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Research Article

Cancer Epidemiology, Biomarkers & Prevention

International Variation in Female Breast Cancer Incidence and Mortality Rates

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Abstract

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death among women worldwide. Herein, we examine global trends in female breast cancer rates using the most up-to-date data available.

Methods: Breast cancer incidence and mortality estimates were obtained from GLOBOCAN 2012 (globocan.iarc.fr). We analyzed trends from 1993 onward using incidence data from 39 countries from the International Agency for Research on Cancer and mortality data from 57 countries from the World Health Organization.

Results: Of 32 countries with incidence and mortality data, rates in the recent period diverged—with incidence increasing and mortality decreasing—in nine countries mainly in Northern/Western Europe. Both incidence and mortality decreased in France, Israel, Italy, Norway, and Spain. In contrast, incidence and death rates both increased in Colombia, Ecuador, and Japan. Death rates also increased in Brazil, Egypt, Guatemala, Kuwait, Mauritius, Mexico, and Moldova.

Conclusions: Breast cancer mortality rates are decreasing in most high-income countries, despite increasing or stable incidence rates. In contrast and of concern are the increasing incidence and mortality rates in a number of countries, particularly those undergoing rapid changes in human development. Wide variations in breast cancer rates and trends reflect differences in patterns of risk factors and access to and availability of early detection and timely treatment.

Impact: Increased awareness about breast cancer and the benefits of early detection and improved access to treatment must be prioritized to successfully implement breast cancer control programs, particularly in transitioning countries. *Cancer Epidemiol Biomarkers Prev; 24(10); 1495–506. ©2015 AACR.*

Introduction

Breast cancer is the most commonly diagnosed cancer among women in the vast majority (140/184) of countries worldwide, representing a quarter of all cancers diagnosed in women (1). It is also the leading cause of cancer-related deaths among women (2). Although once primarily considered a disease of Western women, over half (52%) of new breast cancer cases and 62% of deaths occur in economically developing countries (3). In this article, we examine global patterns and trends in female breast cancer incidence and mortality rates using the most up-to-date cancer registry-based data available.

Materials and Methods

Estimated numbers of new breast cancer cases, cancer deaths, incidence and mortality rates, and 5-year prevalence for 2012 by world region and country were compiled by the International Agency for Research on Cancer (IARC) and obtained from GLOBOCAN (4). GLOBOCAN provides estimates of cancer incidence, mortality, and prevalence for countries and world regions. Regional estimates of breast cancer incidence and mortality rates are the population-weighted averages of incidence and mortality rates of the component countries. Incidence data are derived from population-based cancer registries that vary in coverage and may capture the population of an entire country but more often cover smaller areas, such as major cities. Mortality data are collected annually by the World Health Organization, and while there is national coverage, not all countries achieve the same quality or completeness. Detailed information about sources and methods for GLOBOCAN 2012 incidence and mortality estimates, including estimation methods for countries that lack incidence and/or mortality data, is available online (globocan.iarc.fr) and reviewed by Ferlay and colleagues (1). We calculated mortality to incidence rate ratios by region as a proxy of 5-year survival (5).

Using data extracted from the Cancer Incidence in Five Continents series (6), we present local and national observed incidence rates from population-based cancer registries from 39 countries for 2006–2007, as these are the most current years of data available for the majority of countries. Breast cancer mortality rates from 59 countries for 2008–2012 were extracted from the World Health Organization (WHO) Mortality database (7). The long-term data series from cancer registries and the WHO mortality database were used to assess the respective trends in incidence and mortality rates from 1993 onward in 39 and 56 countries (4, 8–12). In addition, we include breast cancer mortality data from Egypt from 2000 to 2011. All rates are per 100,000 females and were standardized using the direct method and the 1960 World standard population to compare data across

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countries and over time (13). Our analysis was limited to invasive female breast cancers defined by ICD-10/ICD-O-3 site code C50.

Temporal trends in breast cancer rates by country were analyzed using Joinpoint regression analysis, which involves fitting a series of joined straight lines on a logarithmic scale to the trends in annual rates (14, 15). We required a minimum of four years between joinpoints and from a joinpoint to either end of the data series. The direction and magnitude of the resulting trends are described by the annual percent change (APC). To facilitate comparison across countries and to evaluate the most recent time trends, a summary measure, the average annual percent change (AAPC), was calculated for the latest 5 years of available data for each country. A detailed description of this method is provided elsewhere by Clegg and colleagues (16). In describing the change, the terms increase or decrease were used when the APC or AAPC was statistically significant; otherwise the term stable was used.

Results

Geographic variation

Almost 1.7 million new breast cancer cases and 521,900 breast cancer deaths were estimated to have occurred in 2012 worldwide (Table 1). The distribution of breast cancer cases, deaths, and 5-year prevalence by world region is shown in Fig. 1. Asian countries, which represent 59% of the global population, accounted for 39% of new cases, 44% of deaths, and 37% of the world's 5-year prevalent cases. Although North America (US and Canada) represents only 5% of the world population, it accounted for 15% of new cases, 9% of deaths, and 17% of the prevalent cases. In contrast, African countries (15% of the world population) represented 8% of the total new cases and 12% of breast cancer deaths, and 7% of the prevalence.

Estimated age-standardized breast cancer incidence rates in 2012 varied 3-fold worldwide, with the highest incidence rates observed in Northern America, Northern and Western Europe, and Australia/New Zealand; intermediate rates in Central and Eastern Europe, Southern America, and the Caribbean; and the lowest rates in Middle and Eastern Africa, Eastern and South-Central Asia, and Central America (Table 1; Supplementary Fig. S1). Similarly, there was approximately 3-fold variation in breast cancer death rates in 2012; however, the highest death rates were observed in Western and Northern Africa and Melanesia and the lowest death rates were found in Central America and Eastern Asia. Rate ratios comparing mortality rates to incidence rates for world regions are also shown in Table 1. The highest mortality to incidence rate ratios were in parts of Africa (Middle, Western, and Eastern), Melanesia, and South-Central Asia. Rate ratios were lowest in Northern America, Australia/New Zealand, and in Northern and Western Europe.

