Long-term Incidence and Mortality Trends for Breast Cancer in Germany

Langfristige Inzidenz- und Mortalitätstrends für Brustkrebs in Deutschland

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ABSTRACT

Introduction Changes in risk factors and the introduction of mammography screening in 2005 have led to dramatic changes in the breast cancer-associated burden of disease in Germany. This study aimed to investigate long-term disease-related incidence and mortality trends in women from East and West Germany since the reunification of Germany.

Methods Total and stage-specific incidence rates were evaluated based on data obtained from selected cancer registries. Sufficiently complete data going back to 1995 were available for 4 East German and 3 West German regions. The figures were weighted for population size, and rates were calculated for the whole of Germany based on the rates for East and West Germany. The study particularly focused on 3 different age groups: women eligible for mammography screening (50–69 years), younger women (30–49 years) and older women (70+ years). All rates were standardised for age. The mortality rates obtained from the official statistics on cause of death since 1990 were processed accordingly.

Results Incidence rates in the observation period increased, as they were affected by the increasing number of cases with early-stage cancers being diagnosed in the screening age group. The total incidence for this group, which included the incidence of non-invasive breast cancers, increased by 14.5% between 2005 and 2016. Early-stage cancers (UICC stages 0 and I) increased by 48.1% while late-stage diagnoses (UICC stages III and IV) decreased by 31.6%. Qualitatively similar changes were noted for the other age groups, although they were less pronounced. The decrease in breast cancer mortality observed since the mid-1990s ended around 2008 for the group of younger women but continued in the screening age group. After 2008, an increase in mortality was observed in the group of older women. The differences in disease burden between East and West Germany (in favour of East Germany) decreased in younger women during the observation period but tended to increase in the group of older women.

Conclusion The analysis suggests that the introduction of mammography screening contributed to a decrease in the incidence of advanced-stage breast cancers and in breast cancer-related mortality rates but also resulted in a substantial number of overdiagnoses. The relatively unfavourable incidence trend in the group of younger women, particularly in East Germany, should be interpreted in the context of lifestyle changes. The slight increase in mortality observed in the group of older women after 2008 requires further analysis.

ZUSAMMENFASSUNG

Einleitung Änderungen bei den Risikofaktoren und das 2005 eingeführte Mammografie-Screening bedingen eine hohe Dynamik der brustkrebsassoziierten Krankheitslast in Deutschland. Ziel der Studie ist die Untersuchung langfristiger krankheitsbezogener Inzidenz- und Mortalitätstrends bei Frauen in Ost- und Westdeutschland seit der Wiedervereinigung.

Methoden Gesamt- und stadienspezifische Inzidenzraten wurden basierend auf den Daten ausgewählter Krebsregister untersucht. Daten mit hinreichender Vollzähligkeit seit 1995 standen für 4 ostdeutsche und 3 westdeutsche Regionen zur Verfügung. Werte für Gesamtdeutschland wurden populationsgewichtet aus den Raten für Ost- und Westdeutschland errechnet. Besonders betrachtet wurden 3 Altersgruppen: Frauen mit Anspruch auf das Mammografie-Screening (50–69 Jahre), jüngere Frauen (30–49 Jahre) und ältere Frauen (70+ Jahre). Alle Raten wurden altersstandardisiert. Entsprechend wurden Mortalitätsraten aus der amtlichen Todesursachenstatistik seit 1990 aufbereitet.

Ergebnisse Im Beobachtungszeitraum kam es zu einem Inzidenzanstieg, der durch die vermehrte Diagnose früher Stadien in der Screening-Altersgruppe geprägt ist. In dieser Gruppe stieg die Gesamtinzidenz unter Einschluss der nichtinvasiven Brustkrebsfälle von 2005 bis 2016 um 14,5 %. Frühe Stadien (UICC 0 und I) nahmen um 48,1 % zu, während Spätstadien (UICC III und IV) um 31,6 % zurückgingen. In den anderen Altersgruppen kam es zu qualitativ ähnlichen Veränderungen, die jedoch weniger stark ausgeprägt waren. Der seit Mitte der 90er-Jahre zu beobachtende Rückgang der Brustkrebssterblichkeit endete bei den jüngeren Frauen um 2008, während er sich in der Screening-Altersgruppe fortsetzte. Bei älteren Frauen kam es nach 2008 zu einem Anstieg. Ost-West-Unterschiede bei der Krankheitslast (zugunsten Ostdeutschlands) nahmen bei den jüngeren Frauen im Beobachtungszeitraum ab, während sie bei den älteren Frauen eher zunahmen.

