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ORIGINAL RESEARCH

Time Trends in Male Breast Cancer Incidence, Mortality, and Survival in Austria (1983–2017)

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Background: Male breast cancer (MBC) comprises less than 1% of all breast cancer cases globally and remains understudied with persisting sex-specific survival disadvantages. We aim to contribute to better understanding of MBC with a comprehensive analysis of time-trends over several decades in Austria.

Methods: We used Austrian National Cancer Registry data on 1648 cases of MBC cases diagnosed between 1983 and 2017 in Austria. Overall incidence, mortality, and survival rates, as well as age-, stage-, and period-specific incidence and survival rates were calculated. Joinpoint regression was performed to assess trends.

Results: MBC incidence rates increased throughout the whole observation period (1983–2017) with an annual percent change (APC) of 1.44% (95% confidence interval, CI: 0.77 to 2.11). During the same period, morality rates were stable (APC: –0.25, 95% CI: –0.53 to 0.60). Ten-year survival rates showed three phases of decreasing increases with an average APC of 2.45%, 1983–2009 (95% CI: 2.1 to 2.74). Five-year survival rates improved until 2000 (APC: 2.31, 95% CI: 1.34 to 3.30) and remained stable thereafter (APC: 0.10, 95% CI: –0.61 to 0.80). Stage-specific analyses showed a single trend of stable incidence rates of distant disease MBC (APC: –0.03, 95% CI: –1.67 to 1.65). Further, we observed increases in localised, regional, and unknown stage cancer incidence and increases in incidence rates across all age groups over the whole observation period. However, the estimates on these subgroup-specific trends (according to age- and stage) show wider 95% CIs and lower bounds closer to zero or negative in comparison to our findings on overall incidence, mortality, and survival.

Conclusion: Despite improvements in survival rates, MBC mortality rates remained largely stable between 1983 and 2017 in Austria, possibly resulting from a balance between increasing overall incidence and stable incidence rates of distant disease MBC.

Keywords: male breast cancer, male health, cancer epidemiology, cancer trends

Background

Male breast cancer (MBC) is an uncommon disease and generally reported to account for less than 1% of all breast cancer (BC) cases.[1] BC in males is diagnosed at higher age and later stage when compared to female BC.[2] Despite conflicting research on sex-specific survival and mortality differences in the past, more recent studies reported survival disadvantages in males when compared to corresponding cases in women.[2–6] Further, improvements in survival in male patients with BC were slower than in female patients.[7]

Treatment principles of MBC follow recommendations established for female patients. However, MBC patients tend to undergo radical surgery more often, and receive radiotherapy, chemotherapy, as well as hormonal therapy less often than female patients with similar characteristics.[3,8]

In an international comparison of sex-specific BC rates using data spanning from 1988 through 2002, male breast cancer incidence varied notably with the highest numbers observed in Israel (1.24 cases per 100,000 men), the Philippines (0.98 cases per 100,000 men), and Iceland (0.93 cases per 100,000 men). Compared to this, in the same period, the incidence rate in Austria was low with 0.45 cases per 100,000 men.[9] The incidence of MBC over time did not

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generally increase in international comparisons.[9] However, increases in incidence of MBC were reported for the United States with an average annual percent change (AAPC) of 1.0 between 1973 and 2003.[10]

Recent efforts of providing a basis for the better understanding of MBC include the characterisation of clinical features, diagnosis and treatment, prognostic factors for survival as well as biological characteristics, whereas epidemiological evidence of MBC and trends over time information are lacking.[8,11]

With our comprehensive analyses of overall incidence as well as age- and stage-specific incidence, mortality, and survival rates, using a full national sample over 35 years of observation, we aim to contribute to the unravelling of the characteristics of MBC by providing robust evidence of time-trends over several decades.

Methods

The data used for our analyses include all MBC cases recorded between 1983 and 2017. They were collected within the Austrian National Cancer Registry (ANCR) and were provided by Statistics Austria, the national Statistical Institute. Information on all newly diagnosed cancer cases in Austria is collected statutory, grounded in Austria's National Cancer Statistics Act of 1969, with sufficient completeness and quality of data from 1983 on. Further, Austria's cancer registry data is linked to official cause of death statistics.

The provided data comprises information on year of diagnosis, year of death, age at the time of diagnosis, age at the time of death, place of residency (Austria federal state), cancer diagnosis, histological type, stage, and cause of death. Cancer diagnoses were coded using the tenth revision of the International Classification of Diseases (ICD-9 and ICD-10), histological types were coded using the International Classification of Diseases for Oncology, third edition (ICD-O-3).[12] Data on population counts according to sex and age were obtained from Statistics Austria. Mid-year population numbers were estimated by averaging the population counts on January first of a certain year with the count of the respective following year using Microsoft Excel (Version 16.63 for Mac OS).[13]

The calculations of rates and statistical analyses were performed using Stata software (Stata BE 17).[14] MBC-specific deaths were identified using information on case of death (coded using ICD-10) and reflect cases in patients who were diagnosed with BC and died from BC specifically.[12] Age groups were formed using information on age at report with an age group of 18–49 years and ten year-age groups starting at the age of 50. Observation periods were created using information of year of report and yielded seven five year-periods (1983–1987, 1988–1992, 1993–1997, 1998–2002, 2003–2007, 2008–2012, 2013–2017). Groups according to stage were created based on given information (localised cancer, regional cancer, distant disease cancer, death certificate only cases, and unknown stage cases).

