our preventive maneuvering does, in fact, do more good than harm.

A number of studies have demonstrated that the main tool of overdiagnosis, universal screening, is expensive, ineffective, and even dangerous. Therefore, every individual should be informed of the risks, inconveniences, and dangers of each proposed test other than its possible benefits.

However, it seems that apart from these uncertain benefits, political and/or economic cost-effectiveness are some of the advantages of screening, which are enhanced when both objectives coincide.

These premises serve as the foundation for our analysis of a screening that is widely accepted.

## 2. Breast cancer screening

In a review of five Swedish trials, published in *The Lancet* in 1993<sup>[3]</sup>, it was found that screening reduced breast cancer mortality by 29% (however, as we shall discover later, this was not the case). Despite this, the review has also addressed the need to consider other factors, both beneficial and harmful ones, in addition to mortality, before recommending universal screening. Needless to say, that 29% of successes were, in principle, highly appealing, thus concealing other recommendations.

In reality, this reduction in mortality is equivalent to saving one woman in every 1000 screened over 10 years. The benefit of detection is therefore very small. Translating it into standard language, according to the study, in that 10-year period, four women out of 1000 died from breast cancer, while only three died among those screened. Therefore, the absolute reduction in mortality for breast cancer was only 0.1% (1 in 1000) after 10 years. This 0.1%, using relative risk reduction (RRR), became the 29% cited.

Moreover, those figures were "inflated." Later, reviews have found that the reduction in mortality was in fact

smaller. The most exhaustive evaluation was that of a Cochrane review in 2009<sup>[4]</sup>, which included six studies and 600,000 women. After accounting for the biases identified in those studies, the RRR of mortality was in fact half of the aforementioned (15%), or what amounts to the same thing, that it was necessary to screen 2000 women in ten years (twice as much) for one to benefit compared to the group that was not screened (absolute risk reduction: 0.05%). On the other hand, this benefit was non-existent when evaluating the overall mortality since it was the same in both the groups, which could be ascribed to the consequences resulting from overtreatment in the screening group.

The relevance of overdiagnosis and overtreatment was also acknowledged in consideration of the cumulative risk of false positive results. Overdiagnosis reached 30% that is to say that 10 healthy women (who if there had been no screening would not have been overdiagnosed) were treated unnecessarily, and although no one can say with certainty which women have overtreated tumors, there is certainty about what happens to them: they would have to undergo surgery, radiotherapy, hormonal therapy for 5 years or more, chemotherapy, or a combination of all of these to treat abnormalities that otherwise would not have caused disease<sup>[5]</sup>. It has been warned that repeated screening increases the risk of overdiagnosis as shown by the risk ranging from about 20–60% after 10 years of mammography screening.

The review revealed for the first time that psychological harm from breast cancer screening is substantial and long-lasting, affecting a large number of healthy women (over 200 women experienced significant psychological harm).

In 2011, the National Breast Cancer Coalition (NBCC)<sup>[6]</sup>, after two exhaustive reviews on screening, concluded that the general impact on mortality is small and that the existing biases in the trials could either “erase it” or “create it.”

Mammography, which has many limitations, does not prevent or cure breast cancer. Women should discuss with their physicians their own risk profile, the potential benefits and harms, the complexities of screening mammography, and then make informed decisions about the screening. Women who have symptoms of breast cancer, such as a lump, pain, or nipple discharge, should have a diagnostic mammogram performed.

The update on the Cochrane database review, carried out in 2013<sup>[7]</sup>, found no positive effect of screening on mortality from breast cancer, nor on overall mortality. They believe that due to advances in breast cancer treatment and increased general awareness, the absolute effect of screening was likely to be less than that shown in the trials. In fact, recent studies have suggested that screening is no

longer effective<sup>[8,9]</sup>. This finding has led to the abolishment of screening mammography by the Swiss Medical Council in 2014<sup>[10]</sup>.

The importance of women making informed decision to accept screening or not has been emphasized, and an evidence-based informative booklet that is available in several languages has also been published<sup>[11]</sup>.

In a comprehensive review of scientific literature, published in *The BMJ*, Prasad *et al.*<sup>[12]</sup> have found that disease-specific mortality is an unreliable proxy for overall mortality. Even when a screening technique lowers disease-specific mortality rates, which is generally rare or only to a slight degree, there are no significant differences in overall mortality. Negative effects of screening may override any disease-specific benefits.

If screening does not reduce the risk of mortality from cancer (including breast cancer), why are screening campaigns so successful?

### 3. Misinformation and misrepresentations: Misconceptions by women

In 2014, Biller-Andorno and Jüni<sup>[10]</sup> revealed the enormous discrepancy between women’s perceptions of the benefits of mammogram and those expected in reality. Of 1003 women questioned, 71.5% believed that mammogram can reduce the risk of mortality from breast cancer by at least half, while 72.1% believed that it can prevent at least 80 deaths/1000 women screened. Nothing could be further from reality than this.

