Benefits and Risks of Breast Cancer Screening

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Breast Cancer Screening: Pro

Achim Wöckel (Würzburg); Wolfgang Janni (Ulm)

Worldwide, breast cancer remains the most common form of cancer affecting women. In Germany, more than 70,000 women are diagnosed with breast cancer annually, 17,000 of whom die each year from their disease [1]. Nationwide, mammography is used in the group of 50- to 69-year-olds for early detection of breast cancer. Unlike curative mammography, screening examinations are performed at highly specialized centres with a sophisticated quality management programme in place. To be able to participate in the programme, the corresponding qualifications must be verified by annual audits. The outcome rates are verified by special higher-ranking bodies, called reference centres. In total, Germany has 94 screening centres around the country. By definition, the objective of screening mammography is not just to lower overall breast cancer mortality. Rather, the paramount aim is also to discover tumours at an early stage and thereby improve survival and quality of life of the women affected. This definition by itself makes it obvious that numerous different endpoints need to be analysed in order to evaluate the benefits of this type of screening intervention. Besides direct parameters like breast cancer mortality, a more complex analytical approach must also address other rapidly changing surrogate parameters such as increases in incidences and staging shifts in favour of smaller and thus prognostically more favourable tumours. These surrogate parameters also include changes in tumour therapies trending towards less radical locoregional treatments or less aggressive systemic regimens. The above highlights the importance of the current debate surrounding these surrogate parameters, given that mortality effects can only be estimated over relatively long observation periods. Since such a broadly comprehensive and functioning screening programme was not implemented nationwide until 2006, evidence for any specific effects on mortality in Germany is still lacking.

Impact of Screening on Prognostic Surrogate Parameters and Treatment Modalities

Breast cancer is not a singular illness, but comprises a very heterogeneous group of various subtypes with differing prognoses. In general, the survival rate is dependent on specific prognostic factors. These include tumour size, axillary lymph node metastases, distant metastases (TNM classification) and histological differentiation grade. Hypothetically, it should be possible to favourably influence these prognostic surrogate parameters with effective screening interventions. Furthermore, changes in tumour stages and prognostic factors have had a considerable impact on locoregional and systemic therapies, which also might be one reason for an association between certain trends and screening interventions. Recently published studies have impressively demonstrated these effects: As early as 2003, a screening mammography programme was commenced in Bavaria, which was turned over to the national screening programme in 2006. On a total of 75,575 registered breast cancer cases (primary diagnosis 2000–2008) in this Bavarian cohort, an initial analysis of the trends in prognostic factors and standard therapies for the 3 age groups (up to 49 years, 50–69 years, >70 years) was conducted based on annual percentages and 95% confidence intervals (CI) for the percent difference between the year of...
diagnosis, 2000 and 2008; logistical regression models were also calculated [2]. The effects of screening in the age group of 50–69 years were illustrated by comparing the individual groups: The analysis showed a clear increase in the incidence of in-situ carcinomas in the age group of screened women, whereas a constant time curve of incidence rates was registered in the unscreened cohorts. Since 2004, a continual and significant decline in the rate of advanced invasive carcinomas (tumour size > 2 cm) has been registered in the age groups up to 49 years and 50–69 years, whilst this rate remained stable in the group of over 70-year-olds. Concerning the rate of lymph node metastases (pN+) verified by pathology, the data on the screened cohort showed a statistically significant decrease of 9.9 percentage points (95% CI 13.9; –5.9) (2000: 40.1%; 2008: 30.2%). Among the up to 49-year-olds, the reduction was weaker and not significant; in the elderly patients, there was essentially no identifiable trend over time.

In all age groups, the rate of poorly differentiated carcinomas (G3) showed a constant decline, the strongest being in the screened cohort with 11.1 percentage points (95% CI 15.0; –7.1) (2000: 37.9%; 2008: 26.8%). These analyses moreover revealed for the trends in standard therapies that the observed increase in early and more favourable stage distributions might have contributed to the fact that it was the 50- to 69-year-old women in particular who avoided radical surgical procedures like mastectomy (2000: 32.6%; 2008: 19.6%) or axillary lymph node dissection (89 vs. 37%) significantly more frequently. The increase in the number of radiotherapy procedures performed in this cohort (59.7 vs. 66.6%) was attributable to the higher rate of breast-conserving surgeries. In line with the guidelines, the shift to more favourable prognostic factors increased the proportion of singular endocrine therapies (28.5 vs. 40.7%) and decreased monochemotherapy regimens (20.4 vs. 13.1%), and thus led to more gentle locoregional and systemic therapies in the screened cohort overall.

