For some time there have been calls for a change in the quality of the presentation of the benefits and disadvantages of screening. These demands are accompanied by the claim that the conventional epidemiological presentation of the rationale for screening is unclear or even misleading and therefore precludes the provision of accurate information (1). This position is accompanied by the aspiration to develop scientifically based methods of communicating risks (2). However, it misinterprets fundamental relationships and cannot remain unchallenged in the light of increasing public interest in early diagnosis and prevention.

Material and methods
A selective analysis of the literature was performed to determine the main considerations that motivate the decision to attend mammography screening, and to rate the evidential value of different modes of presentation. Based on this literature, the benefits and risks are quantified by our own calculations.

Results
Purpose of early diagnosis
The purpose of screening examinations is to detect a disease in an early, still preclinical stage in order to treat it more effectively and thereby lower morbidity and mortality (3). Mammography screening is the method used to identify still unidentified breast cancer in the asymptomatic population. The goal is to prolong the survival of subjects with already identifiable breast cancer by providing early treatment.

Survival time is defined as the period elapsing between diagnosis and death. In breast cancers discovered by early detection programs, survival times are also prolonged by bringing forward the time of diagnosis in cases in which the disease course is not influenced by providing treatment earlier. The effectiveness of screening therefore cannot be gauged from the survival times. Mortality is the only variable quantifiable without bias for studies on the effectiveness of early detection activities (3–5).

Results of randomized studies
The question addressed in the randomized studies (6) on mammography screening was whether periodic systematic mammography screening is a suitable...
The benefits of screening are balanced by unavoidable disadvantageous effects:

- False-positive findings
- Tissue biopsies of benign lesions
- Radiation exposure
- Overdiagnosis.

The quantitative extent of false-positive findings, associated biopsies, and the extent of overdiagnosis is shown in Table 2. The figures are based on the outcome variables for mammography screening among 1000 attendees as specified in the European guidelines.

Accordingly, within a two-year screening interval an abnormal mammography gives rise to 30 to 50 further investigations, such as magnification mammography, ultrasound or clinical examination, and, to resolve further existing abnormalities, 10 biopsies. A mean 0.5 cases of breast cancer resulting from overdiagnosis may be expected per 1000 attendees in the two-year screening interval.

Cumulated over 10 screening cycles – equivalent to 20 calendar years – these figures represent the anticipated disadvantageous effects from the viewpoint of 50-year-old women: with reference to 1000 women, 50 women develop breast cancer during these 20 years. About 260 to 400 women are invited to further evaluations following discovery of mammographic abnormalities, and 222 to 362 prove to be false-positive. In 100 women in whom the finding still remains abnormal after the follow-up examinations, tissue biopsies, e.g., in the form of core or vacuum biopsies, are recommended. These procedures show another 62 procedures with a diagnosis of breast cancer, 31 will die during the following 10 years without screening attendance and 20 with screening attendance (35% fewer) (box). The probability of developing the disease is also an important factor. It may vary between countries and therefore cannot be meaningfully derived from the Swedish studies. For Germany, it is about 5% for the age range 50 to 69 years.

In terms of health policy it is interesting to define how many cases of death from breast cancer can be prevented by a screening program: the figure is in the range of about 2500 to 3000 cases annually. This estimate is based on an assumed rate of approximately 55,000 new cases per year, of which about 40% to 50% occur between the ages of 50 to 69 years (8), a 70% screening attendance rate, and the mentioned 10-year survival rate of 69%.

A 10-year period, however, is an arbitrary figure on which to base communication of the effect of mammography screening and results in considerable underestimation especially when considering the absolute effects. Follow-up periods of 16 years and more are now available which show that the effect is also maintained after such long periods (9). The actual number of deaths from breast cancer that can be prevented by screening is therefore higher than estimated above. Moreover, even these follow-up periods of 16 years and more do not provide a complete picture of the screening effect, because in all studies screening was also commenced in the control groups after a few screening cycles. A complete presentation of the study outcomes in absolute figures would require the publication of lifelong breast cancer specific survival times, but such data are not available. All the observed absolute figures therefore underestimate the achievable effects.
1000 screening attendees (table 1), this means that, for one prevented death from breast cancer, up to 10 breast operations with benign findings are performed and one case of overdiagnosis occurs. By far the commonest disadvantageous effect, however, is a false-positive mammography result.