He concludes that promoting mammography screening is easy if most women believe that it prevents or reduces the risk of breast cancer and saves lives through early detection of aggressive tumors. We would be in favor of mammography screening only if these beliefs were valid. Unfortunately, they are not, and we believe women need to be told that.

### 4. Incorrect information

Screening advocates and their organizations often emphasize the benefits while omitting information on major harms when providing information materials<sup>[7]</sup>.

In 2016, Gigerenzer<sup>[13]</sup>, in his editorial in *The BMJ*, which is attached to the review by Prasad *et al.*<sup>[12]</sup>, stressed on the influence of language and the persuasiveness of words. Instead of saying “early diagnosis,” supporters of screening use the term “prevention.” This erroneously suggests that screening lowers the chance of developing cancer. Does this then imply that not getting screened for cancer increases the risk of developing cancer?

Three other instances of how language is used to underline the benefits of screening are as follows: (i) presenting the benefits in relative rather than absolute terms; (ii) comparing increases in 5-year survival rates with decreases in mortality rates; and (iii) showing that the women who are screened by mammography are referred to as patients, who could be healthy people.

## 5. Marketing and its benefits: Political profitability

The information women receive when they are invited to participate in mammography screening tends to be biased, insufficient, and misleading.

Information on the internet, for instance, on cancer fundraising websites, often omits the harms or portrays them as the benefits.

These invitations generally focus on the benefits of screening, rather than providing information on the proportion of healthy women who are overdiagnosed or overtreated.

When women are invited for mammography screening, the common practice is that when they receive the letter, they are also given an appointment for the examination. This puts pressure on women, and thus, their participation in screening is less voluntary. In some countries, women are even telephoned at home and encouraged to participate, which is also potentially coercive.

Screening is said to reduce a woman's risk of losing her breast. This is a false fact. Instead, screening increases the risk of lumpectomy or mastectomy as a result of overdiagnosis and overtreatment.

## 6. The collectives

Support groups, organizations, advertising campaigns, community screening events, *etc.*, consider universal screening as an advance or a social achievement, without having awareness of the risks of overdiagnosis. Added to this is the fact that the information they receive is incomplete and sometimes false, exaggerating the benefits and concealing the disadvantages and, above all, the risks. They do not understand that in this case, "less is more and more is less." Direct access to "non-suspicious" and independent information, such as that provided by the NBCC<sup>[6]</sup> or the Nordic Cochrane Center<sup>[12]</sup>, could reassure some sensitivities.

## 7. Sociopolitical profitability

Although we consider that professionals should be familiar with all publications on the subject, and despite the number of existing screening programs in communities,

private medical societies, and organizations, which do not doubt the excellence of the system, we must, in this case, think as follows: "It does not smell rotten in Denmark," but rather it smells like "sardines being pulled up by their own bootstraps" and how can they throw stones, not even sardines, at their own roof?

It is noteworthy that the primary objective of a breast cancer prevention plan in a specific autonomous community is the participation of at least 70% of women who have been invited to participate. If that is the objective, to ensure maintenance budgets, how is screening supposed to be recommended to women in an unbiased manner? On the other hand, there were no assessments for tumor detection, false-positives, adverse events, unnecessary interventions, *etc.* Even the indicator "cancer detection rate within the program" was specified as "Not available" in the findings. Clearly, it takes 10 years and 2000 women to get three!

The last objective, which is the ninth on the list, is to improve the training and knowledge of professionals and the general public on preventive aspects of cancer. However, it does not seem that this objective can be achieved either.

Prasad *et al.*<sup>[12]</sup> have recommended that health-care providers should be frank about the limitations of screening. The first step public health experts should take is to convey the message that mass screening of healthy people for cancer is not equivalent to health preservation. To say explicitly or implicitly that screening saves lives when there is no evidence to support this claim and much to the contrary undermines confidence toward the medical profession.

## 8. Conclusion

From an ethical perspective, it would be difficult to justify the implementation of a public health program that clearly does not bring more benefit than harm. Providing clear and unbiased information, promoting appropriate care, and preventing overdiagnosis and overtreatment would be the best option.

Women, physicians, and health-care policymakers should carefully consider the trade-offs when deciding whether to participate in screening programs.

Given all of that, we are not implying that all cancer screening is futile. People with a higher baseline risk of cancer, such as those with a family history of cancer or environmental exposure, may benefit from screening. Similar to Prasad and the NBCC<sup>[6,12]</sup>, we believe that it is advisable to invest money in research for such patients.

It is understandable that some people, even with objective data at hand, still prefer to be screened. There is also much to be debated on concerning who should

be financially responsible for the application of medical procedures that are not based on scientific evidence.

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Refer to primary version.

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The paper, after translation, has been edited to adapt it to the format and style of *Tumor Discovery*. The most obvious change to the paper is the removal of Summary section (“Resumen” in original).

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