Analysis of Survival and Breast Cancer Mortality

In the past, various individual studies demonstrated a positive effect of mammographic screening examinations on survival [3–6]. A synopsis of several papers suggests a ‘likely’ advantage for the age group between 50 and 69 years. However, the exact effect strengths diverge strongly across the individual data collections. According to current knowledge, mammography screening does not confer any benefit for women under 40–50 years of age because the percentage of false-positive findings is proportionately higher the younger the women are. Among others, one explanation for this is that younger women have a higher breast density which encumbers the general readability of the mammogram. Current data from clinical trials suggests that screening does not lower mortality in elderly women (≥70) either, i.e. due to their age, the women no ‘longer’ benefit from mammography [7].

Past meta-analyses and appraisals have repeatedly addressed the methodological deficiencies in these study populations, some of which were monitored over a decade ago, show differences in risk profiles, and can only be followed up within cohort studies. A recent paper published in the Cochrane Database examined the benefit-risk relationship based on the available evidence [8], thereby updating a systematic review from the year 2011: In sum, the overall analysis only included 7 randomised trials that were methodologically robust and published up to 2012. The data were available from an aggregate total of 600,000 women aged between 39 and 74 years. 4 of these trials showed a significant reduction in breast cancer mortality (relative risk 0.75 (95% CI 0.67–0.83)), whereas 3 studies showed no benefit despite adequate randomisation. The authors did show, however, that the endpoint ‘breast cancer mortality’ in the individual trials had been interpreted variously. This was because there is no uniform classification for the cause of the patients’ deaths. Similarly, other research groups attribute the difficulties associated with interpreting screening interventions to multifactorial effects [2]: The implementation of quality-promoting interventions (e.g. guidelines), the use of modern therapeutic methods (e.g. antibody therapy), and modified surgical techniques all make it very difficult to quantify the impact of screening both on the changes in therapies and on oncologically relevant endpoints. This fact highlights the importance of methodically stringent reviews in the Cochrane Database, as illustrated above, which nevertheless were able to show survival benefits. However, the extent to which more effective therapeutic modalities will overshadow the survival benefits conferred by screening mammography for the endpoint analysis moving forward remains to be seen.

Obviously, these survival benefits cannot be viewed in a vacuum, but must be contrasted against the potential harms that can be incurred through screening interventions. The authors of the Cochrane review estimated the reduction in breast cancer mortality to be around 15% and showed that 1 woman (only) could be saved from death by breast cancer in a cohort of 2,000 women who were screened over a period of 10 years. This contrasts with the 200 healthy women forced to undergo a 10-year period, 0.3–3.2 women avoided breast cancer death because of the screening interventions, whereas 490–670 women received at least one false-positive result that led to further needless interventions. These analyses undertaken by Welch and Passow [9] also clearly illustrate that the effect strengths which, in turn, prove the benefits, vary greatly between the individual age groups (table 1).

| Table 1. Lower and upper bound estimates for the number of breast cancer deaths avoided because of a 10-year course of annual screening mammography (modified according to [9]) |
|---|---|---|---|---|---|
| Relative mortality reduction attributable to screening, % | Lower bound (5% reduction) | Upper bound (36% reduction) |
| 15-y | 22 | 33 | 44 | 55 | 66 |


Janni/Porzsolt/Schmutzler/Wöckel
Table 1. Lower and upper bound estimates for the number of breast cancer deaths avoided because of a 10-year course of annual screening mammograms (modified according to [9])

<table>
<thead>
<tr>
<th>Data</th>
<th>Lower bound (5% reduction)</th>
<th>Upper bound (36% reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>age, years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>SEER 15-year risk of dying from breast cancer</td>
<td>3.27</td>
<td>6.45</td>
</tr>
<tr>
<td>Relative mortality reduction attributable to screening, %</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>15-year risk without screening per 1,000</td>
<td>3.37</td>
<td>6.70</td>
</tr>
<tr>
<td>15-year risk with screening per 1,000</td>
<td>3.20</td>
<td>6.36</td>
</tr>
</tbody>
</table>

