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Original Research

European trends in breast cancer mortality, 1980–2017 and predictions to 2025



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Abstract Background: Breast cancer mortality in European women has been falling for three decades. We analysed trends in mortality from breast cancer in Europe over the period 1980–2017 and predicted number of deaths and rates to 2025.

Methods: We extracted death certification data for breast cancer in women for 35 European countries, between 1980 and 2017, from the World Health Organisation database. We computed the age-standardised (world standard population) mortality rates per 100,000 person-years, by country and calendar year. We obtained also predictions for 2025 using a joinpoint regression model and calculated the number of avoided deaths over the period 1994–2025.

Results: The mortality rate declined from 15.0 in 2012 to 14.4 in 2017 per 100,000 women (–3.9%) for the European Union (EU)-27. This fall was greater in the EU-14 (–5.2%), whereas rates rose in the transitional countries during this period by 1.9%. Mortality rate predictions across Europe are expected to reach relatively uniform levels in 2025. During the studied period, favourable trends in mortality emerged in most countries, with the greatest decrease in Denmark, whereas Poland and Romania showed an upward trend. The largest predicted decrease in breast cancer mortality was estimated for the United Kingdom (12.2/100,000 women in 2025), leading to the estimated avoidance of 150,000 breast cancer deaths over the period 1994–2025 and 470,000 in the EU-27.

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Conclusions: Favourable trends in breast cancer mortality were observed in most European countries, and they will continue to fall in the coming years. Less favourable patterns were still observed among the transitional countries than other European areas.

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1. Introduction

Breast cancer mortality in Europe has been declining for the last three decades [1]. These decreases have been greater in Northern than in Eastern Europe, where lower mortality rates were observed in the past [1]. Such favourable trends are essentially due to improvements in diagnosis and treatment [2–6]. Although the mortality rates are nowadays more uniform in Europe, the pattern observed in the past has been reversed. Breast cancer mortality rates tend to be higher in Central and Eastern countries, where they were lower in the past [1].

Political, economic and social changes have occurred in Central and Eastern Europe over the last three decades, which had a large impact on health policy as well as the public's perception of health. Because of these changes, such countries have been termed 'transitional countries' [7–10].

This study provides recent trends and patterns in breast cancer mortality across Europe, as well as predictions of mortality rates for the largest European countries and selected European regions to 2025.

2. Materials and methods

We extracted official death certification data for breast cancer in women for various European countries, between 1980 and 2017 or the most recent available calendar year (2018 for a few countries), from the World Health Organisation (WHO) database [11]. During the calendar period considered, three different revisions of the International Classification of Diseases (ICD) were used to classify deaths from breast cancer, with the following codes: '174' for the ICD-8 and ICD-9 and 'C50' for the ICD-10 [12–14]. We obtained estimates of the resident populations, based on official censuses, from the same WHO database and, when unavailable, from the Eurostat [15]. We selected 35 countries from Europe, as per death certification coverage. All the selected countries had a coverage over 90%, with the exception of Serbia (84%). Using certified deaths and resident populations, for each country and calendar year, we computed age-specific rates for quinquennia of age (from 0–4 to 85+ years). We then computed the age-standardised mortality rates per 100,000 person-years, based on the world standard population [16], at all ages and at age groups, 20–49, 50–69, 70–79 and 80+. We also obtained age-standardised mortality rates

for the European Union (EU) as a whole, defined as EU-27 (excluding Cyprus, for which data were available only for a limited number of years), for the EU-14 (old member states) and for a group of countries defined as 'transitional countries' (including Belarus, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, North Macedonia, Poland, the Republic of Moldova, Romania, Serbia, Slovakia and Slovenia). We excluded Ukraine because data are not consistent.

For a subset of 20 major countries, plus the EU-27, EU-14 and transitional countries, we carried out a joinpoint regression analysis over the 1980–2018 period [17]. We thus identified the time point(s), called 'joinpoints', when a change in the linear slope (on a log scale) of the temporal trend occurred, by testing from zero up to a maximum of four joinpoints. As a summary measure, we estimated the annual percent change (APC) for each identified linear segment and the weighted average APC over the entire study period [18,19].

We estimated predicted age-specific numbers of deaths and 95% prediction intervals (PIs) for 2025, for France, Germany, Italy, Poland, Spain and the United Kingdom (UK) (i.e. the largest European countries) and for the three geographical areas considered, by applying a linear regression to the mortality data from each age group over the most recent trend segment identified by the joinpoint model. We computed predicted age-specific and age-standardised death rates with 95% PIs using predicted age-specific numbers of deaths and predicted populations from Eurostat [15].

We estimated the number of avoided cancer deaths over the 1994–2025 period (2000–2025 for transitional countries) by comparing observed deaths and expected ones on the basis of the 1993 (1999 for transitional countries) age-specific peak rates.

3. Results

Table 1 presents age-standardised mortality rates from breast cancer at all ages for 35 European countries and the EU-27, EU-14 and transitional countries, around 2012 (2010–2014 quinquennium) and in 2017, with the number of deaths of the last year and percent changes between 2017 and 2012. Fig. 1 gives the mortality rates observed in 2017. Breast cancer mortality rates in the EU-27 declined from 15.0 in 2012 to 14.4 in 2017 per 100,000 women (–3.9%). The fall was greater in the EU-14 (–5.2%), whereas rates rose among the transitional

countries over the studied period by 1.9%. In most EU countries, mortality rates decreased over the last 5 years, with percent changes ranged from –2.1% in Slovenia to –15.3% in Denmark. The fall was –6.9% in the UK. Stable trends were observed in Portugal and Latvia, and some increases were registered in Greece, Ireland, Poland and Romania. As non-EU member states, Belarus showed the greatest decrease in mortality, whereas rates remained stable in Serbia while rose in Iceland.

In 2017, the highest mortality rates were observed in Serbia (20.6/100,000 women), followed by other Eastern countries and Ireland (16.6/100,000). The rate among transitional countries was 15.7/100,000 women, comparable with the one in the Russian Federation. The lowest rate was reported in Spain (10.9/100,000 women), followed by Norway (11.2), Sweden (11.3), Belarus (11.4) and the Czech Republic (12.1).

Table 2 gives age-standardised mortality rates from breast cancer at ages 20–49, 50–69, 70–79 and over 80 years old for 35 European countries and the EU-27, EU-14 and transitional countries, around 2012 (2010–2014 quinquennium) and in 2017, the number of deaths of the last year and percent changes between 2017 and 2012. In women aged 20–49, mortality rates decreased from 2012 to 2017 by 7.1% in the EU-14 and by 5.6% in the EU-27 countries, whereas they remained approximately stable in the transitional countries. Among the EU countries, the greatest decreases were in Denmark (–33.8%), whereas falls higher than 10% were also found in Belgium, Croatia, Lithuania, the Netherlands and Sweden. A similar pattern was observed in Switzerland. In contrast, mortality rates rose in women at this age group in the Czech Republic, Greece, Hungary, Ireland, Malta, Poland, Portugal and Romania. Among women aged 50–69, breast cancer mortality rates decreased by 6.3% and 8.2% in the EU-27 and EU-14, respectively, whereas they remained stable among transitional countries. Rates fell for most European countries, but were stable in Latvia, Portugal, Romania and Iceland. Different patterns were observed among women aged 70–79 years. Rates were stable in the EU-27 and EU-14, while increased in transitional countries (4.2%). The greatest mortality increases were observed in Romania, Poland, Ireland and the Republic of Moldova. Large disparities were observed in the changing rates among the oldest age group, where mortality rates increased over the study period for most countries. The unfavourable change was higher in transitional countries (over 17%) than that in the EU (EU-27, 4.2% and EU-14, 2.7%). Poland showed the largest rises (41%), whereas Croatia and Malta showed the largest decreases.