Observed age-standardized incidence rates in 2006–2007 are presented in Fig. 2. Incidence rates ranged from 25.6 cases per 100,000 females in Thailand (3 registries) to 95.3 per 100,000 in the Netherlands. Incidence rates also varied within region, with rates in Israel approximately 50% higher than other Asian countries. Incidence rates also tended to be elevated in Northern and Western European countries relative to Eastern Europe. Age-standardized female breast cancer death rates for select countries in 2008–2012 are shown in Fig. 3. Breast cancer death rates were highest in Barbados (26.1 per 100,000), Armenia (24.2), and Ireland (19.7) and lowest in Guatemala (4.9), the Republic of Korea (5.2), and Egypt (5.9).

Incidence and mortality trends

Trends in breast cancer incidence and mortality rates for selected countries are shown in Fig. 4 and in Tables 2 and 3. Increasing breast cancer incidence trends during the most recent time period were observed in 22 of 39 countries, with 5-year AAPCs ranging from 0.8% in the Netherlands to 4.8% or more in Thailand (3 registries) and Uganda (Kyadondo County) (Table 2). In five countries [France (6 registries), Israel, Italy (8 registries), Spain (7 registries), and Norway], breast cancer incidence rates decreased 0.8%–1.6% per year and in 12 others, primarily in Northern America, Oceania, and Europe, incidence rates were stable (Table 2). In contrast to incidence trends, death rates significantly decreased in the most recent period in

Table 1. Estimated numbers of new female breast cancer cases and deaths by world area, 2012

	Cases		Deaths		Mortality: incidence
Area	Number	ASR	Number	ASR	Rate ratio
Eastern Africa	33,470	30.4	17,030	15.6	0.51
Middle Africa	10,920	26.8	5,980	14.8	0.55
Northern Africa	39,510	43.2	15,580	17.4	0.40
Southern Africa	10,300	38.9	4,050	15.5	0.40
Western Africa	39,680	38.6	20,520	20.1	0.52
Eastern Asia	277,050	27.0	68,530	6.1	0.23
South-Central Asia	223,900	28.2	104,670	13.5	0.48
South-Eastern Asia	107,550	34.8	43,000	14.1	0.41
Western Asia	42,490	42.8	14,810	15.1	0.35
Caribbean	11,290	46.1	3,930	15.1	0.33
Central America	24,890	32.8	7,270	9.5	0.29
Southern America	115,880	52.1	32,010	14.0	0.27
Northern America	256,220	91.6	48,850	14.8	0.16
Central and Eastern Europe	123,620	47.7	48,720	16.5	0.35
Northern Europe	78,250	89.4	17,910	16.4	0.18
Southern Europe	100,810	74.5	27,470	14.9	0.20
Western Europe	156,050	91.1	37,240	16.2	0.18
Australia/New Zealand	17,550	85.8	3,620	14.5	0.17
Melanesia	1,380	41.0	630	19.7	0.48
Micronesia/Polynesia	350	48.8	80	13.1	0.27
World	1,676,600	43.1	521,900	12.9	0.30

Abbreviation: ASR, age-standardized rate per 100,000.

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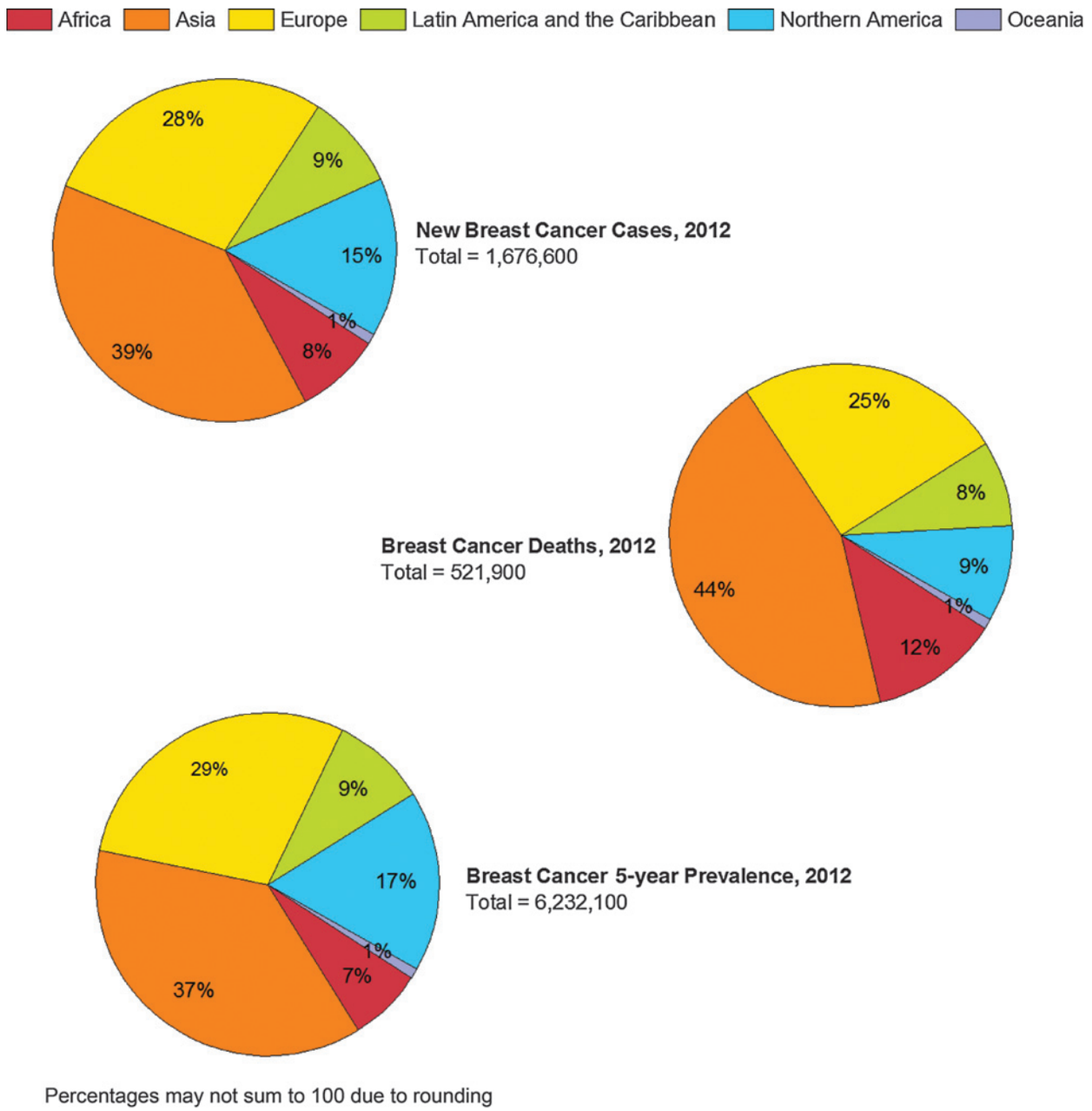