Table 2. The aims of healthcare are described for three different strategies: primary, secondary, tertiary prevention; tools required to complete these strategies are shown

<table>
<thead>
<tr>
<th>Methods</th>
<th>Strategies</th>
<th>primary prevention</th>
<th>secondary prevention</th>
<th>tertiary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>–</td>
<td>first step: early detection</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>–</td>
<td>second step: confirmation</td>
<td>first step: confirmation</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>only step: prevention</td>
<td>third step: treatment</td>
<td>second step: treatment</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion and Interpretation

The aim of this paper was to describe the positive effects of screening mammography. That is the reason why its negative effects have only been addressed in a rudimentary fashion (rate of false-negative findings, overdiagnosis, radiation exposure, mental stress). In aggregate, however, past studies of varying methodological quality have been able to demonstrate a positive impact on breast cancer mortality. Since the methodology of many of these studies has been critically appraised in reviews, however, it is difficult to quantify the exact effect strengths attributable to screening. Additionally, the optimization of therapeutic modalities taking place over the past years has also posed conundrums when it comes to interpreting results from screening studies. Despite these limitations, which encumber any assignment of effects, screening interventions in the desired age groups have moreover led to changes in the incidences, with a trend towards more favourable prognostic factors. This, in turn, has positively impacted the radical and aggressive nature of locoregional and systemic therapies for breast cancer. In addition to weighing the individual benefits and harms, which must certainly be a substantive part of educational measures, the long-term goal of reducing breast cancer mortality should be further evaluated. Proper assessment, however, is only possible by analysing data on screened participants within a functioning and comprehensive nationwide cancer registry.

Breast Cancer Screening: Contra
Franz Porzsolt (Ulm/llerissen)

Different Perspectives and the Consequences

About 90 years ago, Eugen Bleuler, a Swiss psychiatrist, wrote a small but important booklet about the autistic-undi...

Benefits and Risks of Breast Cancer Screening

Examples of systematic errors (bias) which may occur in treatment, screening, or diagnostic studies

<table>
<thead>
<tr>
<th>Methods</th>
<th>Goal of action</th>
<th>Potential effects</th>
<th>Actual effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>confirmation of a suspected but specified disease without signs or symptoms</td>
<td>will be suspected but not confirmed*</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>confirmation of an existing but not yet specified disease with signs or symptoms</td>
<td>confirmation of sensitivity and specificity</td>
<td>confirmation of the significance of the test result</td>
</tr>
<tr>
<td>Therapy</td>
<td>intervention to prevent unwanted consequences in patients with confirmed disease</td>
<td>confirmation of efficacy of the intervention</td>
<td>confirmation of effectiveness of the intervention</td>
</tr>
</tbody>
</table>

*Persons who decide to participate in a screening programme will barely agree not to be screened as members of the control group.

Table 3. Description of goals and effects of screening, diagnosis or treatment under ideal or real-world conditions

<table>
<thead>
<tr>
<th>Methods</th>
<th>Goal of action</th>
<th>Potential effects</th>
<th>Actual effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception/</td>
<td>sampling bias</td>
<td>healthy volunteer bias and incentive bias</td>
<td>pre-test bias (sampling bias)</td>
</tr>
<tr>
<td>performance</td>
<td>selection bias</td>
<td>performance bias</td>
<td>performance bias</td>
</tr>
<tr>
<td>Evaluation</td>
<td>detection bias</td>
<td>detection bias</td>
<td>detection bias</td>
</tr>
<tr>
<td>Interpretation</td>
<td>lack of intent-to-treat analysis</td>
<td>sensitivity/specificity bias</td>
<td>sensitivity/specificity bias</td>
</tr>
</tbody>
</table>

Risk of Bias in Prevention Studies

From the perspective of CE, it is essential to avoid bias in prevention studies. It is demonstrated in table 2 that secondary prevention is the most complex of all prevention strategies and inherits the largest number of potential forms of bias (table 4). This evidence could only be derived from a structured analysis of different prevention strategies. In several ongoing projects, we are analysing studies to prevent glaucoma and cancer of the lung, colon, prostate and breast. In these projects, we are identifying a huge number of systematic errors in diagnostic and screening studies. Some of these errors are

Primary Prevention in Clinical Economics

Table 4. Examples of systematic errors (bias) which may occur in treatment, screening, or diagnostic studies