The age standardisation of rates was performed based on Tiwari et al's method for efficient estimation. The confidence intervals were calculated based on a gamma distribution using the *distrate* command for Stata.[15,16] Kaplan–Meier survival estimates of all MBC cases combined and according to subgroups were created using Stata's *stset* command. In cases where diagnosis and death were reported in the same year, an average survival of six months was assumed. BC-specific survival rates (five year- and ten year-survival rates) were extracted from life tables created using Stata's *ltable* command.[17] Joinpoint regression analysis with significance tests based on Monte Carlo permutations was performed and joinpoints (trend changes), annual percentage changes (APC) as well as average annual percentage change (AAPC) were calculated using the National Cancer Institute's Joinpoint Trend Analysis Software (Desktop Version 4.9.1.0.) in order to quantify trends over time.[18] The maximum number of joinpoints was set to four. Correction for type 1 errors was performed based on the Bonferroni–Holm method. The reporting of the results refrains from using language that categorises based on p-values and the significance of confidence intervals. To enable nuanced interpretation of the results, we provide details on the numbers of observation according to each subgroup, interval estimates (95% confidence intervals, CIs), and indicate p-values <0.05 (Table 1 and Table 2).

Ethical approval for the use of Austrian Cancer registry data for this study in accordance with the guidelines of the Helsinki Declaration was provided by the Ethics Committee of the Medical University of Vienna (Study 1259/2019).

Table 1 Breast Cancer in Men in Austria, Austrian Cancer Registry, 1983–2017

Diagnosis of breast cancer (n=1648)	**n**	**%**
C500-C508	93	5.6
C509	1550	94.1
C809	5	0.3
Stage at diagnosis (n=1648)	n	%
Localised	567	34.4
Regional	597	36.2
Distant	151	9.1
Unknown	245	14.9
Death certificate only	88	5.3
Deaths in men with breast cancer during the observation period (n=1018)	n	%
Any cause of death	1018	100.0
Breast-cancer specific deaths	468	46.0
Age	Median	Range
Age at diagnosis	67	14–95+
Age at death	76	22–95+

Table 2 Annual Percent Changes in Overall Incidence and Mortality of Breast Cancer, Breast Cancer-Specific Five-Year and Ten-Year Survival Rates, and Stage-Specific and Age-Specific Breast Cancer Incidences in Males in Austria, 1983–2017

	n	**Period**	**APC**	**(95% CI)**	**AAPC**	**(95% CI)**
Overall incidence	**1648**	**1983–2017**	**1.44**	**(0.77 to 2.11)**	**–**	
Overall mortality	1018	1983–2017	–0.25	(–0.53 to 0.60)	–	
Five-year survival	**1408***	**1983–2000**	**2.31**	**(1.34 to 3.30)**		
		2000–2014	0.10	(–0.61 to 0.80)	**1.30**	**(0.71 to 1.90)**
Ten-year survival	**1043***	**1983–1989**	**5.53**	**(3.40 to 5.67)**		
		1989–1999	**2.79**	**(2.39 to 3.18)**		
		1999–2009	**0.89**	**(0.66 to 1.12)**	**2.45**	**(2.16 to 2.74)**
Stage-specific incidence						
Localised	567	1983–2017	0.83	(–0.37 to 2.03)	–	
Regional	597	1983–2017	1.14	(–0.07 to 2.36)	–	
Distant disease	151	1983–2017	–0.03	(–1.67 to 1.65)	–	
Unknown stage	245	1983–2017	1.97	(0.233 to 3.73)	–	

(*Continued*)

Table 2 (Continued).

	n	Period	APC	(95% CI)	AAPC	(95% CI)
Death certificate only	88	**1983–2017**	**–3.25**	**(–5.00 to 1.48)**	**–**	
Age group (years)						
18–49**	143	1983–2017	1.26	(–0.30 to 2.85)	–	
50–59	285	1983–2017	0.82	(–0.50 to 2.16)	–	
60–69	494	1983–2017	1.01	(0.00 to 2.02)	–	
70–79	460	1983–2017	1.40	(–0.36 to 2.45)	–	
80+	264	1983–2017	1.71	(–0.52 to 2.92)	–	

Notes: *Cut-offs due to the observation period (censoring). **Two cases were recorded in male persons under the age of 18 which were excluded from this group. Bold: p-value <0.05.
Abbreviations: APC, annual percent change; AAPC, average annual percent change; CI, confidence interval.

Results

Between 1983 and 2017, a total of 1648 cases of MBC were observed in Austria with 468 BC-specific deaths recorded. The median age at diagnosis was 67 years, the median age at death was 76 years. Most cases were coded as C509 ("Malignant neoplasm; Breast, unspecified", 94.1%) whereas a smaller part included a localisation of the tumour (C500-C508). Five cases (0.3%) were coded as unspecific according to the diagnosis (C809) but were identified as breast cancers according to the histological type (intraductal carcinomas).[12] The largest group according to stage of diagnosis over the whole period of observation was that of regional disease cases (36.2%), closely followed by localised stage disease cases (34.4%) (Table 1).