Joinpoint analysis results for 20 major European countries, plus the EU-27, the EU-14 and the transitional countries are presented in Fig. 2 and Table 3. Most European countries showed a downward trend in

mortality from breast cancer, whereas Poland, Romania and Serbia showed less favourable trends over the most recent period. Transitional countries showed an unfavourable trend until the mid-1990s, although they had

Table 1

Age-standardised (world population) mortality rates per 100,000 women with breast cancer at all ages in various European countries around 2012 (2010–2014) and 2017 (or the last available year^a), deaths of the latest year and the corresponding change in rates.

Country	All ages			
	2012	2017	Deaths	% change
EU countries				
Austria	14.1	13.5	1566	–4.5
Belgium	17.6	15.3	2227	–13.3
Bulgaria	15.2	14.9	1312	–2.2
Croatia	18.1	15.8	853	–12.7
The Czech Republic	13.3	12.1	1620	–9.3
Denmark	17.5	14.8	1069	–15.3
Estonia	14.5	13.8	260	–4.7
Finland	13.3	13.0	908	–2.6
France	15.4	14.7	12,434	–4.4
Germany	16.1	15.4	18,396	–4.3
Greece	13.8	14.3	2163	3.8
Hungary	17.7	17.1	2123	–3.2
Ireland	15.2	16.6	678	8.9
Italy	14.8	14.2	12,616	–4.1
Latvia	16.8	17.0	445	1.5
Lithuania	15.6	13.9	521	–10.9
Luxembourg	15.2	14.6	89	–3.6
Malta	16.5	14.4	73	–12.9
The Netherlands	17.4	15.5	3107	–11.4
Poland	14.3	15.1	6670	5.1
Portugal	13.1	13.1	1769	–0.1
Romania	15.2	15.8	3495	4.6
Slovakia	15.9	.	.	.
Slovenia	15.0	14.7	433	–2.1
Spain	11.7	10.9	6489	–7.3
Sweden	12.7	11.3	1413	–11.1
Other European countries				
Belarus	12.8	11.4	1138	–10.7
Iceland	13.8	14.7	47	7.0
North Macedonia	17.1	.	.	.
Norway	12.1	11.2	623	–7.1
The Republic of Moldova	16.6	16.0	505	–4.0
Russian Federation	16.1	.	.	.
Serbia	20.4	20.7	1766	1.2
Switzerland	14.2	13.2	1405	–7.1
The UK	16.2	15.1	11,512	–6.9
The UK, England and Wales	16.1	15.0	10,178	–6.6
The UK, Northern Ireland	16.8	15.2	314	–9.5
The UK, Scotland	16.8	15.6	1020	–6.9
EU (27)	15.0	14.4	81,504	–3.9
EU (14)	14.9	14.2	63,808	–5.2
Transitional countries	15.4	15.7	19,832	1.9

EU, European Union; UK, United Kingdom.

^a Last available year (when it was different from the 2017) was: 2013 for North Macedonia; 2014 for Slovakia and the Russian Federation; 2015 for Bulgaria, Denmark, Ireland, Latvia, Turkmenistan, EU 27, EU 14 and transitional countries; 2016 for Belgium, France, Greece, Italy, Kyrgyzstan, Luxembourg, Malta, Norway, Switzerland, the UK, UK England and Wales, UK Northern Ireland and UK Scotland; 2018 for Belarus, Estonia, Georgia, Iceland, Lithuania and the Republic of Moldova.

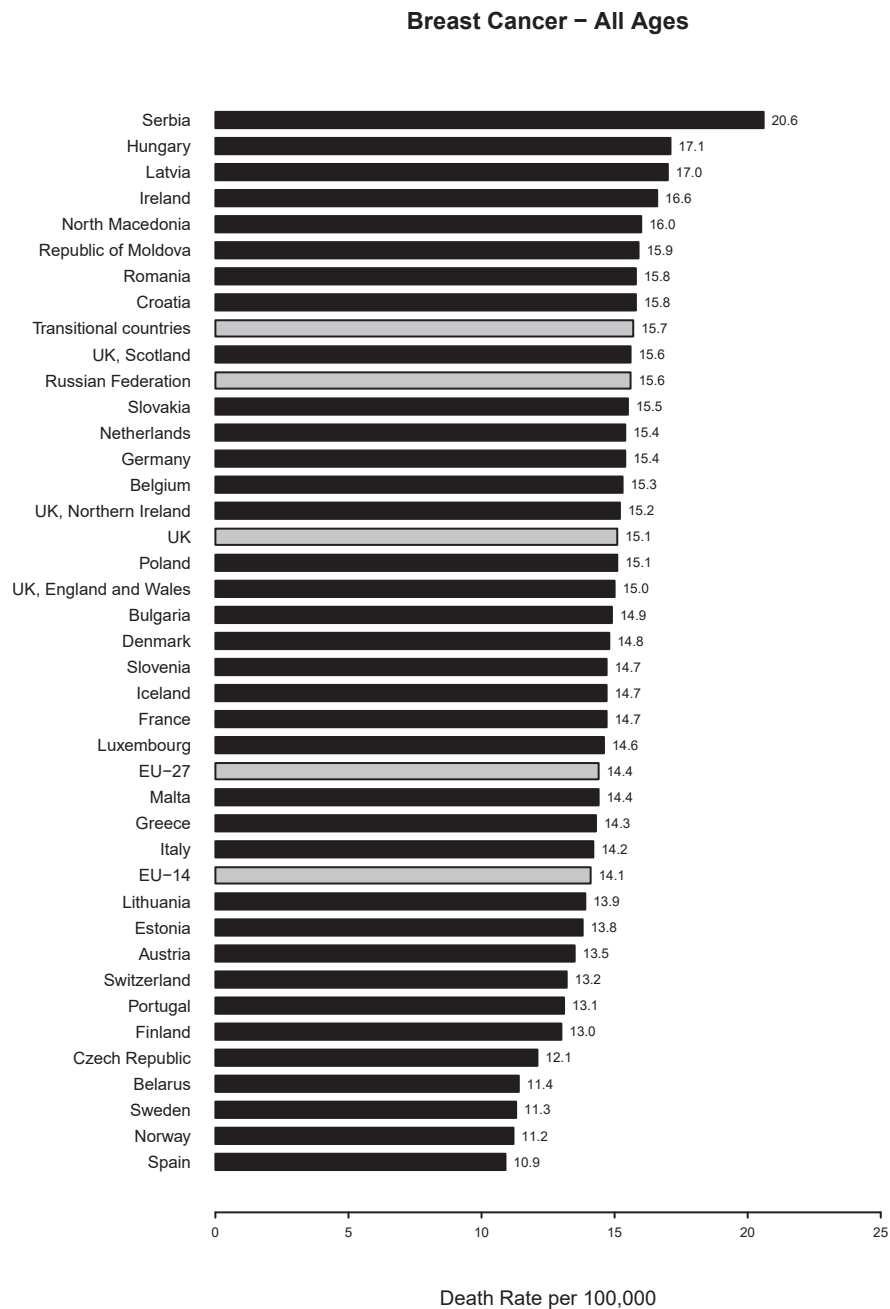


Fig. 1. Bar plot of the age-standardised (world population) rates from breast cancer registered in 2017 (or the last available year) ordered from the highest to the lowest rate. EU, European Union; UK, United Kingdom.

lower breast cancer mortality rates at the beginning of the 1980s than the rest of Europe. In the countries of Western and Northern Europe, despite the higher mortality observed at the beginning of the 1980s, the trend changed at the end of the decade, and such a favourable pattern continued. In the countries of Central and Eastern Europe, the change in trend was observed in the mid-1990s or even later in some countries.