Schlussfolgerung Die Analyse legt nahe, dass die Einführung des Mammografie-Screenings zum Rückgang der Inzidenz fortgeschrittener Brustkrebsstadien und der Brustkrebsmortalität beigetragen, aber auch eine substanzielle Zahl von Überdiagnosen verursacht hat. Relativ ungünstige Inzidenztrends bei jüngeren Frauen, insbesondere in Ostdeutschland, sind vor dem Hintergrund von Lebensstiländerungen zu interpretieren. Die beobachtete leichte Zunahme der Mortalität bei älteren Frauen seit 2008 bedarf eingehenderer Analysen.

Introduction

Breast cancer is the most common type of cancer in women, both in Germany and worldwide. In 2014, 69 220 women in Germany developed invasive breast cancer (ICD-10 C50). Breast cancer was given as the cause of death in 17 670 cases. This makes breast cancer the most common cancer women die from, followed by lung cancer (ICD-10 C33-C34) with 15 524 deaths. Based on these data, 1 in 8 women will develop breast cancer sometime in their lifetime, and 1 in 29 women will die from the disease [1]. According to the Global Burden of Disease Study, in 2017 around 432 000 years of healthy life (disability-adjusted life years [DALYs]) were lost in Germany [2].

Apart from its numerical relevance, breast cancer deserves special consideration, as it is possible to influence the disease burden. Due to the improved treatment options nowadays breast cancer is considered a potentially curable disease, as long as there is no distant metastasis. Mammography provides a means to screen a broad section of the female population with a high probability of detecting early-stage disease. Moreover, some known risk factors (e.g. alcohol consumption and lack of exercise) are modifiable and can, to a certain extent, be amended for the primary prevention of disease. The costs of limiting the breast cancer-related burden of disease place great strain on the healthcare system. Attention has increasingly focused on social and financial consequences for the families of affected patients, many of whom are just middle-aged.

Because of its importance, breast cancer was already included in Germany's 2003 list of national health targets which had aimed at "reducing mortality, improving quality of life". In July 2015, the prevention law (*Präventionsgesetz*) enshrined these health targets in law in Sec. 20 para. 3 No. 2, Book V of the German Code of Social Law (*Sozialgesetzbuch* [SGB] 5). A success in reducing the breast cancer-associated disease burden should be reflected in epidemiological trends. The unspecific impact of improved prevention and therapy would be visible in a decrease in breast cancer mortality. The impact on incidence is expected to be more complex, with greater variation over time and depending to the respective variable. While improvements in treatment basically leave the incidence rate unchanged, a success in primary prevention leads to a decrease in the number of new cases with disease. Secondary prevention (screening) should, if successful, result in a lower rate of cases with advanced breast cancer while the rate of cases with early-stage cancers should increase, particularly in the initial period after the introduction of a screening programme.

This study aimed to provide a description of long-term trends in overall and stage-specific breast cancer incidence and mortality rates in Germany for women of different age groups. The study particularly focuses on the different developments in East and West Germany and on the impact of introducing mammography screening in 2005.

Methods

Data

The incidence rates (of invasive [ICD-10 C50] and in situ [ICD-10 D05] breast cancer) were determined separately for East and West Germany using data obtained from the Centre for Cancer Registry Data at the Robert Koch Institute (RKI) [3]. Sufficient completeness of registry data (≥ 90 % coverage according to the estimates of the RKI) was achieved in different regions of Germany at different times [4]. As the aim was to investigate the longest possible time series, the study used data on incidence starting in 1995.

From this time on and until 2015, complete data were available for all federal states in East Germany (area of the former GDR) with the exception of Saxony-Anhalt. As regards the federal states in West Germany, complete data to 2016 was available for the Saarland, Hamburg and the administrative district of Münster (in the state of North Rhine-Westphalia). As the study aimed to compare East and West Germany, the federal state of Berlin was not considered for study because of its special status. The data used in the study thus covers around 20% of the female population in Germany (reference year 2005) [5].

Data analysis

The rates obtained for the different areas were taken as representative for the two respective German regions and used as the basis for values calculated for all of Germany in the form of weighted averages which took account of the population sizes of the age groups being evaluated in both German regions (see Appendix). Three age groups were investigated: women eligible for mammography screening (50–69 years), younger women (30–49 years), and older women (70+ years). To adjust for demographic shifts within these age groups, the age group-related rates as well as the rates across all age groups were standardised for age (using the old European population as the standard).