Incidence rates of MBC increased with a linear trend between 1983 and 2017. During the same period, mortality rates remained largely stable with a tendency of decline (Table 2, Figure 1). Five-year survival rates increased between 1983 through 2000, followed by stable rates. Ten-year survival rates showed a triphasic trend of increases (Table 2, Figure 2).

Localised and regional MBC incidence rates increased in a single linear trend from 1983 through 2017. Incidence of distant disease BC remained stable throughout the whole observation period. Death certificate only-cases decreased between 1983 and 2017 as part of a single, linear trend. During the same period, incidence of unknown stage MBC showed a single trend of increases (Table 2, Figure 3).

Changes in incidence according to age groups underwent similar changes with single trends of linear increases between 1983 and 2017. The largest increases were observed in persons above 80 years of age, followed by 18–49 years old patients. The increases in incidence in patients aged 60–69 and in the group of 50–59 years old patients were rising more modestly (Table 2, Figure 4). However, these subgroup-specific trends (according to stage and age groups) showed wide 95% CIs with lower bounds closer to zero or negative in comparison to the estimates obtained on the trends in overall incidence, mortality, and five-year and ten-year survival.

Kaplan–Meier survival estimates of BC-specifical survival in men in Austria showed survival rates of 78% (95% CI; 0.76–0.82) after five years and 71% (95% CI: 0.68–0.73) after 10 years (Figure 5, all cases combined).

Survival estimates according to stage showed expected patterns of decreasing survival from early- to late-stage BC in men in Austria (Figure 6). After a slightly lower survival in the first three years, survival estimates in patients with unknown stage of breast cancer remained in range between the survival rates observed in localised and regional stage MBC patients.

Kaplan–Meier survival estimates according to age showed similar five-year survival rates across age groups in patients aged between 18 and 79 but more distinct differences in ten-year survival rates between those age groups. Patients aged 80 years or older show significantly lower survival rates (five-year and ten-year survival rates) as compared to younger patients (Figure 7).

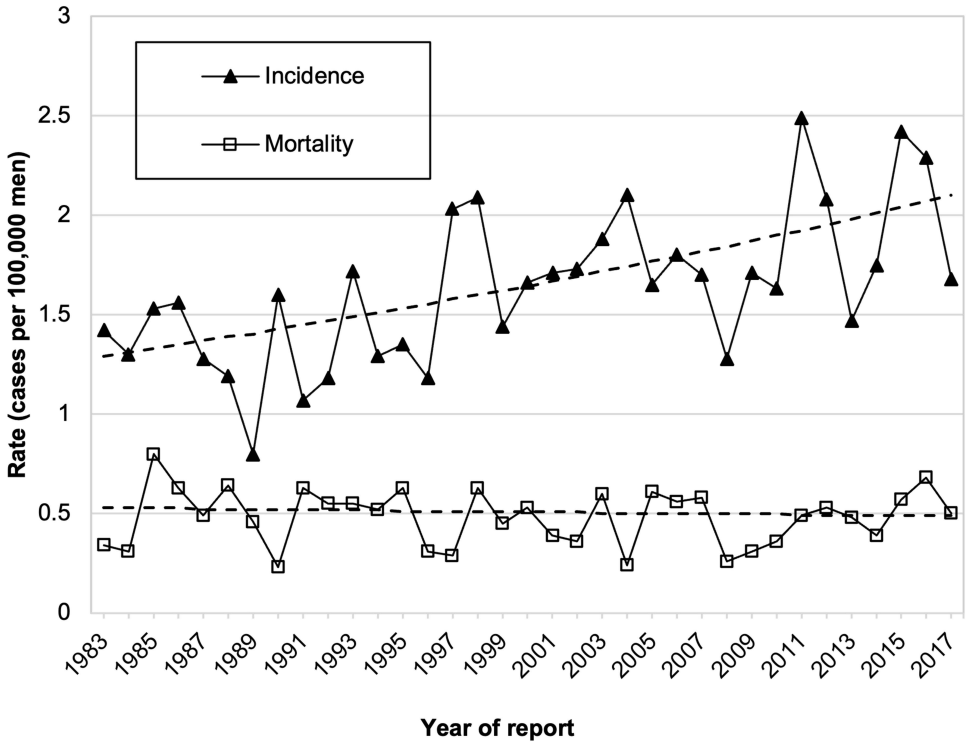

Figure 1 Male breast cancer incidence and breast cancer-specific mortality in Austria, 1983–2017 (age-standardised, European Standard Population 2013).