Table 4 and Fig. 3 present breast cancer mortality predictions to 2025 for the six major EU countries (a) and three groups of countries considered (b). The largest decrease was predicted to be in the UK (about –19%), reaching a predicted mortality rate of 12.2/100,000 women. The predicted declines for France, Germany, Italy and Spain are comparable (between –9 and –10%). Notwithstanding such differences in trends, the lowest predicted death rate in 2025 is in Spain (9.9/

Table 2

Age-standardized (world population) mortality rates per 100,000 women with breast cancer at different age groups in selected European countries around 2012 (2010–2014) and 2017 (or the last available year^a), deaths of the latest year and the corresponding change in rates

Country	Age group 20–49				Age group 50–69				Age group 70–79				Age group 80+			
	2012	2017	Deaths	% change	2012	2017	Deaths	% change	2012	2017	Deaths	% change	2012	2017	Deaths	% change
EU countries																
Austria	6.0	5.9	123	−1.2	43.2	39.3	461	−9.1	91.8	93.0	400	1.3	205.5	202.8	582	−1.3
Belgium	7.1	6.3	158	−11.2	57.5	46.2	691	−19.5	115.6	107.2	514	−7.3	212.7	214.8	864	1.0
Bulgaria	7.5	7.1	118	−5.8	52.7	49.5	542	−6.1	81.3	87.5	339	7.6	133.0	152.4	313	14.5
Croatia	8.1	7.1	64	−11.9	54.5	48.8	302	−10.5	117.5	113.4	250	−3.5	259.3	172.1	237	−33.6
The Czech Republic	4.9	5.2	135	6.3	41.2	35.6	538	−13.7	95.4	85.2	447	−10.7	191.9	176.8	500	−7.9
Denmark	6.3	4.2	54	−33.8	55.3	44.7	339	−19.2	120.2	120.8	312	0.5	252.9	239.1	364	−5.4
Estonia	5.8	5.7	17	−1.9	51.0	44.7	86	−12.3	85.6	83.0	55	−3.1	144.9	190.3	102	31.3
Finland	5.6	5.2	57	−7.3	44.7	42.8	341	−4.4	85.3	87.3	242	2.4	133.5	141.0	268	5.6
France	7.3	7.2	1060	−1.6	49.3	45.2	4073	−8.4	92.3	90.5	2393	−2.0	180.1	188.8	4908	4.8
Germany	6.5	6.6	1195	1.2	51.8	46.5	5537	−10.3	106.7	104.9	4783	−1.7	200.2	216.8	6880	8.3
Greece	6.2	6.9	186	10.1	41.3	43.8	641	6.2	87.5	81.5	478	−6.9	202.5	207.4	858	2.4
Hungary	7.8	8.3	199	5.9	57.4	53.9	791	−6.2	116.6	111.6	578	−4.3	189.0	186.2	555	−1.5
Ireland	6.5	7.6	84	16.2	47.4	49.7	250	4.8	103.9	117.5	164	13.0	188.3	205.0	180	8.9
Italy	7.0	7.0	1072	−0.9	47.4	43.2	3715	−8.8	87.8	88.0	2863	0.3	179.5	187.1	4966	4.2
Latvia	7.8	7.7	35	−0.9	58.8	58.8	175	−0.1	92.7	101.5	125	9.4	146.9	149.2	110	1.5
Lithuania	7.7	6.5	41	−15.8	54.8	47.6	212	−13.1	87.6	82.3	130	−6.1	108.7	119.9	138	10.3
Luxembourg	5.6	5.4	8	−3.4	47.6	35.9	24	−24.6	90.8	146.0	23	60.9	255.6	231.5	34	−9.4
Malta	6.5	7.5	7	14.5	50.0	40.1	26	−19.7	110.7	114.1	22	3.1	258.9	154.8	18	−40.2
The Netherlands	8.0	6.7	256	−15.7	57.2	50.0	1165	−12.6	98.6	90.7	694	−8.0	214.2	203.9	992	−4.8
Poland	6.4	7.1	616	10.8	50.1	47.9	2664	−4.4	83.4	92.9	1399	11.4	126.6	178.6	1991	41.0
Portugal	7.5	7.8	205	4.1	40.8	41.1	613	0.7	66.9	62.2	340	−7.1	152.4	150.5	611	−1.2
Romania	7.1	7.7	389	8.5	52.4	52.3	1421	−0.1	88.6	100.5	911	13.4	128.3	138.4	774	7.9
Slovakia	5.2	.	.	.	52.5	.	.	.	114.6	.	.	.	198.7	.	.	.
Slovenia	6.3	5.9	28	−7.6	44.4	41.6	124	−6.2	97.9	104.3	98	6.5	240.6	252.5	183	5.0
Spain	6.4	6.0	735	−6.3	36.6	33.6	2035	−8.4	63.1	57.3	1171	−9.3	141.9	139.1	2548	−2.0
Sweden	5.6	4.5	95	−19.2	41.1	35.1	436	−14.4	80.0	76.1	365	−4.8	153.9	163.0	517	5.9
Other European countries																
Belarus	6.6	6.3	142	−5.1	48.6	40.3	592	−17.1	60.9	60.1	226	−1.3	49.8	63.2	178	26.9
Iceland	6.3	10.7	8	70.6	38.7	38.4	15	−0.8	108.2	71.9	8	−33.5	180.4	214.2	16	18.8
North Macedonia	7.6	.	.	.	58.6	.	.	.	102.8	.	.	.	155.1	.	.	.
Norway	5.2	5.0	59	−2.1	39.0	35.9	225	−7.9	74.4	69.3	139	−6.8	156.8	139.4	200	−11.1
The Republic of Moldova	7.5	6.8	59	−9.2	61.7	56.5	281	−8.5	96.7	109.7	113	13.4	83.2	89.4	52	7.5
Russian Federation	7.8	.	.	.	58.4	.	.	.	85.7	.	.	.	104.3	.	.	.
Serbia	8.9	8.6	138	−3.0	70.6	69.4	775	−1.6	122.5	132.0	448	7.8	186.8	212.5	405	13.7
Switzerland	5.3	4.8	97	−10.5	45.3	38.1	410	−15.8	98.8	109.0	383	10.3	187.5	193.4	515	3.1
The UK	7.8	7.5	1103	−3.7	50.1	45.1	3722	−10.0	97.1	90.5	2489	−6.8	214.6	215.3	4198	0.3
The UK, England and Wales	7.8	7.3	960	−5.5	49.7	45.4	3310	−8.5	96.9	89.8	2181	−7.3	215.0	213.9	3727	−0.5
The UK, Northern Ireland	7.8	7.5	31	−3.0	52.9	42.5	96	−19.7	105.4	100.6	74	−4.6	205.4	236.5	113	15.1
The UK, Scotland	8.0	9.2	112	15.4	53.4	42.5	316	−20.3	96.4	94.4	234	−2.0	211.8	226.1	358	6.8
EU (27)	6.8	6.4	6642	−5.6	48.5	45.5	27,177	−6.3	92.2	92.1	19,299	−0.2	177.1	184.5	28,384	4.2

EU (14)	6.8	6.3	5130	-7.1	47.7	43.8	19,974	-8.2	92.1	91.7	15,120	-0.4	182.2	187.0	23,583	2.7
Transitional countries	6.8	6.8	1714	-0.9	52.5	52.2	8197	-0.6	92.6	96.5	4732	4.2	146.5	171.9	5188	17.3

EU, European Union; UK, United Kingdom.

^a Last available year (when it was different from the 2017) was: 2013 for North Macedonia; 2014 for Slovakia and the Russian Federation; 2015 for Bulgaria, Denmark, Ireland, Latvia, Turkmenistan, EU 27, EU 14 and transitional countries; 2016 for Belgium, France, Greece, Italy, Kyrgyzstan, Luxembourg, Malta, Norway, Switzerland, the UK, UK England and Wales, UK Northern Ireland and UK Scotland; 2018 for Belarus, Estonia, Georgia, Iceland, Lithuania and the Republic of Moldova.