Figure 1.
Distribution of estimated female breast cancer new cases, deaths, and 5-year prevalence by world region, 2012.

34 of 57 countries analyzed, with AAPCs during the last 5 years ranging from −0.5% in Costa Rica and Lithuania to −3.6% in Iceland (Table 3). In ten countries (Brazil, Colombia, Ecuador, Egypt, Guatemala, Japan, Kuwait, Mauritius, Mexico, and Republic of Moldova), breast cancer death rates increased (0.2%–3.5% per year) during the most recent five years of data available (Table 3). Trends for specific countries/regions are described in more detail below.

Northern America and Oceania

In the United States, Canada (except Quebec), Australia, and New Zealand, the most recent data indicate that breast cancer incidence rates have stabilized, while mortality rates continued to decline.

Central and Southern America and the Caribbean

Local and national incidence data from Central and Southern America and the Caribbean suggest breast cancer incidence rates continued to increase since 1993 in 3 [Colombia (Cali), Costa Rica, and Ecuador (Quito)] of 4 countries included in the study. In Brazil, there was no significant change in incidence rates over this period. Mortality trends in this region are variable. Since 1993, breast cancer death rates increased in Colombia, Ecuador,

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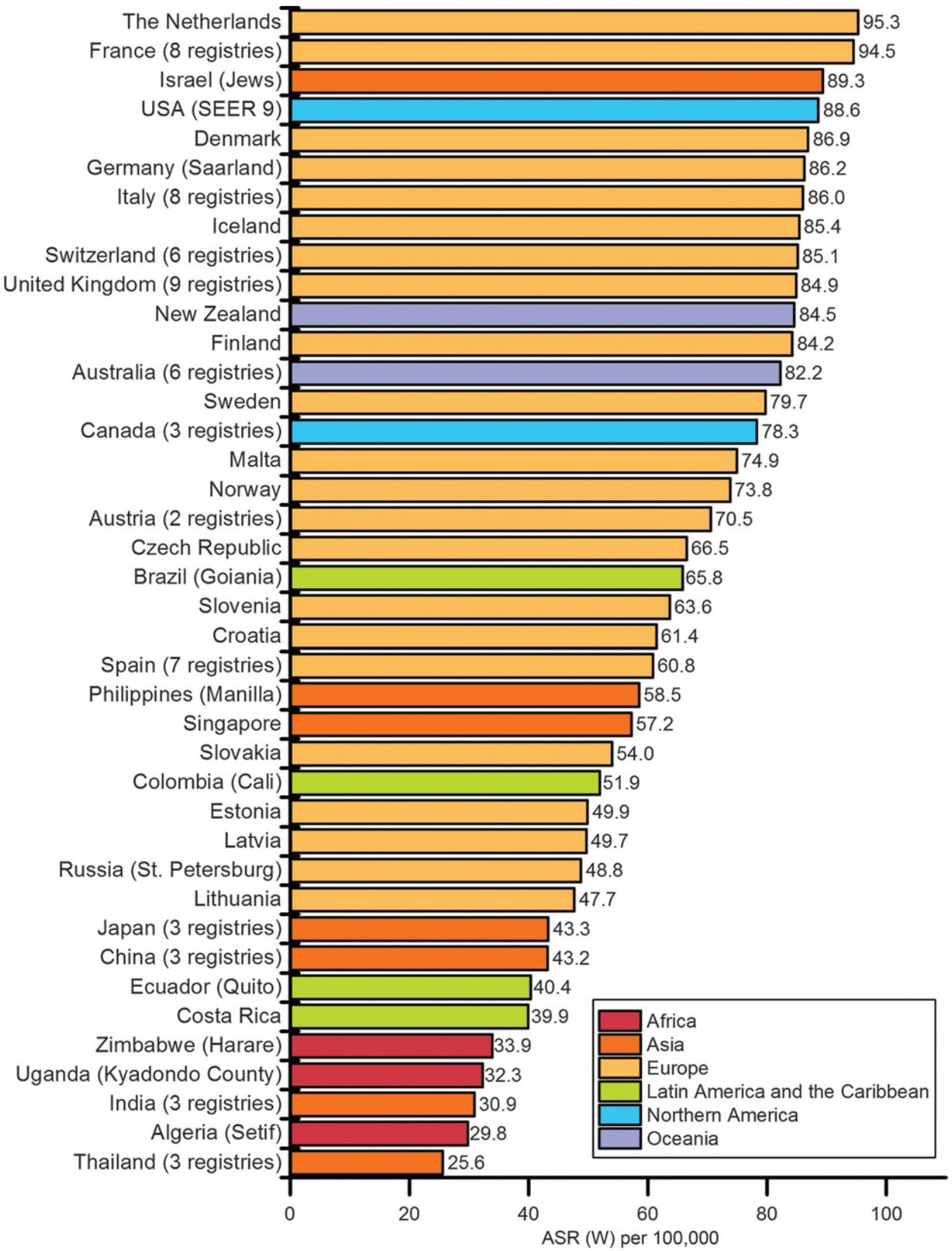

Figure 2.
Age-standardized female breast cancer incidence rates for select registries, 2006–2007.