The stage-specific analysis evaluated UICC stages 0 (in situ), I (summarised as early-stage cancer) and II and stages III and IV (grouped together as late-stage cancer). Invasive tumours of unknown staging were proportionally assigned to stages I to IV [6].

Mortality data were extracted from the official statistics on cause of death, processed and differentiated into the different age groups as described above. Mortality data were available for all federal states in East and West Germany for the period from 1991 to 2017. Berlin was again excluded from the study.

To reduce statistical noise caused by limited case numbers, stage-specific incidence and mortality rates were calculated as sliding averages over 3 years (or 2 years at the edges of the observation period). Because of the limited impact on the overall figures for Germany, missing stage-specific rates for East Germany in 2016 were replaced by the corresponding rates for West Germany.

Results

Incidence

The incidence rates for invasive breast cancer in East and West Germany and for all of Germany are shown in ▶ **Fig. 1 a** to **d**. They show that the incidence rates in the two regions of Germany developed almost in parallel over the entire observation period, although the burden of disease was consistently lower by around 20–25% in East Germany compared to West Germany (▶ **Fig. 1 a**). What is notable is the temporary decrease in incidence rates from 2002, which was most marked among West German women in the group aged 30–69 years. Afterwards, a pronounced, partially reversible increase in incidence rates occurred in connection with the introduction of mammography screening. The incidence rates in West Germany increased after 2004/05. There was a delay before incidence rates in East Germany increased; they only began to increase from 2006/07 but increased more steeply. These increases contribute substantially to the rise in the rates of new cases with disease by around 20% over the entire period of observation. The highest incidence rates for both regions occurred in 2009, after which the overall trend declined. A more differentiated evaluation which looks at changes in age group-related incidence rates over time clearly shows that the development described above was mainly affected by changed incidence rates for the group aged 50–69 years as this was the group in which around 45% of all new cases of disease occurred (▶ **Fig. 1 c**). As it applies to the entire group (all ages), it is notable that the graphs show that incident rates for the intermediate age group in East and West Germany ran largely in parallel. This is not the case for the two other age groups. While the disease burden for younger women (30–49 years) in East and West Germany has tended to gradually converge over time, the rates for older women (70+ years) diverge. Older women in East Germany were not affected by the general increase in incidence rates (▶ **Fig. 1 d**).