100,000). The currently unfavourable trend observed in Poland is predicted to be reversed in the coming years. The predicted decline in Polish rates is, however, lower compared with the other countries (-3.2%), attaining the highest predicted rate in 2025 (14.6/100,000 women). Likewise, mortality rate predictions for the three aforementioned EU groupings are expected to reach comparable levels. The largest predicted decline is about 16% in the transitional countries, although the predicted death rate remains the highest one (13.1/100,000 women). The predicted falls in the EU-27 and EU-14 are 15.6% and 15%, respectively, to reach both a predicted rate of about 12/100,000.

Fig. 4 shows the number of avoided breast cancer deaths estimated (light grey area) for the six major European countries (a) and three analysed groups of European countries (b), between 1994 and 2025. The estimated number of avoided deaths between 1994 and 2017, the predicted to 2025, and for the single year 2025 is given in Table 5. We estimated a total of about 230,000 avoided breast cancer deaths in the EU-27 over the period 1994–2015 and over 470,000 until 2025. Up to 2025, these are predicted to be over 150,000 in the UK, 113,000 in Germany and 50,000 to 87,000 in France, Italy and Spain. Poland is the only country where no avoided deaths from breast cancer were predicted.

4. Discussion

The present study confirms a steady decrease in breast cancer mortality trends across Europe [1,20]. It also confirms that breast cancer is no longer the leading cause of cancer death in women, being overcome by lung cancer over the last few years [20]. Despite the favourable trends observed in mortality throughout Europe, there have been notable exceptions, such as Poland and Romania. The reason is the relatively newly introduced and ineffective breast cancer early detection program in those countries. In Poland, a program was implemented in 2006. Until 2015, women received personal invitations to participate in screening, encouraging them to perform mammography. In 2015, the program funds were reduced, and the sending of invitations was abandoned, which resulted in a steady decrease of the coverage population eligible for the examination, from almost 42% in 2016 to 37% in 2019 [21]. In Romania, the breast cancer early detection program has been in operation since 2015 but is not legally established [22]. Another reason for the unfavourable epidemiological trends in both of these countries is the inefficient management of patients. The average time from diagnosis to start of breast cancer treatment in Poland is about 9.5 weeks [23] and in extreme cases even 38 weeks [21]. In Romania, this time is on average 20.5 weeks [23]. For comparison, in the UK, this time does not exceed 8

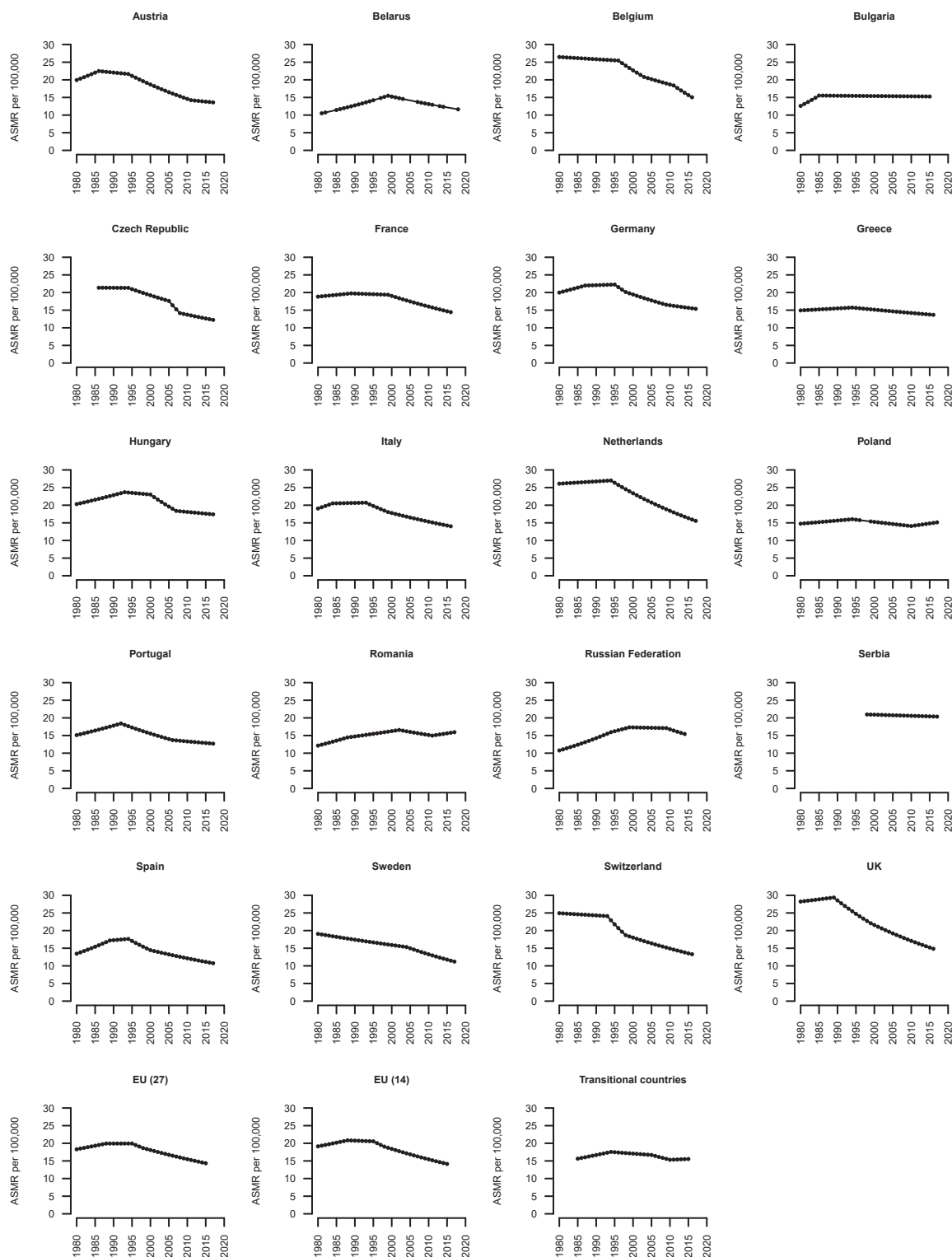


Fig. 2. Joinpoint analysis of trends in breast cancer mortality rates in major countries worldwide since 1980 to 2017 as per data availability. EU, European Union; UK, United Kingdom.

weeks [24]. An additional problem in the case of some Central and Eastern European countries, including Romania, is the lack of access to modern forms of

pharmacological therapy for breast cancer [25]. There is still a gap in access to the agents directed against the human epidermal growth factor receptor 2 (anti-HER2

Table 3

Joinpoint analysis for breast cancer mortality trends in 20 major European countries, plus EU (27), EU (14) and transitional countries, over the period 1980–2018 (as per data availability).