Radiosensitivity of mammary tissue is age dependent. It is highest in the age group between 10 and 20 years and decreases with age. The German Radiation Protection Commission (Strahlenschutzkommission, SSK) states that two-yearly mammography screening in the 50 to 69-year-old age group cumulatively leads to an additional risk of 0.01% to 0.24% of a 50-year-old woman developing breast cancer during her lifetime. The benefit (number of prevented deaths from breast cancer) therefore exceeds the risk (number of breast cancer deaths caused by radiation exposure) at least 100 fold.

**Presentation based on absolute risks**

The method of presentation used by Mühlhauser and Höldke (1) is based on the view that statements of relative risk – such as the statement that mammography screening reduces the risk of dying of breast cancer by 30% – are unclear or misleading.

The authors therefore avoid stating relative probabilities and report the results of the randomized studies to which the relative risk data refer, in the form of absolute percentages or frequency data. For example, it is stated: "Without mammography screening, 4 of 1000 women die of breast cancer within a 10-year period. With mammography screening, 3 of 1000 women die of breast cancer within a 10-year period".

### TABLE 1

**Estimated breast cancer mortality**

<table>
<thead>
<tr>
<th>Event</th>
<th>Number</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of women followed up</td>
<td>100 000</td>
<td>Age range 50 to 69 years</td>
</tr>
<tr>
<td>New breast cancer cases per year</td>
<td>250</td>
<td>0.25% of 50 to 69-year-olds</td>
</tr>
<tr>
<td>New breast cancer cases in 2 years</td>
<td>500</td>
<td>2 x 0.25% of 50 to 60-year-olds</td>
</tr>
<tr>
<td>Of these, death within 10 years after diagnosis</td>
<td>155</td>
<td>About 31% (see 10-year survival rates; [7])</td>
</tr>
<tr>
<td>Number of breast cancer patients who survive for at least 10 years – without screening –</td>
<td>500 – 155 = 345</td>
<td>About 69% of affected persons</td>
</tr>
<tr>
<td><strong>With screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of women attending screening</td>
<td>100 000</td>
<td></td>
</tr>
<tr>
<td>New breast cancer cases in 2 years (one two-year screening cycle)</td>
<td>500</td>
<td>Of these, about ¾ detected in screening (375 cases) and ¼ in the interval (125 cases, see [12])</td>
</tr>
<tr>
<td>&quot;Overdiagnoses&quot; which would not have appeared as disease without screening</td>
<td>50</td>
<td>10% overdiagnosis with reference to incidence without screening (see [13])</td>
</tr>
<tr>
<td>Of these, death within 10 years from breast cancer</td>
<td>0.65 × 0.31 × 500 = 101</td>
<td>65% of mortality without screening due to 35% mortality reduction by screening; 31% mortality with 69% 10-year survival rate (see above); overdiagnosed cases do not die of the disease</td>
</tr>
<tr>
<td><strong>Mortality balance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer mortalities prevented by one screening cycle</td>
<td>155 – 101 = 54</td>
<td>Per 100 000 screening attendees and 500 persons with disease, 54 breast cancer mortalities are prevented within a 10-year period</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Or: per 100 persons with disease, 54 without screening and 20 with screening die within 10 years of breast cancer</td>
</tr>
<tr>
<td>Breast cancer mortalities prevented by 10 screening cycles (total duration of screening program)</td>
<td>540</td>
<td>540 breast cancer mortalities are prevented (about 5 per 1000) per 100 000 screening attendees on attendance at all 10 screening cycles offered</td>
</tr>
</tbody>
</table>

*1 with reference to new cases of breast cancer diagnosed in 50 to 69-year-old women taking into account a follow-up period of 10 years without screening and in screening attendees (own calculations based on the cited literature)

*2 This is the only randomized study to date from which overdiagnosis could be directly quantified
Keystone statements