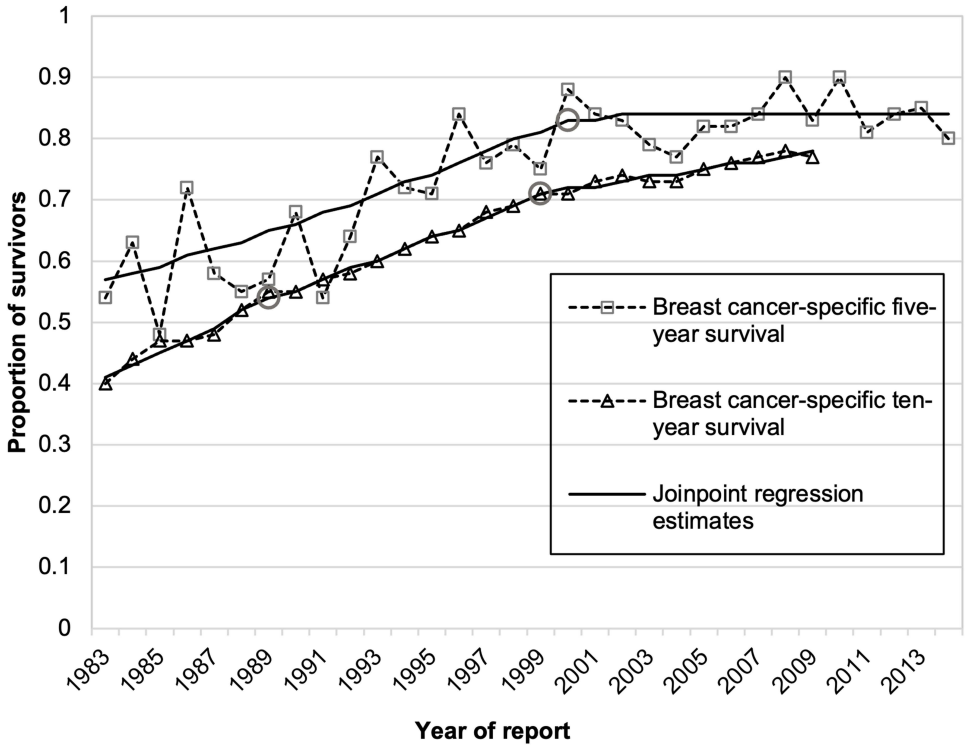

Figure 2 Breast cancer-specific five-year and ten-year survival among men in Austria, 1983–2014 and 1983–2009 - Circles indicate joinpoints (breast cancer-specific five-year survival: 2000, breast cancer-specific ten-year survival: 1989, 1999).

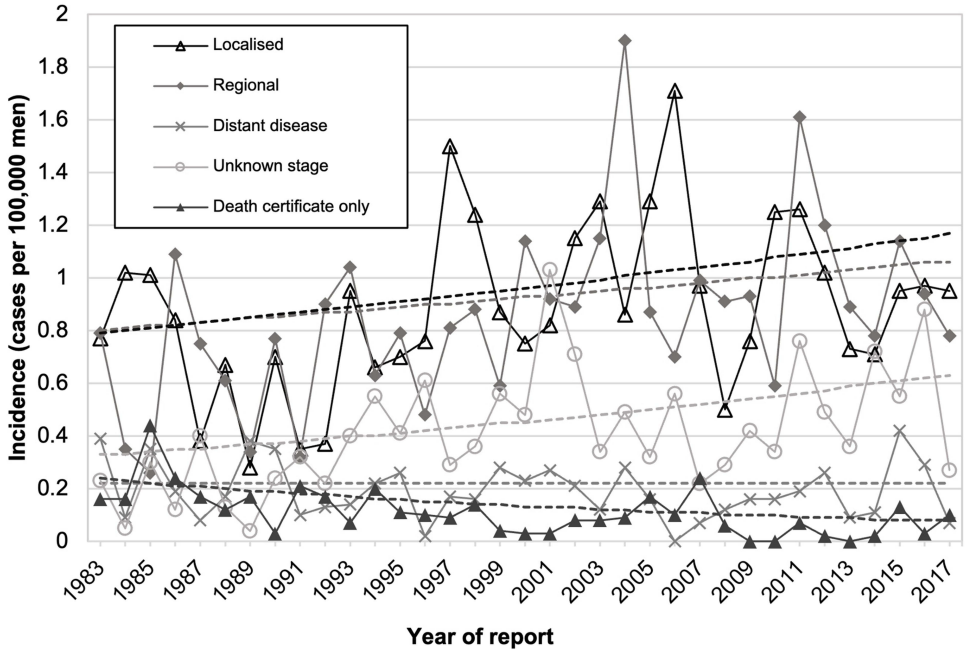

Figure 3 Breast cancer incidence in males in Austria according to stage, 1983–2017 (age-standardised, European Standard Population 2013).