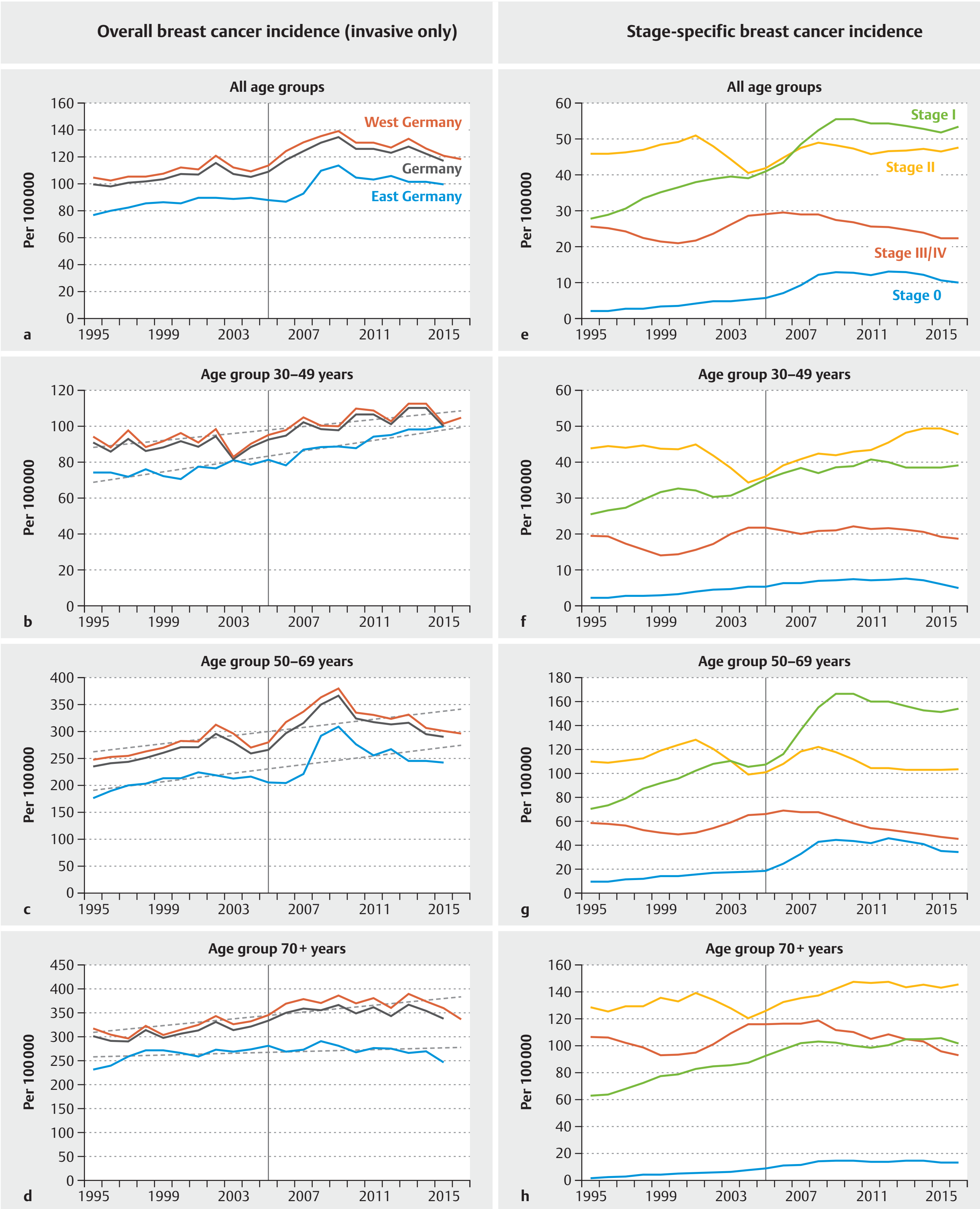
Stage-specific incidence

The course of stage-specific incidence rates is shown in ▶ **Fig. 1 e** to **h**. For reasons of clarity, the graphs do not differentiate between East and West Germany, as the stage-specific incidence rates in the two regions follow a very similar course. The change in incidence over time described above was accompanied by a significant shift in distribution across cancer stages (▶ **Fig. 1 e**). The temporary decrease in the incidence rate after 2002 was largely caused by a decrease in UICC stage II cancers, which was partially compensated for by an increase in stage III tumours. The subsequent increase, which correlates chronologically with the introduction of mammography screening, is mainly the result of an increased number of in situ cancers (stage 0) and stage I tumours accompanied by a decrease in late-stage cancers.