- The effectiveness of an invitation to periodic mammography screening is the result of the reduction of breast cancer mortality among all invited women (not all of whom follow the invitation) and is 25%. The effectiveness of the screening procedure is the result of the reduction of breast cancer mortality among the women who did follow the invitation and is 35% (5).
- For individual decision making, the risk reduction in the event of illness is decisive and can be expressed as a frequency: of 100 women with a diagnosis of breast cancer, 31 will die within the following 10 years without screening and 20 with screening (35% fewer).
- In the actuarial definition of risk the probability of the undesired event is multiplied by the expected magnitude of loss if the undesired event occurs. This takes into account the fact that it is also advisable to insure against very rare events if they could result in significant loss. In mammography screening this explains why women decide in favor of screening even if they rate the probability of developing breast cancer as relatively low.

"unconventional, but accurate" presentation: "Of 1000 women with mammography screening over 10 years, 999 have no benefit because they would also not have died of breast cancer without mammography screening" (1).

The presentation of the results in the form of relative probabilities (breast cancer mortality decreases by 35%) is also open to doubt (1, 2) because studies have shown that both physicians and potential screening attendees were unable to correctly convert the usual relative percentages into absolute figures.

Discussion

In view of the possible modes of presentation, the question arises as to which is most suitable and is properly understood by physicians and the lay public who are relatively unfamiliar with epidemiological topics.

Conditional probabilities, relative risk, and the actuarial definition of risk

Various concepts are available for the assessment of risk. The epidemiological definition of risk comprises only the likelihood of an undesired event occurring. The actuarial definition of risk also includes the magnitude of loss: the probability of the undesired event is multiplied by the presumed magnitude of loss if the event occurs. This takes into account the fact that it is also advisable to insure against very rare events which, if they occur, could spell economic ruin for the person concerned.

The assessment of risks is a task which has to be continuously mastered in everyday life. When assessing for what risks provisions should be made, attention is focused mainly on the magnitude of the potential harm and only secondarily on the probability of its occurrence. In these cases one usually thinks in terms of conditional probabilities (e.g. "if the house burns down, then I’ll be ruined"). Although the event is extremely unlikely in individual cases, building insurance is virtually universal and in Baden-Württemberg, Germany, is even compulsory. Other examples could be given which prove that thinking in terms of conditional probabilities and a concept of risk that includes the extent of possible harm is not unusual and, on the contrary, permeates social life on many levels.

There is thus good evidence that for many women the reason for attending mammography screening is not the actual probability of the event, i.e. the likelihood of becoming ill or dying, but the thought of the consequences of the illness. The high participation rates in the Scandinavian countries and in the German model projects, as well as in the first screening units of the nationwide screening program in the Federal Republic of Germany support this interpretation.

This means: a 50-year old woman who perceives the approximately 5% probability of developing breast cancer over the next 20 years as comparatively low, may possibly nevertheless decide in favor of screening because she rates the consequences of a disease as significant both for herself and her social environment. From this perspective, the benefit of screening emerges as the conviction that – in the event of becoming ill – one has done everything possible according to existing medical knowledge to limit the serious consequences. All attendees in screening programs benefit from this aspect, not only the women who actually become ill, and among those who do become ill, not only those whose death could be prevented.

The method of presentation propagated by Mühlhauser and Höldke (1) completely disregards this aspect. The authors combine the two variables most important for deciding whether to attend – the risk of becoming ill and the increased probability of survival in the event of disease onset during screening attendance – in a manner which is misleading for individual decision making. In responding to a woman's question about the benefits of screening attendance, it is unsuitable to quote a figure that relates the affected person's improved chances of cure to all women entitled to attend, i.e., to the 95% who do not develop breast cancer. This is the basis on which Mühlhauser and Höldke ([11], table 1) arrive at the stated 0.07% absolute risk reduction by screening with reference to breast cancer mortality (see also [10] and the response in [11]). The question remains as to whether a presentation of the numerical data with conditional probabilities need necessarily be difficult to understand.