Country	Period 1	APC 1	Period 2	APC 2	Period 3	APC 3	Period 4	APC 4	Period 5	APC 5	AAPC
Austria	1980–1986	2 ^a	1986–1994	−0.5	1994–2011	−2.4 ^a	2011–2017	−0.7			−1 ^a
Belarus	1981–1999	2.2 ^a	1999–2018	−1.5 ^a							0.3
Belgium	1980–1996	−0.2 ^a	1996–2003	−2.8 ^a	2003–2011	−1.5 ^a	2011–2016	−3.9 ^a			−1.6 ^a
Bulgaria	1980–1985	4.3 ^a	1985–2015	−0.1							0.5 ^a
The Czech Republic	1986–1994	0	1994–2005	−1.7 ^a	2005–2008	−7	2008–2017	−1.6 ^a			−1.8 ^a
France	1980–1989	0.5 ^a	1989–1999	−0.2	1999–2016	−1.7 ^a					−0.7 ^a
Germany	1980–1987	1.4 ^a	1987–1995	0.2	1995–1998	−3.3	1998–2009	−1.8 ^a	2009–2017	−0.9 ^a	−0.7 ^a
Greece	1980–1994	0.4	1994–2016	−0.6 ^a							−0.2 ^a
Hungary	1980–1993	1.2 ^a	1993–2000	−0.4	2000–2007	−3.2 ^a	2007–2017	−0.5			−0.4
Italy	1980–1984	1.9 ^a	1984–1993	0.1	1993–1999	−2.3 ^a	1999–2016	−1.5 ^a			−0.8 ^a
The Netherlands	1980–1994	0.2	1994–2017	−2.4 ^a							−1.4 ^a
Poland	1980–1994	0.6 ^a	1994–2010	−0.8 ^a	2010–2017	1 ^a					0.1
Portugal	1980–1992	1.6 ^a	1992–2006	−2.1 ^a	2006–2017	−0.7 ^a					−0.5 ^a
Romania	1980–1988	2.2 ^a	1988–2002	1 ^a	2002–2011	−1.1 ^a	2011–2017	1.1 ^a			0.7 ^a
Russian Federation	1980–1994	2.8 ^a	1994–1999	1.7 ^a	1999–2009	−0.1	2009–2014	−2 ^a			1.1 ^a
Serbia	1998–2017	−0.2									−0.2
Spain	1980–1989	2.8 ^a	1989–1994	0.5	1994–2000	−3.3 ^a	2000–2017	−1.7 ^a			−0.6 ^a
Sweden	1980–2004	−0.9 ^a	2004–2017	−2.4 ^a							−1.4 ^a
Switzerland	1980–1993	−0.3	1993–1998	−5 ^a	1998–2016	−1.9 ^a					−1.7 ^a
The UK	1980–1989	0.4 ^a	1989–1999	−2.8 ^a	1999–2016	−2.3 ^a					−1.8 ^a
EU (27)	1980–1988	1.1 ^a	1988–1995	0	1995–1998	−2.2 ^a	1998–2015	−1.5 ^a			−0.7 ^a
EU (14)	1980–1988	1.1 ^a	1988–1995	−0.2	1995–1998	−2.5 ^a	1998–2015	−1.7 ^a			−0.9 ^a
Transitional countries	1985–1994	1.3 ^a	1994–2005	−0.5 ^a	2005–2010	−1.7 ^a	2010–2015	0.3			0

APC: annual percent change; AAPC: average annual percent change; EU: European Union; UK: United Kingdom.

^a Significantly different from 0 ($p < 0.05$).

Table 4

Number of predicted deaths and mortality rate for the year 2025 and comparison figures for 2017^a, for the six major countries and the three studied areas, with 95% prediction intervals (PIs).

Country	Observed number of deaths 2017	Predicted number of deaths 2025 (95% PI)	Observed ASR 2017	Predicted ASR 2025 (95% PI)	% difference 2025 vs. 2017
France	12,434	13,200 (12,693–13,759)	14.72	13.20 (12.55–13.85)	–10.3
Germany	18,396	19,400 (18,522–20,339)	15.4	13.96 (13.20–14.71)	–9.4
Italy	12,616	12,700 (12,238–13,169)	14.21	12.73 (12.17–13.29)	–10.4
Poland	6670	8200 (7554–8865)	15.07	14.58 (13.31–15.85)	–3.2
Spain	6489	6400 (5978–6795)	10.87	9.88 (9.22–10.53)	–9.1
The UK	11,512	10,500 (10,016–11,016)	15.08	12.19 (11.5–12.87)	–19.2
EU (27)	81,504	84,500 (82,993–86,097)	14.43	12.18 (11.89–12.47)	–15.6
EU (14)	63,808	65,300 (63,989–66,589)	14.15	12.02 (11.68–12.37)	–15.0
Transitional countries	19,832	22,200 (21,119–23,258)	15.68	13.13 (12.17–14.08)	–16.3

ASR: age-standardised mortality rates (using the world standard population as reference); EU: European Union; UK: United Kingdom.

^a Last available year (when it was different from the 2017) was 2015 for EU 27, EU 14 and transitional countries and 2016 for France, Italy and the UK.

agents) between individual European countries [26]. In most countries of Western Europe, the availability of this form of therapy in 2013 covered its demand, whereas among the countries of Central and Eastern Europe, this condition was only applicable to Slovenia and the Czech Republic. The quality of access to other modern methods of therapy, such as CDK4/6 inhibitors, between European countries is unknown. In Poland, these drugs are not reimbursed from public funds [27].

Four decades ago, mortality from breast cancer was lower among transitional countries than that among Western and Northern European countries. However, trends have reversed. Thus, transitional countries have

slightly higher mortality rates nowadays than the rates in the 1980s and at the higher rates than in the EU-14 countries.

Previous studies showed a greater decrease in breast cancer mortality rates of women aged below 50 than of middle-aged ones [1]. The present study does not confirm such observations. Reduced mortality rates in women aged 50–69 years were –6.3% and –8.2% for the EU-27 and EU-14 countries, respectively, compared with –5.6% and –7.1% for younger women. The mortality trends for younger and middle-aged women in transitional countries were constant. Middle-aged women are covered by mammography screening,

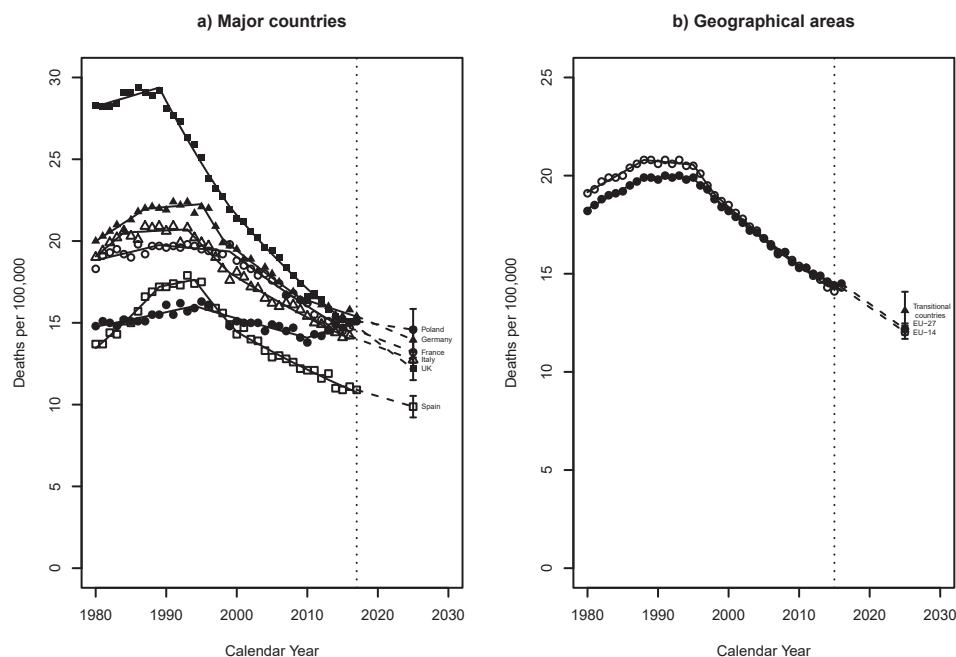


Fig. 3. Annual breast cancer age-standardised (world population) mortality rates per 100,000 at all ages, over the period 1980 to 2018, the resulting joinpoint regression models and predicted rates for the year 2025 with 95% prediction intervals (PIs), in the six major countries (a) and the three studied geographical areas (b). EU, European Union; UK, United Kingdom.