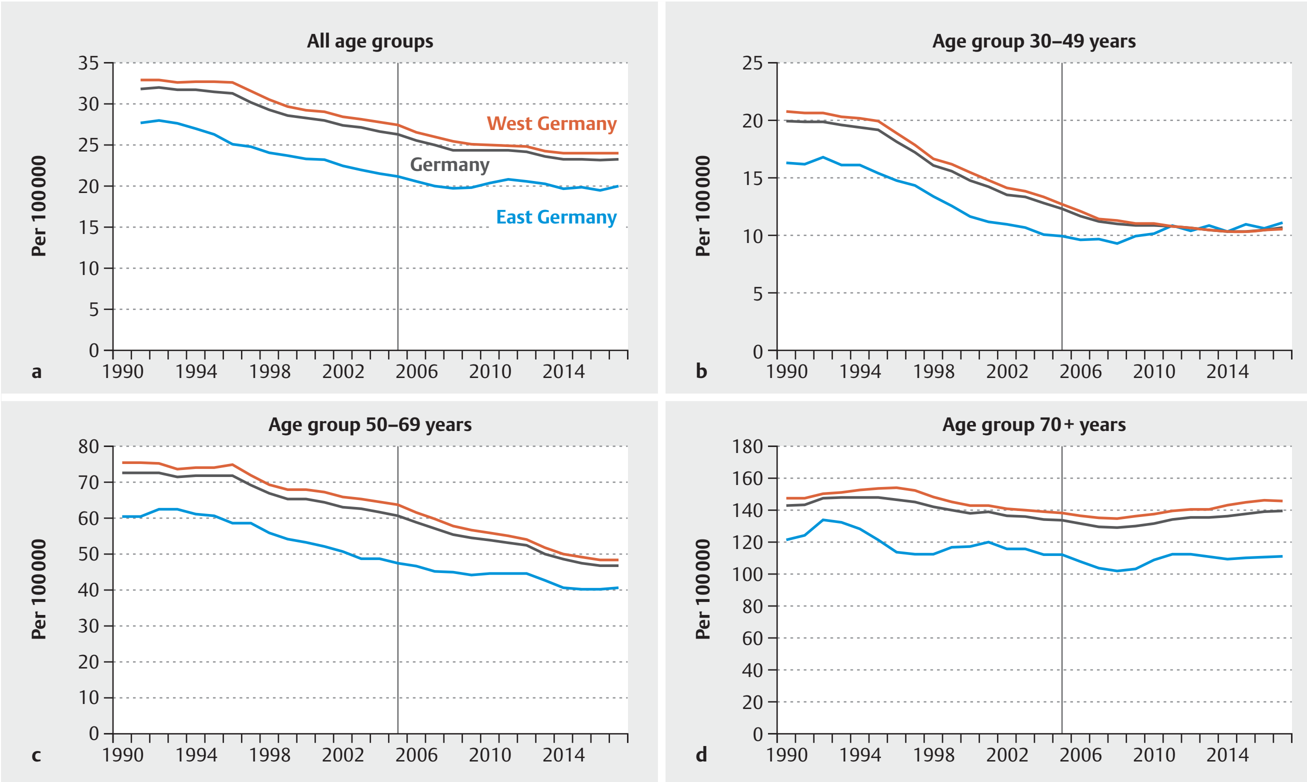
As expected, these shifts are more pronounced in the screening age group (50–69 years; ▶ **Fig. 1 g**). Compared to 2005, the rate of new cases with disease in this age group had increased by 48.1% in 2016 (stage 0: + 79.8%, stage I: + 42.5%). There were no relevant changes in UICC stage II tumours over the same period of time (+ 2.4%). The rate for advanced stage cancers decreased in parallel by 31.6%. The total incidence, including in situ cancers, increased by 14.5%; in terms of the incidence rate for 2016, additional diagnoses accounted for 12.6%. It should be noted, however, that an even higher relative increase in the incidence of early-stage cancers had already occurred in the screening age group between 1995 and 2005 (+ 58.2%). From 2005, qualitatively similar shifts in cancer stages also occurred in the group of younger (▶ **Fig. 1 f**) and of older women (▶ **Fig. 1 h**); however, these shifts were less pronounced. Increases of 8.4% (age group 30–49 years) and 13.2% (70+ years) can be set against decreases in late-stage cancers of 15.1 and 19.7%, respectively. Here too, the incidence of early-stage cancer already began to increase prior to 2005 although it started from lower levels.

Mortality

Mortality from breast cancer decreased strongly across all age groups in both regions of Germany, declining by around 27% (▶ **Fig. 2 a**). This positive change started around the middle of the 1990s and ended around 2008 in East Germany and 2014 in



▶ **Fig. 1** Overall and stage-specific incidence of breast cancer in Germany over time, differentiated according to age groups. Age-standardised overall (**a–d**) and stage-specific (**e–h**) incidence of breast cancer (using the old European population as the standard). Stage-specific incidence rates are presented as sliding averages over three years. The vertical lines indicate the year in which mammography screening was introduced (2005); the dotted lines show trends (smallest squares method).



▶ **Fig. 2** Breast cancer mortality in Germany according to age group over time. Age-standardised breast cancer mortality rates (using the old European population as the standard). The rates are shown as sliding averages over three years. Vertical lines indicate the year when mammography screening was introduced (2005).

West Germany. However, the trends in the different age groups differed significantly: while mortality in the group of younger women remained stable from around 2008 (▶ **Fig. 2b**), mortality in the group of older women increased from this time on (▶ **Fig. 2d**). Mortality continued to decrease in the group of women aged 50–69 years (▶ **Fig. 2c**).

In parallel to what occurred with incidence rates, mortality rates in East Germany were on average 20% lower over the entire observation period than those in West Germany. Here too, the differences between age groups were also evident. After 2011, the mortality rates for younger women in East and West Germany converged entirely. In the intermediate age group, the relative distance between mortality rates in the different regions remained stable at around 20% over the entire observation period. In the group of older women, there was a tendency for the gap between East and West Germany to widen. What is notable for this age group is that there was no marked decrease in mortality rates during the entire observation period.