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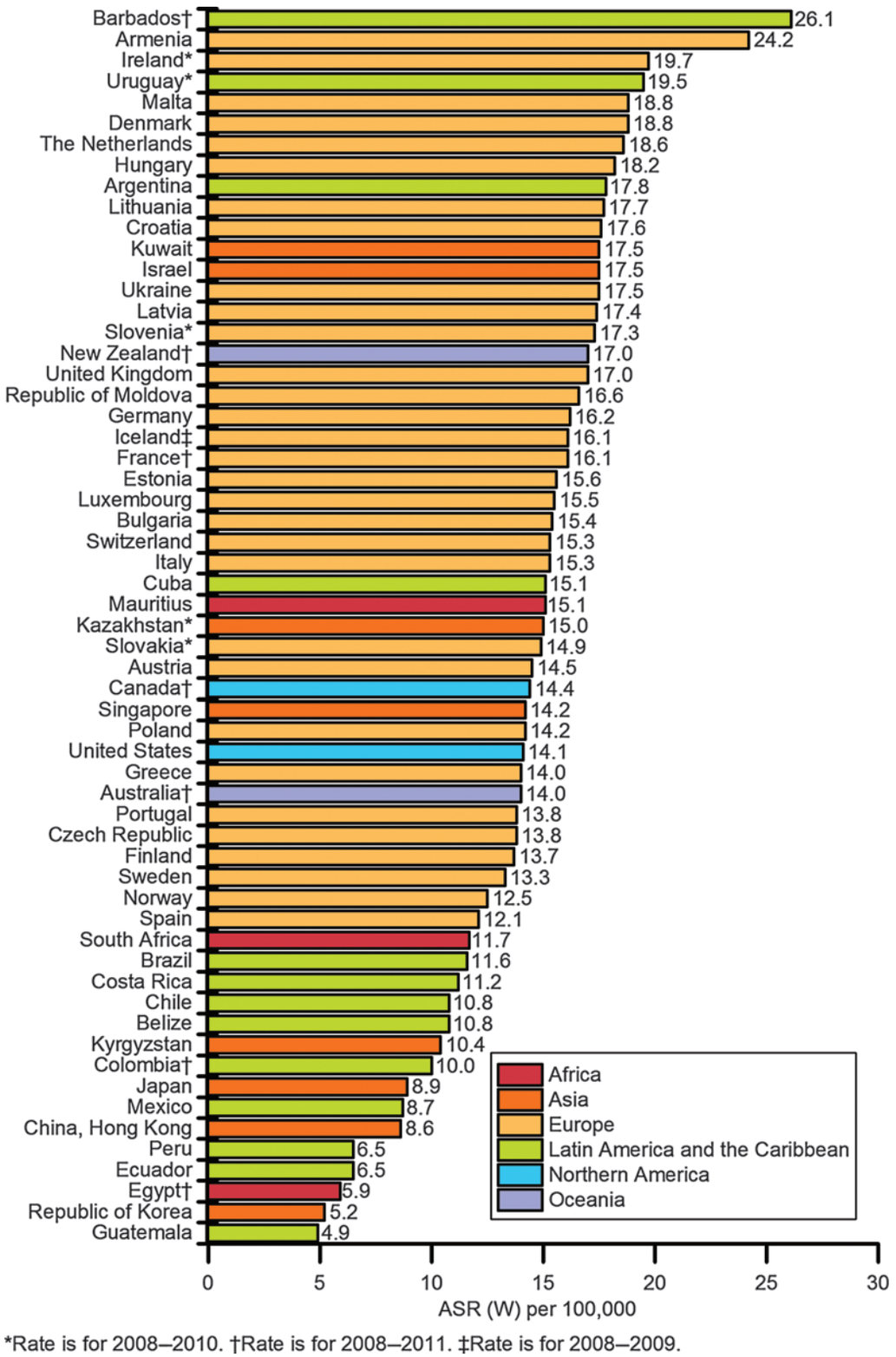

Figure 3.
Age-standardized female breast cancer mortality rates for select registries, 2008–2012.