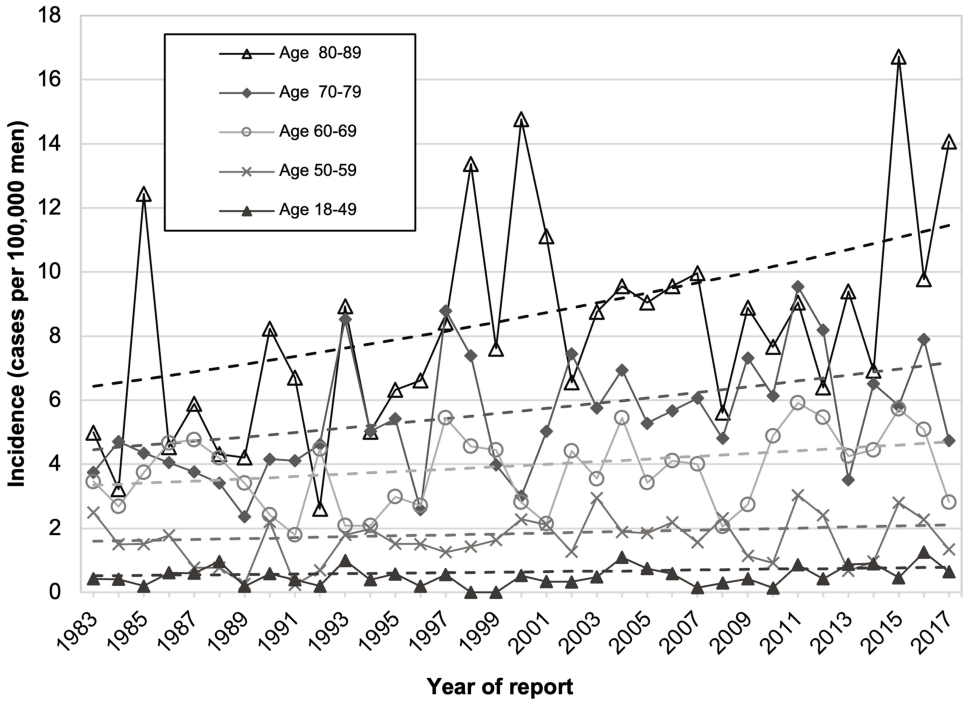

Figure 4 Breast cancer incidence in males in Austria according to age, 1983–2017 (crude rates).

Kaplan–Meier estimates of MBC-specific survival rates according to periods of diagnosis (five-year groups of diagnosis, Figure 8) displayed comparably low survival rates in the two earliest observation groups (1983–1987 and 1998–1992), and distinctly higher survival rates in patients diagnosed from 1993 onwards, with diminishing differences between patients diagnosed between 1998 and 2017.

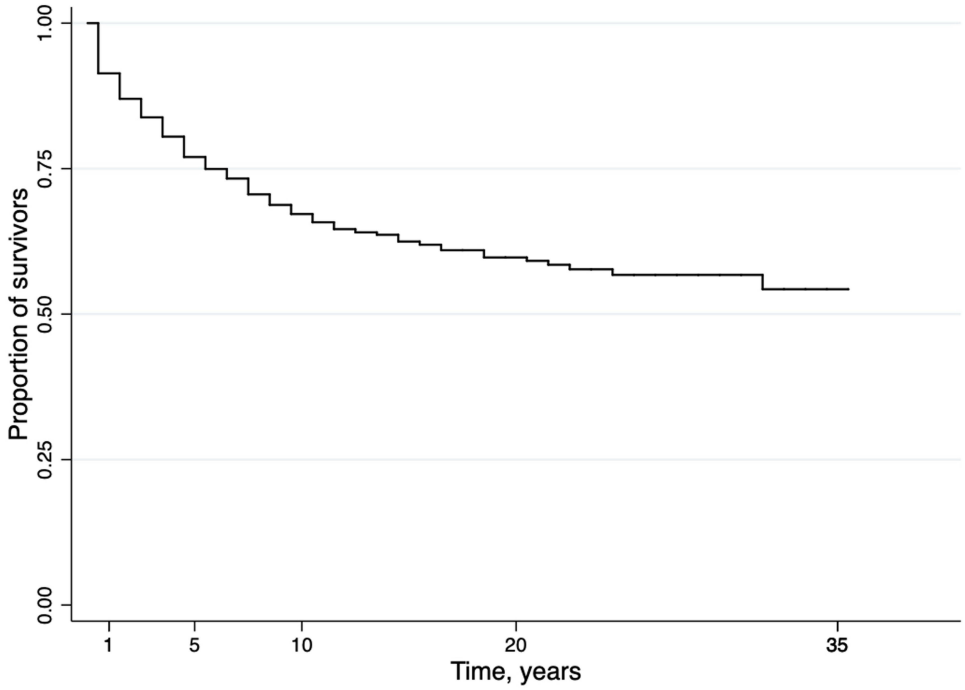

Figure 5 Overall breast cancer-specific survival in men in Austria, 1983–2017 (end of follow-up 2018).