Discussion

The main finding of this study is that breast cancer mortality in the overall female population in Germany decreased during the observation period while the breast cancer incidence rates increased. Age-specific trends and shifts in cancer stages suggest that both of these developments were affected by the introduction of mammography screening in 2005. Differences in incidence and mortality rates which existed in East and West Germany throughout the age groups in the period shortly after German reunification still persisted.

As expected, there was an initial increase in overall incidence rates in the group of women eligible for screening (50–69 years) followed by a decrease, although incidence rates did not drop to the levels prior to the introduction of screening. This temporary excess (also referred to as the "prevalence peak") is a typical consequence of the introduction of screening and is largely caused by early diagnosis of already prevalent cases. The chronological course of the prevalence peak which reached its maximum in 2009 correlated with the phase of successive implementation of the programme, whereby implementation in East Germany was slightly delayed [7]. The prevalence peak is a necessary and intended consequence of screening. In contrast, the excess number of cases remaining after the prevalence peak indicates a relevant harm caused by the intervention. It is caused by screening-induced diagnoses which would not have been made without screening, typically because the affected person dies before the (possibly slow-growing) tumour becomes clinically apparent. The individual occurrence of these so-called overdiagnoses including the treatment triggered by the diagnoses (overtreatment) is also unavoidable, although on a case-by-case basis it can usually not be ascertained whether the specific diagnosis is an overdiagnosis. With regard to the overall population, the number of overdiagnoses can be offset by the number of averted diagnoses (among other screening participants) if screening is capable of detecting relevant numbers of pre-stage lesions of the target disease. This is not the case with breast cancer screening if in situ carcinomas are not defined as pre-stage lesions but as a target disease. If it is assumed that the incidence trend in the group of women aged 50–69 years is not affected by secular trends, then our data shows that 12.6% of the diagnoses made in 2016 were programme-induced overdiagnoses. This figure is within the wide range of values reported elsewhere [8]. The decline in incidence rates visible since 2009 primarily affects women in the intermediate and older age groups. The unfavourable development in the group of younger women could indicate a cohort effect (see comparison between East and West below).

The observed temporary decrease in incidence rates from 2002 was most probably caused by the drop in the prescription of hormone replacement therapies, after two large studies (Women's Health Initiative and Million Women Study) reported an increased risk of breast cancer as a result of hormone replacement therapy. This is supported by the fact that the decrease was limited to West Germany, where hormone preparations are far more commonly used to treat symptoms of menopause than in East Germany [9]. It is difficult to interpret why this decrease was also observed in the group of West German women aged 30–49 years, as hormone treatment is rarely indicated and prescribed in this age group. It is possible that the observed decrease could be a random fluctuation.

The stage-specific analysis supports the assumption that the changes in incidence rates after 2005 are a direct consequence of mammography screening. The strong increase in early-stage cancers in the screening age group can ideally be set against a subsequent decrease in advanced stage cancers. Low changes in incidence rates for UICC stage II tumours can be explained by the rate shifting towards more stage 0 and I cancers but with this decrease being cancelled by a corresponding shift from the rate of higher stage cancers.

It can be assumed that the observed decrease in advanced stage cancers is a successful outcome of the screening programme if corresponding changes do not occur in the age groups not eligible for screening. Our data does not fully bear this out. After 2005, changes in the incidence of early and late-stage cancers typical for screening programmes occurred both in the group of younger and the group of older women, although they were lower than in the group eligible for screening. A possible reasons for this favourable development are an increased awareness of the disease and opportunistic screening. The detection of in situ carcinomas is a clear indicator, as they are almost only found during imaging-based screening and also increased after 2005 in the age groups not eligible for screening. It should also be noted that when screening was introduced, a non-negligible incidence of cases with non-invasive breast cancer was recorded for all age groups. In accordance with our data, a study done in the Saarland showed that between 2002–2004, 45.3% of women aged 55 years and above had a mammography in the previous 2 years [10]. Such a high number cannot be explained by diagnostic necessity. It is expected that the effects of opportunistic screening examinations will continue to affect the disease burden even after 2005. Based on the currently available data, it is not possible to make a sharp distinction between the effects of opportunistic and of organised screening. The overall picture of the observed findings suggests, however, that the decreased incidence of advanced stage cancers is a result, at least in part, of the success of quantitatively and qualitatively improved screening. The size of the observed effect is in line with findings reported in other studies [11].