Early diagnosis is concerned with prolonging the survival of the affected persons, but this cannot be
directly quantified empirically for the reasons explained. The consideration of mortality is only the unavoidable detour required in order to nevertheless obtain an answer to the question whether survival is prolonged by early detection.

A presentation in the form of conditional probabilities (reduction of lethality in the event of disease onset) is the most suitable way of approaching the problem. The fact that an incorrect understanding of such variables has been observed in surveys cannot be used as a justification for arguing against its use if it is appropriate for the purpose. Since conditional probabilities frequently play a role in decision making in daily life, the main concern is to achieve understanding of the facts about screening by establishing a relationship to such everyday life experiences.

It should be emphasized once again at this point that the figures presented in table 1 are fictional values synthesized from partial results as a means of presenting and quantifying the basic approaches in a simplified form. Data that are repeatedly requested in order to illustrate the procedures followed in screening and which are to be seen in table 1 cannot be obtained empirically. Survival times in screening for example are necessarily systematically biased. Constructive procedures are therefore required.

The problems addressed are not peculiar to an organized screening program but reflect the difficulties generally involved in screening. They occur in the same manner in colorectal and cervical screening, and become quantitatively visible in an organized, quality assured program in contrast to opportunistic screening. In opportunistic screening, which does not allow systematic quality assurance, much more unfavorable figures must be assumed. The unavoidable side effects described underline the necessity for strict quality assurance (in all kinds of screening) in order to minimize their extent as far as possible.

### TABLE 2

<table>
<thead>
<tr>
<th>Event</th>
<th>Number</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women attending screening</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>Screening cycle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conspicuous findings per screening cycle</td>
<td>30–50</td>
<td>3% to 5% of attendees within 2 years (12)</td>
</tr>
<tr>
<td>Biopsy based diagnoses</td>
<td>10</td>
<td>1% of attendees within 2 years (Swedish guidelines, see also [14])</td>
</tr>
<tr>
<td>Overdiagnoses</td>
<td>0.5</td>
<td>10% overdiagnosis with reference to the incidence without screening*2</td>
</tr>
<tr>
<td>Number of new disease cases and events of undesirable adverse reactions within 10 screening cycles in 50-year-old women</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>Number of women who develop breast cancer within the next 20 years (=10 screening cycles)</td>
<td>50</td>
<td>Cumulative probability of 5% of developing disease (20 × 0.25%*2)</td>
</tr>
<tr>
<td>Number of women with breast cancer diagnosis due to overdiagnosis</td>
<td>5</td>
<td>10% of breast cancer incidence without screening*2</td>
</tr>
<tr>
<td>Number of women with positive mammography findings</td>
<td>260–400</td>
<td>Cumulative probability of 26% to 40%; consequence is repeat invitation for further diagnostic evaluations</td>
</tr>
<tr>
<td>Number of women with false-positive mammography findings</td>
<td>223–363</td>
<td>Cumulative probability of 22.25% to 36.25%; Positive findings minus correct positive findings (10 × 1.5 × incidence = 3.75%*2)</td>
</tr>
<tr>
<td>Number of women with biopsy</td>
<td>100</td>
<td>Cumulative probability of 10% (10 × 1%*2)</td>
</tr>
<tr>
<td>Number of women with a false-positive indication for a biopsy</td>
<td>63</td>
<td>Cumulative probability of 6.25%; Proportion of biopsies minus the biopsies with correct positive findings (10 × 1.5 × incidence*2)</td>
</tr>
<tr>
<td>Number of women with breast cancer operation resulting in benign findings</td>
<td>&lt;10</td>
<td>Cumulatively &lt; 25% of the detection rate (10 × 1.5 × incidence, see [12])</td>
</tr>
</tbody>
</table>

*1 Own calculations based on the cited literature.  
*2 see table 1
Conflict of interest statement
The authors declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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Corresponding author
Prof. Dr. rer. nat. Nikolaus Becker
Deutsches Krebsforschungszentrum
Abteilung Krebsepidemiologie
Im Neuenheimer Feld 280
69120 Heidelberg
Germany
n.becker@dkfz.de