<table>
<thead>
<tr>
<th>Methods</th>
<th>Treatment study</th>
<th>Screening study</th>
<th>Diagnostic study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception/</td>
<td>sampling bias</td>
<td>healthy volunteer bias and incentive bias</td>
<td>pre-test bias (sampling bias)</td>
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</tr>
</tbody>
</table>

Secondary Prevention in Clinical Economics

The aims of diagnostic studies are different under ideal or under real-world conditions. Under ideal study conditions, the aim is to investigate the investigate the sensitivity and specificity of a test. Under real-world conditions, the clinical significance of the test result should be demonstrated. A test has no clinical significance at all if the derived consequences are completely independent from the test result. On the other hand, the clinical significance of a test may be considered high if the derived consequences strongly correlate with the test results. In relation to therapy, the aim of studies conducted under ideal conditions is the assessment of efficacy, while effectiveness can be assessed in studies conducted under real-world conditions.
Table 4. Examples of systematic errors (bias) which may occur in treatment, screening, or diagnostic studies

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Lack of intent-to-treat analysis</th>
<th>Sensitivity/specificity bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluation</td>
<td>Detection bias</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conception/Therapy

Intervention to prevent unwanted consequences

Screening

Confirmation of a suspected but specified disease

Table 3. Methods, Goal of action, Potential effects, Actual effects

<table>
<thead>
<tr>
<th>Selection of an Appropriate Goal</th>
</tr>
</thead>
</table>
| The most powerful form of bias in any type of management is related to imprecise or inappropriate goals. The example of secondary prevention of breast cancer shows that inadequate confirmatory endpoints are used in a large number of studies to confirm the effectiveness of mammography screening. A high compliance rate with mammography screening or high sensitivity and/or specificity of a detection method or an impressive mammography-related increase in breast cancer incidence are no reliable indicators to demonstrate effectiveness of mammography screening. A high compliance rate with screening indicates a convincing quality of the screening campaign, and a high sensitivity/specificity indicates a high correlation of imaging methods with the results of histopathologic examinations. Any of these results are important and describe a necessary but not sufficient prerequisite to demonstrate effectiveness of mammography screening. Screening cannot be considered effective unless the number of breast cancer-related deaths can be reduced by it. Unfortunately, the sensitivity of disease-specific death is hard to confirm as the prevalence of both conditions, death and disease, are each 100% in a diseased person. Instead of assessing disease-specific death, we suggest the assessment of advanced stages of the disease. Advanced stages of disease can be assessed much more reliably than ‘disease-specific death’. The reliability is high because advanced stages of disease can be confirmed by signs while disease-specific death is an assumption which may or may not be true.

Reliable Screening Studies

Screening studies which measure the incidence of advanced stages of disease are more reliable than screening studies which measure other indicators such as compliance with the screening programme or incidence of early-stage breast cancer. All of the mentioned results, compliance as well as incidence of early-stage and late-stage disease, were reported in a recent study on 30 years’ experience with breast cancer screening [21]. This study demonstrated that the only indicator which did not change at all during the last 30 years – despite an increasing compliance with screening – was the incidence of late-stage distant disease. The authors of this publication did not discuss the possible consequences from this important finding [21]. Our letter to the editor which expressed the need to discuss the absence of reduction of advanced-stage distant disease was rejected. The editor did not want to publish a minority opinion. Even if the New England Journal of Medicine did not want to grasp this nettle, I strongly encourage the discussion about appropriate endpoints of screening programmes.

Screening – A Conflicting Topic of Science and the Public/Politics

Politicians and a considerable part of the public [22] believe in the effectiveness of screening programmes despite a considerable volume of contradictory observations. There is probably only a single reason which feeds this belief and the associated discussions: the induced perception of safety.

Most doctors favour screening programmes for two reasons. First, they are convinced that screening programmes generate patient benefit. This conviction can be explained by the doctors’ lack of ability to assess the validity of screening studies (table 4) and the lack of knowledge to distinguish final endpoints or their surrogates (e.g. reduction of the incidence of late-stage disease from intermediate endpoints (e.g. increased incidence of detected early-stage breast cancer). Based on this lack of understanding, doctors would even feel unsafe when not offering screening. Second, doctors who offer screening programmes generate earnings from the offered programmes and react predictably to an economic incentive. As long as our society is offering this incentive, doctors cannot be blamed for acting accordingly.