The increase in stage III and IV tumours observed between 2001 and 2004 combined with the simultaneous decrease in stage II tumours should be viewed in the context of the changes made to the 6th edition of the TNM classification (2002). These changes resulted in some tumours which had previously been classified as UICC stage II in the 5th edition being subsequently considered as UICC stage III tumours [12].

The observed decrease in breast cancer mortality which began in the mid-1990s had its counterparts in many other western countries [13]. There are many possible reasons for the decrease. Improved chemotherapies, antihormone therapy, immunotherapy and combined treatment have significantly improved the prognosis for breast cancer in the last 20 to 30 years. This study suggests that opportunistic screening which was already being carried out before 2005 also contributed to this trend. The fact that a continued decrease in mortality rates in the target population of women aged 50–69 years was observed even after 2008 but not in the other age groups points to the additive effect of organised mammography screening. Alternative explanations for the favourable changes observed in the age group eligible for screening, such as the more intensive utilisation of new therapies, should also be considered. More intensive therapies may play a role compared to the 70+ age group (see more on this point below). But it is unlikely that this is the only explanation for the more favourable development of breast cancer mortality in the age group eligible for screening, given that the benefits of decreased mortality correlate with changes in stage-specific incidence rates. The decrease in the rate of cases with advanced stage breast cancer is a reliable indicator for a screening-related success in decreasing disease-specific mortality [14]. The observed age-dependent trends in stage-specific incidence rates are therefore an indication that breast cancer mortality in the group of women aged 50–69 years is affected by mammography screening.

Comparable studies from other countries on the impact of mammography screening on mortality present a mixed picture. Numerous authors have carried out systematic reviews of the confusing range of studies and data currently available. Mandrik et al. summarised the results of 58 systematic reviews in a comparative overview [15]. Qualitative and quantitative syntheses consistently find a screening-related decrease in breast cancer mortality. Meta-analyses of observational and population-related studies report a pooled effect estimate for screening-related risk reduction of 28–56%. Lower effects based on randomised controlled studies and models are also reported. It can be concluded from this that observational studies tend to lead to an overestimate of screening-related effects on disease-specific mortality. Mandrik et al. emphasised the large methodological heterogeneity in both primary studies and in systematic reviews. They also noted that studies interpret their findings differently in terms of the clinical relevance, particularly in relation to possible harms from screening (overdiagnosis, false-positive results). It should be emphasised in this context that, taken by themselves, the age-specific trends for breast cancer mortality we observed in our study do not provide conclusive evidence for the positive effects of mammography screening. In line with international studies, they do suggest, however, that the screening programme contributed to reducing mortality in the target group.

The finding that since 1990 there has been no discernible trend of decreased mortality for the group of women aged 70+ years and that mortality rates in the group even increased after 2008 needs to be discussed. Corresponding trends in incidence rates which could explain this observation are not apparent; the rate of new cases with disease did not increase more in the group of older women than in the group of younger women. This suggests that older patients do not share in or benefit from improved treatment options in the same way as younger patients do. Observations for the years 1998–2008 showed that, compared with patients of the same age in the USA, the survival rates of older women with breast cancer (aged ≥ 70 years) in Germany were poorer, but those of younger women were not. Another study found that older patients (aged 70 years and above) received chemotherapy, radiotherapy and trastuzumab less often than younger women [16]. This may be justified by medically relevant co-morbidities or the individual patient's age-related preferences. Whether this difference also indicates genuine deficits in healthcare provision is being investigated further.

The fact that there is a considerable difference in breast cancer-related disease burden between East and West Germany has been known for quite some time. This difference is primarily associated with the difference in reproductive behaviour in the two German regions. The different risk factors for postmenopausal breast cancer, which accounted for around 83% of all breast cancer cases in 2014, have been investigated in detail [3]. Women who are at least 30 years old when they give birth to their first child have a 1.34 higher risk of postmenopausal breast cancer compared to women who give birth to their first child before the age of 25. Childlessness increases the risk by a factor of 1.23 [17]. Until the end of the 1990s, women in East Germany were on average 2–4 years younger when they gave birth to their 1st child than women in West Germany [18]. Following the study by Tamini et al. [17], this would correspond to a risk reduction of about 10%. The total fertility rate in East Germany between 1974 and 1990 was 1.7 children per woman, which was higher than that of West Germany (1.4 children per woman). Childlessness among East German women born in the period 1965–69 was 12.3% and thus less frequent than among West German women of the same generation, of whom 21.9% did not have children [18]. Based on the above-mentioned figures, this difference could explain another 2–3% difference in risk between East and West Germany. Changes in reproductive behaviour over time would fit the observed differences in incidence trends for the different age groups. The trends in East and West Germany have converged, both in regard to the birth rate and in regard to maternal age at birth of the 1st child. The effects this has had on breast cancer incidence are more likely to be found in the younger age group than in older age groups for whom the different conditions in a divided Germany continue to have an impact.