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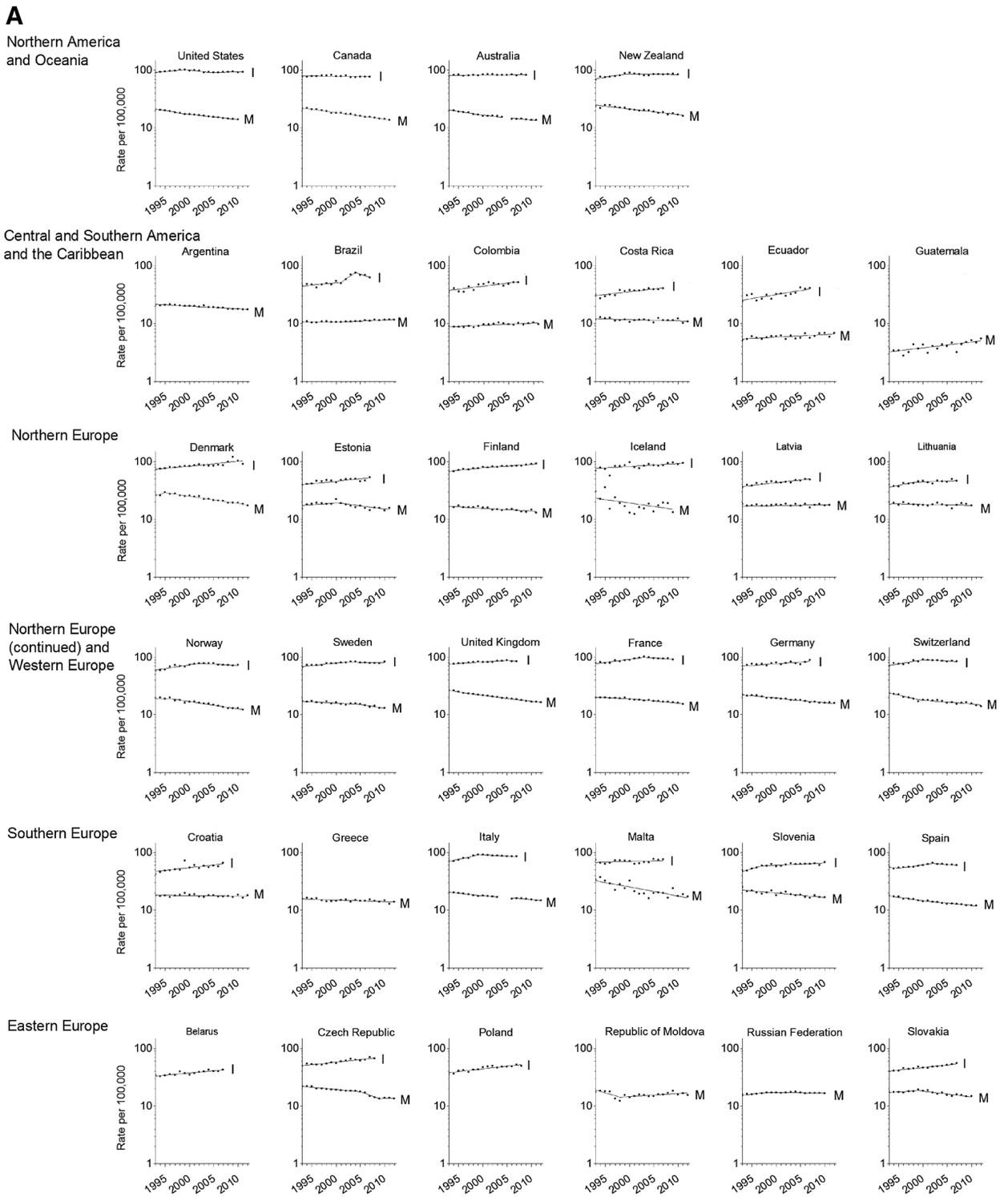

I indicates incidence data and M indicates mortality data.
Lines represent fitted values based on Joinpoint analyses; squares represent observed rates.

Figure 4.
Trends in age-standardized female breast cancer incidence (I) and mortality (M) rates, select countries. (*Continued on the following page.*)

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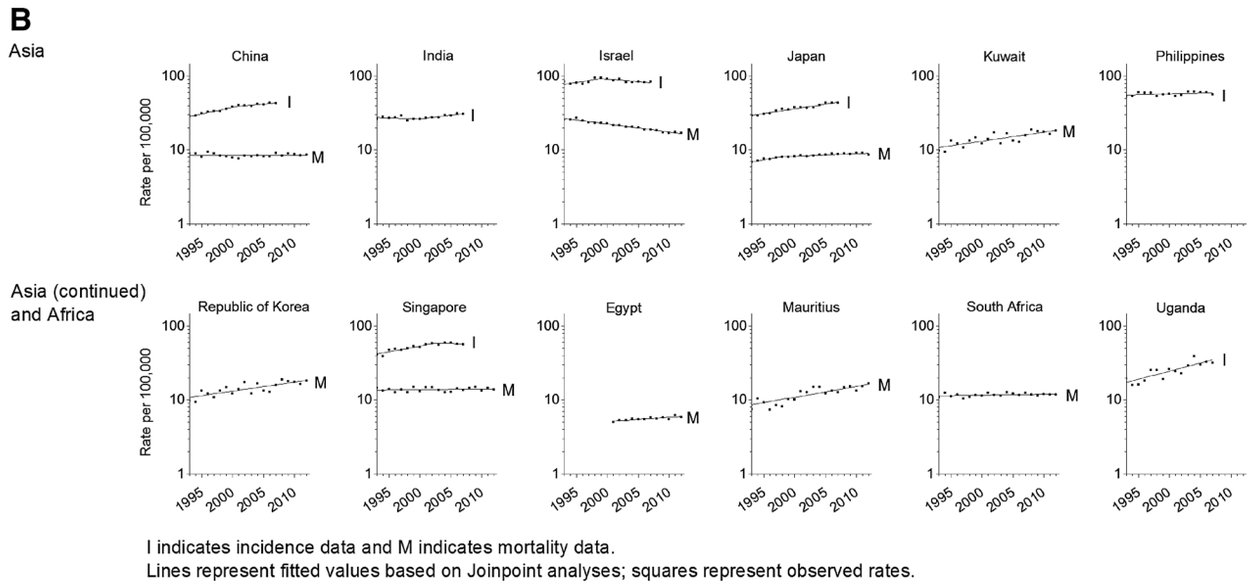

Figure 4.
(*Continued.*)

Guatemala, and Mexico; decreased in Costa Rica, Chile, and Uruguay; and did not change significantly in Belize and Cuba. Breast cancer death rates also increased in Brazil, by 0.9% per year from 2001 to 2012.

Northern Europe

Incidence and mortality trends diverged in five Northern European countries (Denmark, Estonia, Finland, Iceland, and Lithuania), with incidence rates increasing and mortality decreasing since the mid-1990s. In Latvia, Sweden, and the United Kingdom, increasing incidence trends were also observed; however, incidence rates stabilized in the most recent period in Sweden and the UK. In contrast, incidence rates decreased in Norway by 1.2% per year from 2002 to 2010. Of the 10 countries in Northern Europe in this analysis, death rates decreased since the mid-1990s in all except Latvia, where rates were stable since 2002. Despite the steady decrease in mortality rates by 2.9% per year from 1996 to 2012, Denmark has one of the highest breast cancer death rates in the region (Fig. 3).