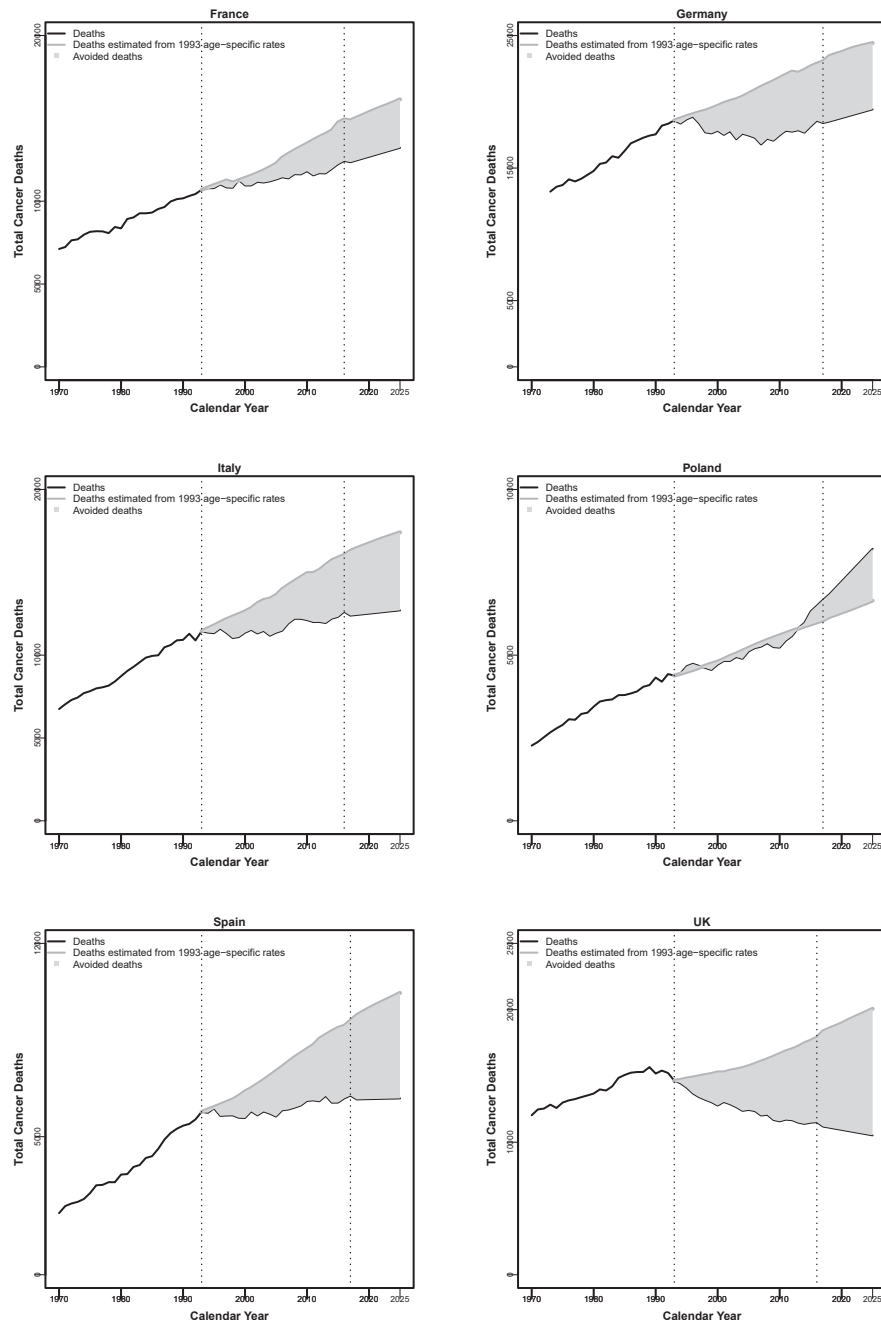


Fig. 4. Total avoided breast cancer deaths for the six major EU countries (a) and the three studied areas (b) between the top rate in 1993 (or 1999 for transitional countries) and 2025 (light grey area); observed numbers of cancer deaths from 1970 to 2017 (or 2016) and predicted cancer deaths from 2018 (or 2017) to 2025 (black line); estimated numbers of total cancer deaths by applying 1993 (or 1999 for transitional countries) age-specific peak mortality rate (dark grey). EU, European Union; UK, United Kingdom.

which thereby reduces their mortality. A favourable trend is, however, also observed for younger women, which may have arisen from increased diagnostic attention, as well as improved management and treatment. This includes breast ultrasonography, which is, however, not a recognised method of breast cancer screening and bears high rates of false-positive results [28–30].

Within Europe, changes in reproductive health and lifestyle have been observed, generally increasing the

potential risk of developing breast cancer [31]. Women are increasingly giving birth to their first child at a later age and have fewer children [32–34]. The fertility rate for the EU-27 has remained approximately stable for almost twenty years [34]. Among all the WHO regions, European women breastfeed their babies least frequently and for a shorter time [35]. Moreover, no favourable changes were observed in the age of menarche or menopause [31]. The prevalence of obesity in women did not decline in most countries or even

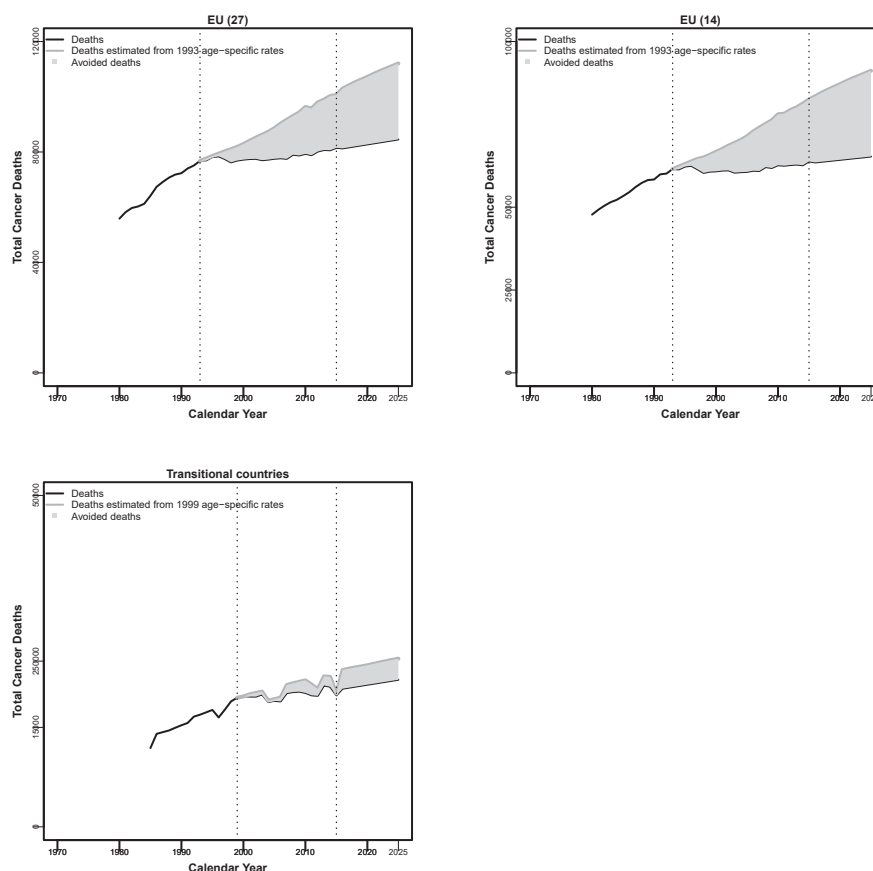


Fig. 4. (continued).

increased in some of them [34]. Thus, the favourable mortality trends observed in Europe today cannot be attributed to changes in risk factors for breast cancer. Nevertheless, identification and quantification of modifiable risk factors and the implementation of appropriate programs to encourage lifestyle change can have tangible effects on breast cancer mortality rates. About one-third of breast cancer cases can be avoided by appropriate lifestyle modification, which includes limiting alcohol consumption, as well as sugar-sweetened drinks and red and processed meat, eating meals

rich in vegetables, fruits, whole grains and beans, limiting fast foods and avoidance of overweight and obesity in adult life, as well as being physically active [36,37]. The differential role of these factors in various areas of Europe is difficult to quantify, but probably explains only a minor part of the diverging trends observed. The widening mortality gap is consequently largely attributable to differences in screening, early diagnosis, clinical management and treatment across Europe.