Body mass index (BMI) is another important factor affecting the incidence of breast cancer. A higher BMI when entering adulthood is protective, while weight gain in later years increases the risk [17]. In this respect women in East Germany had an advantage at the start of the observation period. Overweight and obesity was more common among young women in East Germany at the beginning of the 1990s compared to West Germany. However, weight gain trends in adulthood were very similar in East and West Germany when we look at prevalence in the different age groups [19]. The benefit accruing to East German women from this difference disappeared in subsequent decades. While the prevalence of overweight decreased in the group of younger women until it reached the level of West Germany in 2003, it increased significantly in the intermediate age groups. If the changed age-specific prevalence rates are assumed to be static, then women in East Germany could be expected to have a significantly higher risk compared to women in West Germany, particularly with regard to postmenopausal breast cancer. The fact that such a trend was not visible for the analysed data could be due to cohort effects again: as with their reproductive behaviour, older women continue to benefit from the protective factors generated by their lifestyle in younger years.

The strengths and limitations of this study are largely based on the underlying data. These limitations are very relevant for the incidence data. Because the aim was to carry out a long-term trend analysis, the data used in this study only covers around 20% of the female population of all of Germany. The percentage for West Germany is even lower. In addition to the associated sampling error, it is possible that the available data are not representative for East Germany, West Germany or all of Germany. Information is lacking which would make it possible to estimate the direction and extent of any resulting systematic mistakes (bias). Another unavoidable uncertainty results from the incompleteness of reports on TNM categories, which were particularly common in West Germany in the early years of the observation period. The proportional distribution across cancer stages of missing UICC stages which was done in this study offers correct results if the lack of information does not depend on the actual stage of disease. If this is not the case, bias consisting of over- or under-estimation of early or late stages must be considered. The descriptive nature of the analysis should also be noted. The observational data used in the study are contaminated by screening activities undertaken prior to 2005 as well as by activities in other non-screening age groups and can therefore not be used to make definitive statements about the extent of the benefit of mammography screening. To do so would require a comparison between groups with a known exposition to screening. In terms of the reasons given for the differences between East and West Germany, the only explanatory factors considered in this study were reproductive behaviour and BMI. Other risk factors such as size, age at onset of menstruation and menopause, alcohol consumption, and lack of exercise were not investigated.

Conclusions

The introduction of mammography screening in 2005 had a strong impact on the incidence of breast cancer in Germany as did the rates of opportunistic screening. The decreasing incidence of late-stage breast cancer observable since about 2005 and the continued decrease in breast cancer mortality rates from 2008 on in women between the ages of 50 and 69 years could be partly explained as a successful outcome of the screening programme. On the downside, screening also led to a substantial number of overdiagnoses. Relatively unfavourable incidence trends in younger women, particularly in East Germany, can be explained in the context of changes to lifestyle factors (e.g. reproductive behaviour, overweight). Interpreted as a cohort effect, these incidence trends suggest a prospective increase in older age goups, particularly in East Germany. An unfavourable mortality rate trend was noted for older women. Further research is required to determine whether and to what extent this points to deficits in healthcare provision.

Appendix

Annual rates for all of Germany were calculated using the formula

$$\text{Rate}_G = \frac{\text{Pop}_E}{\text{Pop}_E + \text{Pop}_W} \times \widehat{\text{Rate}}_E + \frac{\text{Pop}_W}{\text{Pop}_E + \text{Pop}_W} \times \widehat{\text{Rate}}_W$$

whereby Pop_E and Pop_W are the number of female inhabitants in the respective age group in East and West Germany, respectively. $\widehat{\text{Rate}}_E$ and $\widehat{\text{Rate}}_W$ are the annual estimated rates for East and West Germany respectively, based on the incident cases and deaths (numerator), and the underlying female population (denominator), each applying to the regions, covered by the selected cancer registries.

Conflict of Interest

The authors declare that they have no conflict of interest.

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