Western Europe

Incidence rates increased over the entire study period in Germany (Saarland) and The Netherlands. Incidence rates also increased in France (6 registries) and Switzerland (6 registries) in the beginning of the study period, but subsequently declined in France (1.2% per year since 2003) and stabilized in Switzerland (since 2000). Breast cancer incidence rates were stable in Austria during 1993–2007. In contrast to the incidence trends, breast cancer death rates decreased in all six Western European countries in the study.

Southern Europe

Similar to France, incidence trends reversed over the study period in Italy and Spain, with rates decreasing since 1999 and 2002, respectively. Incidence rates continued to increase in Croatia and Slovenia since 1993 and were stable over the entire period in Malta. Death rates decreased in six of seven Southern European countries; the trend was stable in Croatia.

Eastern Europe

Incidence rates increased (1.7%–2.2% per year) from 1993 to 2007/2008 in all four Eastern European countries considered in the incidence trend analysis. Trends in death rates in Eastern Europe were variable. In Romania and the Russian Federation, death rates declined since the early 2000s, after previously increasing. Breast cancer death rates also decreased over the study period in Hungary and Slovakia, but they were stable in Bulgaria and Ukraine since 1993 and in Czech Republic since 2009. In contrast, in the Republic of Moldova, breast cancer death rates increased by 1.2% per year from 1998 to 2012.

Asia

Breast cancer incidence rates increased sharply since 1993 in China (3 registries), Japan (4 registries), and Thailand (3 registries). In Singapore, incidence rates increased through 2002 and then stabilized. An increasing incidence trend was also observed in India beginning in 2000. In contrast, incidence rates decreased by 1.6% per year from 1999 to 2007 in Israel. Breast cancer death rates also decreased in Israel. Death rates increased in Japan and Kuwait over the study period and in Kazakhstan and Republic of Korea through 1999 and 2005, respectively. Death rates were relatively stable over the entire study period in China (Hong Kong), Kyrgyzstan, and Singapore.

Africa

Limited data are available for African countries: one metropolitan registry (Uganda, Kyadondo County) for incidence and three countries for mortality. Breast cancer incidence rates increased in Uganda (Kyadondo County) by 5.2% per year during 1993–2007.

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Table 2. Trends in female breast cancer incidence rates in selected registries

	Trend 1		Trend 2		Trend 3		AAPC	
	Years	APC	Years	APC	Years	APC	Last 5 years	
Northern America								
Canada (except Quebec)	1993–2007	−0.2					2003–2007	−0.2
United States (SEER 9)	1993–1999	1.8[a]	1999–2004	−2.2[a]	2004–2012	0.2	2008–2012	0.2
Oceania								
Australia	1993–2009	0.2					2005–2009	0.2
New Zealand	1993–1999	3.2[a]	1999–2010	−0.1			2006–2010	−0.1
Central and Southern America and the Caribbean								
Brazil, Goiania	1993–2001	1.9	2001–2004	14.1	2004–2007	−6.3	2003–2007	−1.6
Colombia, Cali	1993–2007	2.5[a]					2003–2007	2.5[a]
Costa Rica	1993–2007	2.3[a]					2003–2007	2.3[a]
Ecuador, Quito	1993–2007	3.3[a]					2003–2007	3.3[a]
Northern Europe								
Denmark	1993–2011	1.8[a]					2007–2011	1.8[a]
Estonia	1993–2007	1.4[a]					2003–2007	1.4[a]
Finland	1993–2000	2.5[a]	2000–2008	0.9[a]	2008–2011	2.6[a]	2007–2011	2.2[a]
Iceland	1993–2011	1.4[a]					2007–2011	1.4[a]
Latvia	1993–2007	1.8[a]					2003–2007	1.8[a]
Lithuania	1993–2007	1.5[a]					2003–2007	1.5[a]
Norway	1993–2002	3.2[a]	2002–2010	−1.2[a]			2006–2010	−1.2[a]
Sweden	1993–2002	1.9[a]	2002–2010	−0.3			2006–2010	−0.3
United Kingdom (9 registries)	1993–2004	1.2[a]	2004–2007	−0.6			2003–2007	−0.2
Western Europe								
Austria (2 registries)	1993–2007	0.3					2003–2007	0.3
France (6 registries)	1993–2003	2.6[a]	2003–2009	−1.2[a]			2005–2009	−1.2[a]
Germany, Saarland	1993–2007	1.4[a]					2003–2007	1.4[a]
Switzerland (6 registries)	1993–2000	3.3[a]	2000–2007	−1.0			2003–2007	−1.0
The Netherlands	1993–2007	0.8[a]					2003–2007	0.8[a]
Southern Europe								
Croatia	1993–2007	2.2[a]					2003–2007	2.2[a]
Italy (8 registries)	1993–1999	4.6[a]	1999–2007	−0.8[a]			2003–2007	−0.8[a]
Malta	1993–2007	0.5					2003–2007	0.5
Slovenia	1993–1997	5.7[a]	1997–2010	0.9[a]			2006–2010	0.9[a]
Spain (7 registries)	1993–1995	−2.1	1995–2002	2.8[a]	2002–2007	−1.3[a]	2003–2007	−1.3[a]
Eastern Europe								
Belarus	1993–2007	1.7[a]					2003–2007	1.7[a]
Czech Republic	1993–2008	2.1[a]					2004–2008	2.1[a]
Poland (3 registries)	1993–2008	2.2[a]					2004–2008	2.2[a]
Slovakia	1993–2007	2.1[a]					2003–2007	2.1[a]
Asia								
China (3 registries)	1993–2001	4.1[a]	2001–2007	1.6[a]			2003–2007	1.6[a]
India (3 registries)	1993–2000	−0.7	2000–2007	2.4[a]			2003–2007	2.4[a]
Israel	1993–1999	2.9[a]	1999–2007	−1.6[a]			2003–2007	−1.6[a]
Japan (4 registries)	1993–2007	3.0[a]					2003–2007	3.0[a]
Philippines (2 registries)	1993–2007	0.6					2003–2007	0.6
Singapore	1993–2002	3.8[a]	2002–2007	−0.1			2003–2007	−0.1
Thailand (3 registries)	1993–2007	4.8[a]					2003–2007	4.8[a]
Africa								
Uganda, Kyadondo County	1993–2007	5.2[a]					2003–2007	5.2[a]

Abbreviations: APC, annual percent change; AAPC, average annual percent change.
[a]The APC or AAPC is statistically different from zero.