The highest incidence rates are currently observed in Western Europe. Slightly lower ones are recorded in the countries of Southern and Northern Europe. The countries of Central and Eastern Europe have the lowest incidence rates [38].

Also in the United States of America (USA), mortality from breast cancer was increasing until the 1980s. From the beginning of the 1990s to 2017, the mortality rate in the USA decreased by 40%. Over recent years, trends remained favourable, but the slope of the decline decreased. Between 1998 and 2011, the annual decrease was 1.9% and 1.3% between 2011 and 2017 [39]. At the beginning of this century, the mortality rate from breast cancer in the USA was 16.8/100,000 women. In 2012, there was a decrease to 13.8/100,000 women [40]. About 376,000 female deaths have been avoided in the last thirty years in the USA [39].

Table 5

Number of avoided breast cancer deaths, for the six major countries and the three studied areas.

Country	1994–2017 ^a	1994–2025 ^b	2025
France	26,600	51,200	2900
Germany	73,000	113,000	5000
Italy	11,000	87,000	4700
Poland	310	–8700	–1500
Spain	35,600	63,100	3800
The UK	80,800	156,000	9500
EU-27	229,000	477,000	27,400
EU-14	220,000	450,000	25,800
Transitional countries	14,100	44,000	3100

^a For France, Italy and the UK: 1994–2016; for the EU-27 and EU-14: 1994–2015; for the transitional countries: 2000–2015.

^b For transitional countries: 2000–2025.

It is generally assumed that about two-thirds of the decline in breast cancer mortality in Western Europe, and North America, is due to innovative treatment options and about one-third to screening and better diagnosis. Breast cancer treatment includes surgery, radiotherapy and a long list of medications, making breast cancer treatment personalised [6]. The use of anthracycline-containing regimens, followed by the addition of a taxane significantly reduced mortality [41]. In the management of hormone receptor-positive breast cancers, the use of the tamoxifen or aromatase inhibitor led to a substantial decrease in mortality over a 15-year period [42,43]. In the management of patients with HER2-positive breast cancer, the use of anti-HER2 agents (i.e. trastuzumab, pertuzumab) along with chemotherapy also appreciably reduced the risk of death from this cancer [44–46]. The type of systemic treatment depends on the biological cancer subtype determined by immunohistochemistry. In addition, computerised risk models of recurrence, such as PREDICT, are useful tools for assessing the benefit of systemic adjuvant therapy, allowing individualisation of therapy [6]. Improved radiotherapy has also had a significant impact on the reduction of mortality from breast cancer. Its use, both after breast-conserving surgery and after mastectomy, contributed to the reduction of the risk of cancer recurrence and death from it [4,47].

We did not consider the potential impact of the COVID-19 pandemic on future trends in breast cancer mortality. The major short-term impact was on delayed screening in 2020 [48]. This may have some unfavourable impact on breast cancer mortality in the next several years, unless screening is promptly resumed. Such potential impact is, however, difficult to assess now.

In line with earlier predictions, breast cancer mortality in Europe continues to decline [1]. However, the selection of the transitional country group in our study confirmed the inequalities in health between the countries of Northern and Western Europe and the countries of Central and Eastern Europe. These changes require immediate action to achieve reductions in breast cancer mortality. In the next few years, mortality from breast cancer is predicted to decline, even in Poland, where, together with Romania, we are currently seeing an unfavourable mortality trend. However, the interventions undertaken should be aimed at maintaining and strengthening the predicted trend.

5. Conclusions

We are seeing a decline in mortality from female breast cancer in Europe. This trend will continue in the next five years. We observed a less favourable epidemiological situation in transitional European countries, compared with the countries of Western and Northern Europe. In addition, there is still an increase in mortality

from breast cancer among these countries (Poland and Romania). Poland is the only country where no avoided deaths from breast cancer were predicted.

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Author contributions

Cezary Wojtyla: Conceptualization, Methodology, Writing - Original Draft, Visualisation

Paola Bertuccio: Methodology, Software, Formal analysis, Resources, Data curation, Visualisation

Andrzej Wojtyla: Validation, Writing - Review & Editing, Supervision

Carlo La Vecchia: Conceptualization, Methodology, Validation, Writing - Review & Editing, Supervision, Project administration

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

References

- [1] Carioli G, Malvezzi M, Rodriguez T, Bertuccio P, Negri E, La Vecchia C. Trends and predictions to 2020 in breast cancer mortality in Europe. *Breast* 2017;36:89–95. <https://doi.org/10.1016/j.breast.2017.06.003>.
- [2] Sestak I, Cuzick J. Update on breast cancer risk prediction and prevention. *Curr Opin Obstet Gynecol* 2015;27:92–7.
- [3] Cardoso F, Costa A, Senkus E, Aapro M, Andre F, Barrios CH, et al. ESOESMO international consensus guidelines for advanced breast cancer (ABC 3). *Ann Oncol* 2017;28:16–33.
- [4] EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* 2014 21;383(9935):2127–35. [https://doi.org/10.1016/S0140-6736\(14\)60488-8](https://doi.org/10.1016/S0140-6736(14)60488-8).
- [5] Kalager M, Zelen M, Langmark F, Adami HO. Effect of screening mammography on breast-cancer mortality in Norway. *N Engl J Med* 2010;363:1203e10.
- [6] Hensing W, Santa-Maria CA, Peterson LL, Sheng JY. Landmark trials in the medical oncology management of early stage breast cancer. *Semin Oncol* 2020;30(20):30088–9. <https://doi.org/10.1053/j.seminoncol.2020.08.001>. S0093-7754.
- [7] Wojtyla C, Janik-Konieczny K, La Vecchia C. Cervical cancer mortality in young adult European women. *Eur J Canc* 2020;126: 56–64. <https://doi.org/10.1016/j.ejca.2019.11.018>.
- [8] Bobadilla JL, Costello CA, Mitchell F. Premature death in the new independent states. Washington (DC): National Academies Press (US); 1997.
- [9] Gerry CJ, Raskina Y, Tsyplakova D. Convergence or divergence? Life expectancy patterns in post-communist countries, 1959–2010. *Soc Indic Res* 2018;140(1):309–32.