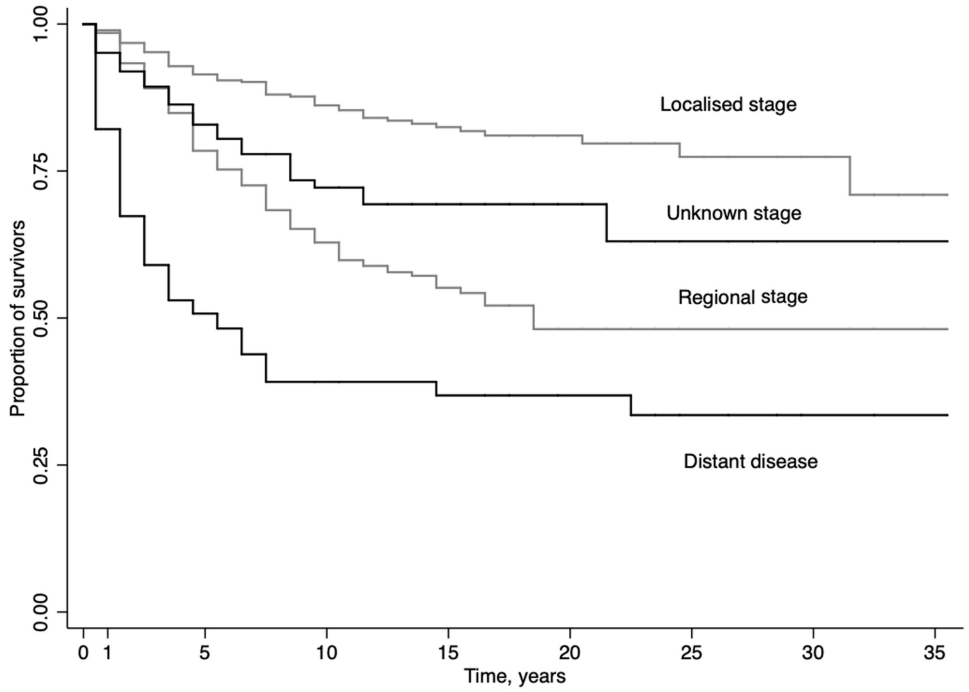

Figure 6 Male breast cancer-specific survival in Austria according to stage, 1983–2017. (end of follow-up 2018).

Discussion

Our analyses of all MBC cases diagnosed in Austria between 1983 and 2017 showed increases in overall incidence while mortality rates remained stable. BC-specific five year-survival rates increased until the year 2000 and were stable in the following years, whereas ten-year survival rates showed a triphasic trend of increases. Stage-specific trends varied, with

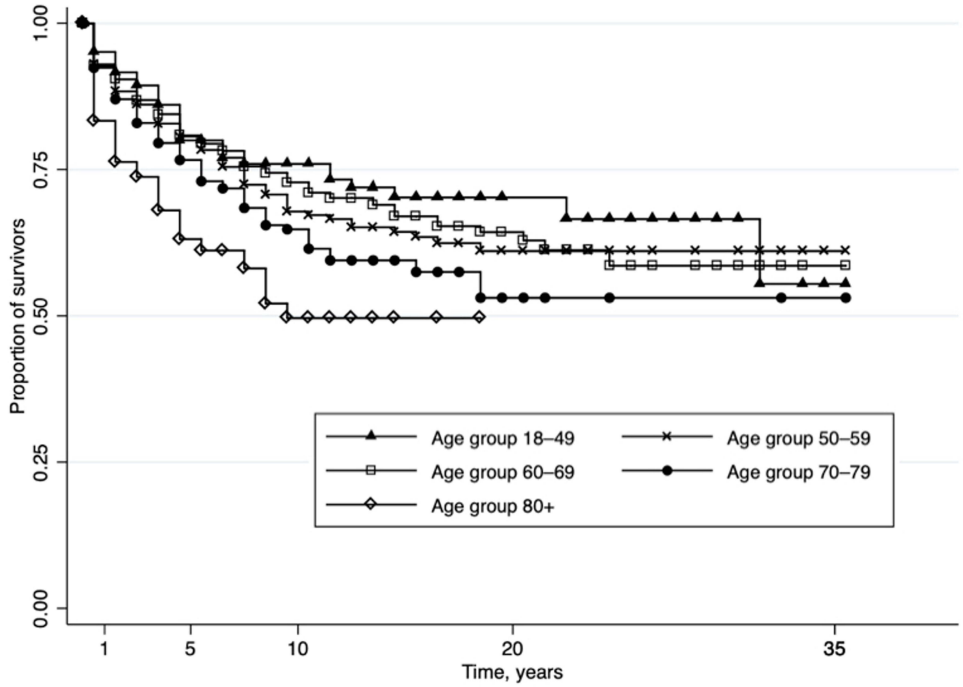

Figure 7 Male breast cancer-specific survival in Austria according to age, 1983–2017. (end of follow-up 2018).