Death rates increased in Egypt (1.3% per year during 2000–2011) and Mauritius (3.5% per year during 1993–2012), while rates were stable in South Africa.

Discussion

The highest breast cancer incidence rates continue to be observed in high-income countries, including countries in Northern America, Australia, and Northern and Western Europe, with intermediate rates in Central and Eastern Europe, Southern America, and the Caribbean, and the lowest incidence rates in Middle and Eastern Africa, Eastern and South-Central Asia, and Central America. Of the 32 countries with both incidence and mortality breast cancer data, rates diverged in nine countries mainly in Northern and Western Europe (Costa Rica, Denmark, Estonia, Finland, Germany, Iceland, Lithuania, Slovenia, and the Netherlands). Both incidence and mortality rates decreased in the recent period in Norway, France, Italy, Spain, and Israel, whereas they increased in Colombia, Ecuador, and Japan. The wide geographic and temporal variations in breast cancer rates and trends reflect differences in the patterns of risk factors and access to and availability of early detection and timely treatment.

Rate ratios were used to compare breast cancer mortality rates to incidence rates by region. The highest rate ratios (corresponding to the poorest survival) were in Africa, South-Central Asia, and Melanesia. A recent worldwide study of cancer survival found that breast cancer 5-year net survival ranged from 53% in South Africa to 89% in the United States (17). In general, high ratios in

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Table 3. Trends in female breast cancer mortality rates for selected countries

	Trend 1		Trend 2		Trend 3		AAPC	
	Years	APC	Years	APC	Years	APC	Last 5 years	
Northern America								
Canada	1993–2011	−2.6[a]					2007–2011	−2.6[a]
United States	1993–1999	−3.0[a]	1999–2012	−2.0[a]			2008–2012	−2.0[a]
Oceania								
Australia	1993–2000	−3.1[a]	2000–2011	−1.8[a]			2007–2011	−1.8[a]
New Zealand	1993–2011	−2.2[a]					2007–2011	−2.2[a]
Central and Southern America and the Caribbean								
Argentina	1993–2012	−1.0[a]					2008–2012	−1.0[a]
Belize	1993–2012	2.3					2008–2012	2.3
Brazil	1993–2001	0.0	2001–2012	0.9[a]			2008–2012	0.9[a]
Chile	1993–2012	−0.8[a]					2008–2012	−0.8[a]
Colombia	1993–2011	0.8[a]					2007–2011	0.8[a]
Costa Rica	1993–2012	−0.5[a]					2008–2012	−0.5[a]
Cuba	1993–2012	0.0					2008–2012	0.0
Ecuador	1993–2012	1.0[a]					2008–2012	1.0[a]
Guatemala	1993–2012	2.3[a]					2008–2012	2.3[a]
Mexico	1993–2012	0.2[a]					2008–2012	0.2[a]
Uruguay	1993–2010	−1.4[a]					2006–2010	−1.4[a]
Northern Europe								
Denmark	1993–1996	2.3	1996–2012	−2.9[a]			2008–2012	−2.9[a]
Estonia	1993–1996	8.3	1996–2012	−1.9[a]			2008–2012	−1.9[a]
Finland	1993–2012	−1.2[a]					2008–2012	−1.2[a]
Iceland	1993–2009	−3.6[a]					2005–2009	−3.6[a]
Ireland	1993–2010	−1.9[a]					2006–2010	−1.9[a]
Latvia	1993–2012	−0.1					2008–2012	−0.1
Lithuania	1993–2012	−0.5[a]					2008–2012	−0.5[a]
Norway	1993–2012	−2.7[a]					2008–2012	−2.7[a]
Sweden	1993–2012	−1.5[a]					2008–2012	−1.5[a]
United Kingdom	1993–1997	−3.4[a]	1997–2012	−2.3[a]			2008–2012	−2.3[a]
Western Europe								
Austria	1993–2012	−2.4[a]					2008–2012	−2.4[a]
France	1993–1999	−0.7[a]	1999–2011	−1.7[a]			2007–2011	−1.7[a]
Germany	1993–2012	−1.8[a]					2008–2012	−1.8[a]
Luxembourg	1993–2012	−2.5[a]					2008–2012	−2.5[a]
Switzerland	1993–1999	−4.4[a]	1999–2012	−1.6[a]			2008–2012	−1.6[a]
The Netherlands	1993–2012	−2.3[a]					2008–2012	−2.3[a]
Southern Europe								
Croatia	1993–2012	−0.2					2008–2012	−0.2
Greece	1993–2012	−0.6[a]					2008–2012	−0.6[a]
Italy	1993–1999	−2.3[a]	1999–2012	−1.5[a]			2008–2012	−1.5[a]
Malta	1993–2012	−3.5[a]					2008–2012	−3.5[a]
Portugal	1993–2012	−1.4[a]					2008–2012	−1.4[a]
Slovenia	1993–2010	−1.9[a]					2006–2010	−1.9[a]
Spain	1993–1999	−3.2[a]	1999–2012	−1.9[a]			2008–2012	−1.9[a]
Eastern Europe								
Bulgaria	1993–2012	−0.1					2008–2012	−0.1
Czech Republic	1993–2005	−1.7[a]	2005–2009	−6.5[a]	2009–2012	0.5	2008–2012	−1.3
Hungary	1993–2012	−1.8[a]					2008–2012	−1.8[a]
Republic of Moldova	1993–1998	−5.6[a]	1998–2012	1.2[a]			2008–2012	1.2[a]
Romania	1993–2001	1.1[a]	2001–2012	−1.1[a]			2008–2012	−1.1[a]
Russian Federation	1993–2003	1.0[a]	2003–2011	−0.8[a]			2007–2011	−0.8[a]
Slovakia	1993–1999	1.3	1999–2010	−2.3[a]			2006–2010	−2.3[a]
Ukraine	1993–2012	−0.1					2008–2012	−0.1
Asia								
China, Hong Kong	1993–2012	0.0					2008–2012	0.0
Israel	1993–2012	−2.5[a]					2008–2012	−2.5[a]
Japan	1993–1998	3.3[a]	1998–2012	0.8[a]			2008–2012	0.8[a]
Kazakhstan	1993–1999	2.7[a]	1999–2010	−0.6			2006–2010	−0.6
Kyrgyzstan	1993–2012	0.4					2008–2012	0.4
Kuwait	1993–2012	2.8[a]					2008–2012	2.8[a]
Republic of Korea	1993–2005	2.8[a]	2005–2012	0.9			2008–2012	0.9
Singapore	1993–2012	0.2					2008–2012	0.2
Africa								
Egypt	2000–2011	1.3[a]					2007–2011	1.3[a]
Mauritius	1993–2012	3.5[a]					2008–2012	3.5[a]
South Africa	1993–2012	0.3					2008–2012	0.3