Patients are overwhelmed with information provided by doctors and other players on the beneficial effects of screening although it is clear that this information is often imbalanced [23, 24]. Following this information, patients feel unsafe without screening and consequently request screening programmes.

Politicians would most likely compromise their career if they did not support strong public demand.

Another group of players who promote screening programmes are the health insurance companies. These companies reimburse the costs of screening and in doing so achieve two important effects: They satisfy the demands of the patients as well as the demands of the doctors. Hence, it would be absolutely counterproductive not to support screening programmes.

In summary, there are four powerful players – doctors, patients, politicians and health insurances – who disagree with scientists concerning the value of screening. We have to decide whether the opinion of these four players or that of the scientific community is more important.
thing that can be counted counts and not everything that
tists should count. This decision is not a scientific but a politi-
cal one. Albert Einstein’s saying explains the existing difference
between scientific and political decisions: ‘Not everything
that can be counted counts and not everything that
counts can be counted’.

Possible Approaches to Solving Existing Conflicts Surround-
ing Breast Cancer Screening

The healthy volunteer bias will probably persist in the fu-
ture, i.e. healthy people will continue to accept screening pro-
grammes more often than others. The conflict of interest
of any players of the system will also persist. It will stay the same
as long as the education of doctors and the information of the
public about the effects of screening does not change. Both
the education of doctors and the information of the public
cannot change unless more people understand how to assess
the validity of scientific publications and how to collect real-
world data which describe the actual and not only the poten-
tial outcomes of screening programmes. Theoretically, both
aspects are easy to achieve.

We offer courses to teach medical students how to assess
the validity of scientific papers [25]. These courses get ac-
cepted by students as they can earn good money with the as-
sement of the validity of scientific publications instead of
doing night shifts in hospitals or accepting jobs in pubs.
Healthcare professionals working with scientific associations
or guideline groups will not accept these courses for three rea-
sons: they probably lack the time which is necessary to com-
plete a complex critical appraisal; they also lack the experi-
ence that grows with learning by doing; and, finally, they lack
the necessary interest in doing this type of work.

Healthcare professionals should care about the legal
framework supporting the collection of real-world data. Meth-
ods to collect these data were recently published [26], and
are presently tested in pilot studies. Without these data, we will
continue to accept tangible costs (i.e. monetary dimensions)
and intangible costs (i.e. quality of life dimensions) of screen-
ing without knowing the real benefit for our patients. We de-
definitely must continue the research into breast cancer screening;
however, there is considerable room for improvement.

Breast Cancer Screening: Comment
Rita Schmutzler (Cologne)

The papers by A. Wöckel and F. Porzsolt were well received
as they comprehensively discuss the pros and cons of screening
mammography in the light of updated data on the outcome
of screening mammography trials, especially by the groups
of Welch et al. [9] and Goetzsche [8]. Their elaborations dem-
strate the ongoing professional debate and disagreement about
the interpretation of the data while largely agreeing on the ac-
curacy of the data. While a net benefit derived from the reduc-
tion in breast cancer-specific mortality is undisputed, the de-
bate concentrates on weighing up benefits and harms. As out-
lined in both papers, the absolute reduction in breast cancer
mortality of (only?) 1 woman per 1,000 women screened for 10
years comes at a price of about 650 women with at least one
false-positive result within this time span and an overdiagnosis
of 30% of all detected breast cancers and thus an about 10-fold
excess of the number needed to treat to safe one woman’s life
(according to Welch and Passow [9]). Incidentally, in the paper
by F. Porzsolt there seems to be a misunderstanding concerning
Bleyer’s/Welch’s data on the effect of screening mammog-
raphy on the incidence of metastatic breast cancer [9, 21].
While Bleyer and Welch [21] outline that screening mammog-
raphy has no effect on the incidence of primarily metastasized
breast cancer, Porzsolt misinterprets this as a lack of effect of
mammography screening on the reduction of all breast cancers
that may eventually metastasize.