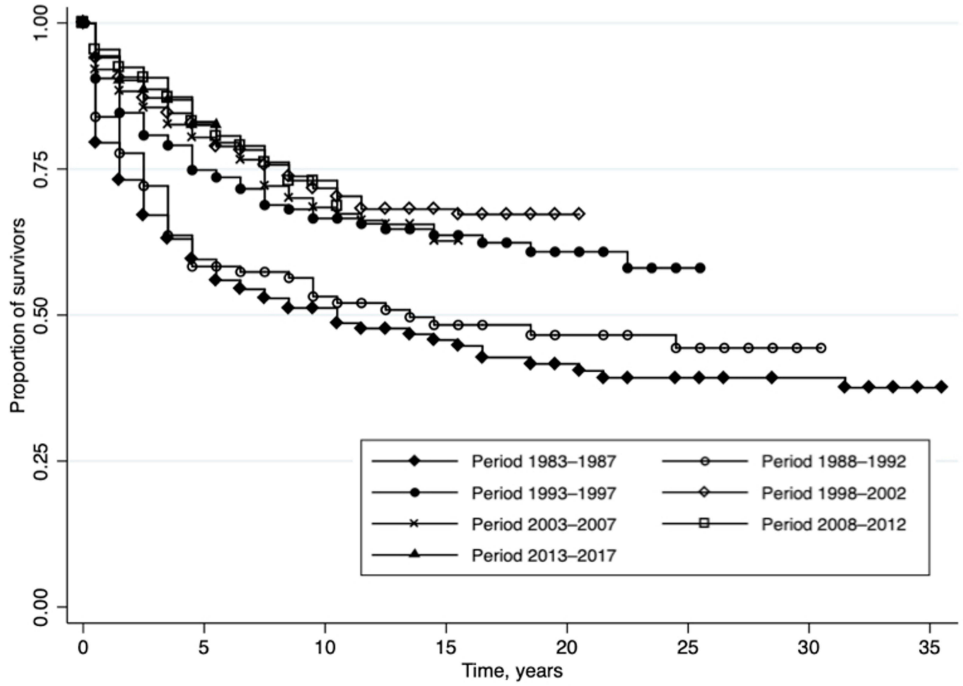

Figure 8 Male breast cancer-specific survival in Austria according to period, 1983–2017. (end of follow-up 2018).

increases in localised, regional, and unknown stage cancer-incidence, fairly stable incidence rates of distant disease BC, and a substantial decline of cases recorded only at death. After a leap in survival between the periods of 1988–1992 and 1993–1997, improvements in survival were less pronounced.

With 1648 cases, 1.0% of all breast cancer cases in Austria (165,354 in total) were diagnosed in males (1983–2017) which is comparable to the expected portion of male breast cancer cases in the United States in 2022 (0.94%) and in

alignment with an international average incidence rate ratio of 122 (female-to-male, 1988–2002).[1,19] The incidence was 1.63 cases per 100,000 men in 2017 (age-standardised, European Standard Population 2013) in Austria, a clear increase from previously reported 0.45 cases per 100,000 men in the period 1988–2002.[9]

Austria's growth in MBC incidence is comparatively high, with an APC of 1.44% (1983–2017, CI: 0.77 to 2.11), as part of a linear trend. The increases in incidence observed in our study are somewhat higher than those reported in a study using data from the United States (US, AAPC=1.0%), but also span a more recent time-period (Austria: 1983–2017 vs US: 1973–2003).[10] An analysis of MBC trends in Scotland covering a more similar observation period to our study, showed an increase in the age-standardised incidence (cases per 100,000) of 0.8 in 1992 to 1.3 in 2017, translating to an AAPC of 1.96%.

As opposed to female BC trends, there is a lack of an apparent contributor to growing incidence rates, such as the start of a screening programme. The growth in incidence may be derived from other diagnosis-related factors, such as increased awareness of male breast cancer or improved imaging quality. Further, the increases in incidence may also be rooted in changes attributable to biological risk factors, particularly those that may have primary or secondary effects on oestrogen-levels. These range from an increase in alcohol consumption, possible effects of radiation exposure, increasingly common obesity and physical inactivity or improper diet, but also hormone treatment as received by transgender women.[9,10,20,21] However, large-scale longitudinal studies on sex-hormone levels in men in Austria or countries comparable in lifestyle and socioeconomic characteristics are lacking.

While incidence increased between 1983 and 2017, BC-specific mortality changed little, with a slight tendency of decrease and an APC of –0.25 (1983–2017, CI: –0.53 to 0.60), whereas BC-specific survival rates improved. Five-year survival rates display an average increase over the whole period of observation of 1.3% (AAPC, CI: 0.71 to 1.90) despite stable mortality rates since 2000. In the last years of observation (2010–2014), BC-specific five-year survival rates ranged from 80% to 90% (Figure 2), somewhat higher than the average relative five-year survival of 78%, as reported officially for the same observation period.[22] Ten-year survival rates show a triphasic trend of decreasing increases with an AAPC of 2.45% (CI: 2.16 to 2.74). These changes likely reflect the uptake of improved treatment derived from female BC management, but they also may come from an increase in early stage-BC incidence with, at the same time, largely unchanged incidence of more lethal, distant disease BC. Improvements in survival of men with BC were reported previously, albeit at slower rates as compared to female BC patients.[7] The lack of change in overall MBC mortality in Austria stands in contrast to decreases of 10 to 40% in mortality between 2000–2004 and 2015–2017 observed in North-Western European countries, Russia and the US. A possible explanation may be a balance between increasing survival rates, and increasing incidence of MBC in Austria, leading to stable overall mortality.[23]

To facilitate the interpretation of possible underlying factors of these trends (increasing incidence, stable mortality, and increasing survival), an overview and graphical representation of all overall as well as subgroup-specific trends was compiled ("Trends at a glance", Figure 9).[24] While overall incidence, mortality, and survival rates describe broader trends and hint at possible cancer control success, the analysis of subgroup-specific rates may point to potential underlying factors influencing the frequency of a disease and leading to changes in survival rates. Such *trends at a glance* (Figure 9) may be particularly interesting from a public health perspective to enable the interpretation of trends and possible underlying factors. For instance, the largely unchanged mortality rates observed in our data may come from a balance of increasing overall and early stage-BC incidence (Figures 3 and 6), offset by a largely unchanged incidence rates of late stage-BC incidence (Figures 3 and 6), the largest contributors to case fatality and thus mortality. Further, the increases in survival rates were accompanied by increases in the incidence rates of localised and regional breast cancer. Our findings are in alignment with the previously described decreases in relative mortality among men with BC in the United States.[3]