- [10] Cornia GA, Panizza R. The mortality crisis in transitional economies. Oxford: University Press; 2000.
- [11] World Health Organization Statistical Information System. WHO mortality database; http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html [Accessed on 20th July 2020].
- [12] World Health Organization. International classification of disease: 8th revision. Geneva, Switzerland: World Health Organization; 1967.
- [13] World Health Organization. International classification of disease: 9th revision. Geneva, Switzerland: World Health Organization; 1977.
- [14] World Health Organization. International classification of disease and related health problems: 10th revision. Geneva: World Health Organization; 1992.
- [15] European Commission. Eurostat population database; <http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data/database> [Accessed on 20th July 2020].
- [16] Doll R, Smith PG, Waterhouse JAH, Muir CS, Shanmugaratnam K, Powell J, et al. Comparison between registries: age-standardized rates. IARC Sci 1982;vol. IV:671–5. Cancer Incidence in Five Continents.
- [17] National Cancer Institute. Joinpoint regression program, version 4.6.0.0.
- [18] Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK. Estimating average annual per cent change in trend analysis. Stat Med 2009;28:3670–82.
- [19] Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. (Erratum in: stat Med 2001;20: 655). Stat Med 2000;19:335–51.
- [20] Malvezzi M, Carioli G, Bertuccio P, Boffetta P, Levi F, La Vecchia C, et al. European cancer mortality predictions for the year 2019 with focus on breast cancer. Ann Oncol 2019;30(5): 781–7. <https://doi.org/10.1093/annonc/mdz051>.
- [21] Koczkodaj P, Sulkowska U, Gotlib J, Mańczuk M. Breast cancer mortality trends in Europe among women in perimenopausal and postmenopausal age (45+). Arch Med Sci 2020;16(1):146–56. <https://doi.org/10.5114/aoms.2019.85198>.
- [22] Ponti A, Anttila A, Ronco G, Senore C, Basu P, Segnan N, et al. Cancer screening in the European union. Report on the implementation of the council recommendation on cancer screening. Lyon: IARC; 2017.
- [23] Jassem J, Ozmen V, Bacanu F, Drobnienė M, Eglitis J, Lakshmaiah KC, et al. Delays in diagnosis and treatment of breast cancer: a multinational analysis. Eur J Publ Health 2014;24:761–7.
- [24] Cancer Research UK. Breast cancer treatment statistics, <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/diagnosis-and-treatment#ref-2> [accessed 24 March 2021].
- [25] ISRA Center. Female oncologic Diseases in Romania. Bucharest: ISRA Center; 2016.
- [26] Ades F, Senterre C, Zardavas D, de Azambuja E, Popescu R, Piccart M. Are life-saving anticancer drugs reaching all patients? Patterns and discrepancies of trastuzumab use in the European Union and the USA. PloS One 2017;12(3):e0172351. <https://doi.org/10.1371/journal.pone.0172351>.
- [27] Jassem J, Krzakowski M, Bobek-Billewicz B, Duchnowska R, Jeziorski A, Olszewski W, et al. Breast cancer. Oncol Clin Pract 2018;14. <https://doi.org/10.5603/OCP.2018.0027>.
- [28] Scheel JR, Lee JM, Sprague BL, Lee CI, Lehman CD. Screening ultrasound as an adjunct to mammography in women with mammographically dense breasts. Am J Obstet Gynecol 2015;212: 9–17.
- [29] Sprague BL, Stout NK, Schechter C, van Ravestein NT, Cevik M, Alagoz O, et al. Benefits, harms, and cost-effectiveness of supplemental ultrasonography screening for women with dense breasts. Ann Intern Med 2015;162(3):157–66. <https://doi.org/10.7326/M14-0692>.
- [30] Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27 825 patient evaluations. Radiology 2002;225: 165–75.
- [31] Gallus S, Lugo A, Murisic B, Bosetti C, Boffetta P, La Vecchia C. Overweight and obesity in 16 European countries. Eur J Nutr 2015;54(5):679–89. <https://doi.org/10.1007/s00394-014-0746-4>.
- [32] Eurostat. Women are having their first child at an older age. <https://ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20190318-1> [Accessed 25th October 2020].
- [33] Eurostat. Women in EU have first child on average at 29. <https://ec.europa.eu/eurostat/documents/2995521/8774296/3-28032018-AP-EN.pdf/fdf8ebdf-a6a4-4153-9ee9-2f05652d8ee0> [Accessed 25th October 2020].
- [34] European Commission. European core health indicators. https://ec.europa.eu/health/indicators_data/indicators_en [Accessed 25th October 2020].
- [35] Theurich MA, Davanzo R, Busck-Rasmussen M, Díaz-Gómez NM, Brennan C, Kylberg E, et al. Breastfeeding rates and programs in Europe: a survey of 11 national breastfeeding committees and representatives. J Pediatr Gastroenterol Nutr 2019; 68(3):400–7. <https://doi.org/10.1097/MPG.0000000000002234>.
- [36] Turati F, Dalmartello M, Bravi F, Serraino D, Augustin L, Giacosa A, et al. Adherence to the world cancer research fund/American institute for cancer research recommendations and the risk of breast cancer. Nutrients 2020;12(3):607. <https://doi.org/10.3390/nu12030607>.
- [37] Mezzetti M, La Vecchia C, Decarli A, Boyle P, Talamini R, Franceschi S. Population attributable risk for breast cancer: diet, nutrition, and physical exercise. J Natl Cancer Inst 1998;90(5): 389–94. <https://doi.org/10.1093/jnci/90.5.389>. Erratum in: J Natl Cancer Inst 2000 May 17;92(10):845.
- [38] Dafni U, Tsourti Z, Alatsathianos I. Breast cancer statistics in the European union: incidence and survival across European countries. Breast Care 2019;14(6):344–53. <https://doi.org/10.1159/000503219>.
- [39] DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, et al. Breast cancer statistics, 2019. Ca - Cancer J Clin 2019;69(6):438–51. <https://doi.org/10.3322/caac.21583>.
- [40] Carioli G, Malvezzi M, Rodriguez T, Bertuccio P, Negri E, La Vecchia C. Trends and predictions to 2020 in breast cancer mortality: Americas and Australasia. Breast 2018 Feb;37:163–9. <https://doi.org/10.1016/j.breast.2017.12.004>.
- [41] Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, Godwin J, Gray R, Pan HC, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet 2012;379(9814): 432–44. [https://doi.org/10.1016/S0140-6736\(11\)61625-5](https://doi.org/10.1016/S0140-6736(11)61625-5).
- [42] Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365(9472):1687–717. [https://doi.org/10.1016/S0140-6736\(05\)66544-0](https://doi.org/10.1016/S0140-6736(05)66544-0).
- [43] Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Davies C, Godwin J, Gray R, Clarke M, Cutter D, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 2011;378(9793):771–84. [https://doi.org/10.1016/S0140-6736\(11\)60993-8](https://doi.org/10.1016/S0140-6736(11)60993-8).
- [44] Goldhirsch A, Gelber RD, Piccart-Gebhart MJ, de Azambuja E, Procter M, Suter TM, et al. Herceptin Adjuvant (HERA) Trial Study Team. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomised controlled trial. Lancet 2013;382(9897):1021–8. [https://doi.org/10.1016/S0140-6736\(13\)61094-6](https://doi.org/10.1016/S0140-6736(13)61094-6).

- [45] Slamon D, Eiermann W, Robert N, Pienkowski T, Martin M, Press M, et al., Breast Cancer International Research Group. Adjuvant trastuzumab in HER2-positive breast cancer. *N Engl J Med* 2011;365(14):1273–83. <https://doi.org/10.1056/NEJMoa0910383>.
- [46] Perez EA, Romond EH, Suman VJ, Jeong JH, Davidson NE, Geyer Jr CE, et al. Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: joint analysis of data from NCCTG N9831 and NSABP B-31. *J Clin Oncol* 2011; 29(25):3366–73. <https://doi.org/10.1200/JCO.2011.35.0868>.
- [47] Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011; 378(9804):1707–16. [https://doi.org/10.1016/S0140-6736\(11\)61629-2](https://doi.org/10.1016/S0140-6736(11)61629-2).
- [48] Nyante SJ, Benefield TS, Kuzmiak CM, Earnhardt K, Pritchard M, Henderson LM. Population-level impact of coronavirus disease 2019 on breast cancer screening and diagnostic procedures. *Cancer* 2021 Feb 26. <https://doi.org/10.1002/cncr.33460>. Epub ahead of print.