The crucial question of this debate is whether we should
call screening mammography into question at this moment.
Although more precise data on the effects of screening mammog-
raphy have become available, the main facts have not
changed since its introduction. As outlined by Porzsolt, the in-
tervention of this programme was a value judgement that
emerged out of an intensive debate between self-help groups,
doctors, health insurances, and healthcare politicians. I do not
see, however, that this decision thwarts scientific findings. It is
rather mandatory to guarantee that women who consider par-
ticipation in screening mammography get all the information
on hand to be able to make an informed decision. Although
this is recognized by all parties involved and strongly recom-
dended by the position paper on informed decision making of
the National Cancer Plan, there is still a sore lack of knowl-
dge and ability on the doctors’ side to communicate the rel-
ent facts of screening mammography as stated by Porzsolt.
Even going through the papers of Wöckel and Porzsolt, it is
challenging to extract the important information. For instance,
can all readers understand table 1 in the Wöckel paper and
communicate these data in layman’s terms to their patients?

In the updated analyses of screening mammography com-
mented on by Wöckel and Porzsolt, the following facts and ab-
solute risks are calculated for women between 40–70 years of
age, who participate for 10 years in screening mammography:

i) The risk of getting a false-positive result is 1/2; hence,
women should be advised to stay calm if they are called for a
revisit as approximately 90% of suspicious findings turn out to
be harmless.

ii) The risk of getting a breast cancer diagnosis is doubled.
This means that the absolute risk of being diagnosed with
breast cancer increases by approximately 1.2%, i.e. 23 instead
of 11 women out of 1,000 women within 10 years.

iii) In the case of a breast cancer diagnosis, 1/3 of women
would never have required treatment. That means that
approximately 8 of 1,000 women who participate in screening
considerably.
mammography for 10 years (and 8 of 23 women who are diagnosed with breast cancer within this time span) undergo overtreatment, although this treatment will predominantly be restricted to surgical intervention as more favourable tumour stages do not require chemotherapy.

iv) The chance of being saved from dying of breast cancer is 2 in 1,000 women participating in screening mammography (0.2%) and 2 in 23 patients diagnosed with breast cancer by screening (10%). It is, however, unclear how much mortality reduction is caused solely by screening benefits and how much by treatment improvements. 5 women die irrespective of screening mammography. In particular, screening mammography is not able to improve the prognosis of those 1–2 women that develop highly aggressive tumours. These tumours largely escape screening mammography and are diagnosed in the metastatic stage.

ev) Whether or not this is worth it is a decision every woman has to make for herself.

For the German situation, it has to be considered that screening mammography is not offered before 50 years of age, leading to a better outcome of screening mammography as reflected by higher breast cancer incidence rates and lower false-positive rates documented in the evaluation report of the ‘Kooperationsgemeinschaft Mammographie’.

In cooperation with others, German Cancer Aid is devoted to providing an information platform that allows informed and non-directive decision making and is updated on a regular basis. Although this helps to fill the knowledge gap of doctors and patients, additional educational programmes are indeed desirable as stated by Porzsolt.

Questions that are not yet sufficiently answered concern the impact of increasing life expectancy on long-term mortality reduction by screening mammography and the importance of secondary endpoints such as improvement of quality of life due to less radical therapeutic interventions. The latter can, however, be weighed against overtreatment as outlined by Wöckel.

Benefits and Risks of Breast Cancer Screening

Beyond the conflicting debate on the benefits and harms of screening mammography, we are facing an even bigger challenge in dealing with risk prediction and preventive options in the post-genomic era. Already, numerous genetic risk factors have been identified for most common solid tumours, i.e. breast, colon, and prostate cancer. Based on these data, risk prediction models have already been established and will be further refined that will ultimately allow individual risk prediction on a continuous risk scale in the near future. This raises numerous questions, e.g. what are the requirements for the introduction of genetic risk factors into clinical risk prediction and consequently clinical prevention? How can genotype-phenotype studies be performed under the assumption of an extreme genetic heterogeneity and therefore small cohorts of patients? Who decides what risk factor should be tested and sets threshold levels for offering risk-adapted preventive measures? Can screening mammography and other cancer screening programmes then be abolished for the general population? Is there a right or an obligation both to undergo risk prediction and prevention? How does this effect non-directive counselling, the right to not know, and the legally guaranteed protection against discrimination? The National Cancer Plan has approached this new field of action in a position paper on risk-adapted prevention that provides a meta-level concept for the translation of genetically driven risk prediction into clinical prevention. On this basis, players in healthcare politics now have the chance to frame this field of action before opportunistic screening activities gain ground, with the introduction of structured programmes based on the principles of mutual solidarity.

Disclosure Statement

AW: No conflict of interest. WJ: Nothing to disclose.
FP: The author did not provide a conflict of interest statement.
RS: Nothing to declare.

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