Our stage-specific analyses show that the increases in incidence are driven by early stage and regional cancer. There is also a high increase in the incidence of unknown stage BC. This finding corresponds to an analysis of female breast cancer rates in Austria (Austrian Cancer Registry Data) and reports from German cancer registries. The large numbers of unknown stage cancer cases may come from a lack of diagnostic information in the early phase of diagnosis when data are collected and provided to the Austrian and German Cancer registries.[19,25–27] Age-specific incidence analysis exhibited linear increases in all age groups (Figure 4). The biggest increase was observed in the oldest patients, aged

	Observed trend	Graphical representation
Overall incidence:	increasing rates (single trend)	
Overall mortality:	stable rates	
Five-year survival:	increasing rates + stable rates	
Ten-year survival:	increasing rates (triphasic trend with lower increases more recently)	
Incidence according to stage		
Localised:	increasing rates (single trend)	
Regional:	increasing rates (single trend)	
Distant disease:	stable rates	
Unknown stage:	increasing rates (single trend)	
Death certificate only cases:	decreasing rates (single trend)	
Incidence according to age (years)		
18–49	increasing rates (single trend)	
50–59	increasing rates (single trend)	
60–69	increasing rates (single trend, lowest increases among age groups)	
70–79	increasing rates (single trend)	
80+	increasing rates (single trend, highest increases among age groups)	
Survival according to subgroups		
Periods:	separated groups (early observations years vs. later observation years)	
Age:	increasing survival with increasing age	
Stage:	increasing survival in lower stages, unknown stage cases with survival	

Figure 9 Trends at a glance: Male breast cancer trends in Austria, 1983–2017.

70 to 79 and 80+. These findings are different to trends observed in women in Austria, where the largest increase in age-specific incidence was observed for women under 35 years of age.[19]

Survival analysis with Kaplan–Meier plots shows an expected pattern of lower survival in older patients and those with more progressed disease (Figures 6 and 7). Furthermore, the stage-specific analyses hint at unknown stage cancer cases in our data set which may be comprised of localised and regional breast cancer cases as the survival rates of unknown stage cases lie between these two groups (Figures 3 and 6). This indicates, that unknown stage MBC cases may be comprised of different stage MBC cases with unavailable staging information at the time of registration of these milder cases.[26]

Analyses of survival according to periods of diagnosis (five-year periods, Figure 8) showed a biphasic improvement in survival with a leap between the periods 1988–1992 and 1993–1997. For the group of patients diagnosed between 1993 and 2017, less pronounced improvements over time were observed. The large majority of MBCs are oestrogen or androgen receptor positive and tamoxifen represents the most widely used pharmaceutical therapy for MBC. Nonetheless, a study using data from the US showed that most MBC patients received surgery only.[3,8] Tamoxifen was introduced in 1977 for the treatment of female BC and was probably adopted for wide use in MBC patients only with a delay and may have had an impact on the observed improvement in survival of Austrian MBC patients.[7,8,28] Similarly, more recent cohorts of MBC patients may benefit from the subsequent introduction of aromatase inhibitors as a therapeutic option for patients with contraindications for tamoxifen.[28,29] Further, as the management of MBC follows guidelines and recommendations developed for female BC patients, in principle, any other technological advancements may lead to increases in survival of MBC patients, whether through improved diagnostic procedures or treatment.[29] However, as currently there is no publication on the provision of treatment to MBC patients using population-wide data, the relative contribution of surgery, hormonal treatment, or other combinations of treatments to the increases in survival rates remains open to future research.

A strength of our study is the use of a full national sample of MBC cases recorded over four decades. The data likely reflects all MBC cases in Austria, as both information from death certificates and newly diagnosed cancer cases from statutory reporting were compiled. A limitation of our analyses comes from the lack of information on further broadly clinical characteristics such as treatment, genetic risk, and family history, but also biological characteristics such as receptor status. Thus, we can only assume that most MBC in Austria are comprised of hormone-receptor positive tumours, as seen in other countries with comparable socioeconomic characteristics.[30] Further, the large number of unknown stage cases introduce difficulty in the interpretation of the results. The relatively low number of cases with long periods of observation of up to 35 years in certain subgroups leads to diminished statistical power (Table 2).

Conclusion

Our comprehensive analysis of MBC over four decades showed increases in incidence while mortality remained stable. Subgroup-specific analyses revealed increasing incidence rates across all age groups and stage-specific trends, in accordance with the absence of a screening-program. Analyses of survival rates according to periods showed a slowdown in progress in the most recent periods, after leaps between 1988–1992 and 1993–1997. Further investigation of possible underlying factors for observed trends in stable five-year survival and mortality is necessary. A particular interest for future research may lie in the role of changing sex-hormone levels in male populations over time.

Data Sharing Statement

The data analysed in this study were provided by Statistics Austria. Restrictions apply to the availability of these data, which were used under license for this study.

Ethics Approval and Participation Consent

Ethical approval for the use of Austrian Cancer registry data for this study in accordance with the guidelines of the Helsinki Declaration was provided by the Ethics Committee of the Medical University of Vienna (Study 1259/2019). Participation consent was sought with information on consent provided in accompanying cover letters sent out with the survey forms.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors disclose no financial interests or competing interests of personal nature for this work.

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