Abbreviations: APC, annual percent change; AAPC, average annual percent change.

[a]The APC or AAPC is statistically different from zero.

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low- and middle-income countries reflect the large proportion of women presenting with advanced disease and limited access to affordable quality cancer treatment (18). In many low-income countries, screening is neither cost-effective nor feasible, and access to healthcare is limited, thus the majority of breast cancer patients are diagnosed with advanced stage disease. For example, during 2009–2010, 76% of breast cancer patients in Nigeria were diagnosed with stage III or IV breast cancer (19). The lowest ratios were observed in Northern America, Australia/New Zealand, and in Western and Northern Europe reflecting moderate death rates despite high incidence rates. Countries with lower breast cancer death rates despite higher incidence rates in part reflect the more favorable survival as a result of earlier stage at diagnosis and greater access to effective cancer treatments (20).

Breast cancer incidence rates have continued to rise in several high-income countries, particularly in Northern and Eastern Europe, as well as in many countries of Latin America, Africa, and Asia, regions with historically lower breast cancer rates. Increasing trends in breast cancer incidence in high-income countries over the past several decades are thought to reflect increases in the prevalence of known risk factors (e.g., reproductive patterns and obesity) and increased detection through mammography (20, 21). Increases in the use of postmenopausal hormone therapy may have also contributed to the increases in breast cancer incidence rates through the early 2000s (22–28). Although mammography screening is currently the most effective method for detecting breast cancer at an early stage, it also results in the overdiagnosis of some breast cancers. Estimates of overdiagnosis are highly variable, ranging from <5% to >30% (29–35).

Similarly, the increasing incidence trend in low- and middle-income countries is due largely to increases in risk factors associated with economic development and urbanization, including obesity and adaptation of a Western-type diet, physical inactivity, delayed childbearing and/or having fewer children, earlier age at menarche, and shorter duration of breastfeeding (20, 36–44). For example, average body mass index (BMI) among women has increased over the past several decades in many countries around the world, such as in Costa Rica where the average female BMI increased from 23.3 in 1980 to 27.1 in 2008 (45, 46). Increased access to contraceptives and other voluntary family planning initiatives have led to sustained declines in fertility rates in Asia, Latin America, and Africa (47). Increased awareness of the disease may also contribute to rising incidence rates in low and middle-income countries.

Incidence rates declined in the recent period in five high-income countries (France, Israel, Italy, Norway, and Spain) and rates were stable in 13 other countries. Previous studies have documented a decline in breast cancer incidence in a several high-income countries related to decreased use of menopausal hormone therapy around the early 2000s (22–28). In the United States, breast cancer incidence rates dropped nearly 7% between 2002 and 2003, coinciding with the publication of the results of Women's Health Initiative trial on the adverse health effects of menopausal hormone therapy use in postmenopausal women (48). The continued decline or stabilization in some Western countries has also been attributed to plateaus in participation of mammography screening (20, 22).

Although breast cancer incidence rates continued to increase or stabilize in many countries, mortality rates have declined in 34 of 57 countries in the most recent time period (Table 3). Most of the decreasing trends, as well as the most rapid declines, occurred in high-income countries. These reductions have been attributed to early detection through mammography and improved treatment; although the respective contributions of each are unclear and likely vary depending on the level of participation in regular screening and the availability and prompt administration of state-of-the-art treatment (21, 49–54). A study of cancer survival in 67 countries reported that 5-year breast cancer survival increased steadily in most high-income countries, as well as in several countries in Central and Southern America (17).

In contrast to the decreasing trends observed in most countries, breast cancer mortality rates increased in ten countries (Brazil, Colombia, Ecuador, Egypt, Guatemala, Japan, Kuwait, Mauritius, Mexico, and Republic of Moldova) reflecting increasing incidence trends and in some cases, limited access to treatment (55, 56). Increasing mortality rates in Asia, Latin America, and Africa have been previously documented (38, 57–59). It has been reported that the increase in breast cancer death rates in Japan began in the 1960s, approximately 10 years after the country experienced a transition from a traditional Asian plant-based diet to a Western meat-based diet and subsequently an increase in the prevalence of overweight and obesity (58). In addition, even in some high-income countries such as Japan, mammography screening has not been widely embraced at a population level for reasons including cultural attitudes toward screening, lack of knowledge and/or encouragement from family and physician, and concerns about modesty (60).

Optimal breast cancer treatment is often not available in low-income countries. Effective treatment may be limited by small numbers of trained medical personnel, insufficient modern equipment, including pathology services and radiotherapy machines, and the high cost of cancer drugs (18). There are currently more than 25 countries, primarily in Africa, without a single radiotherapy unit (61). The International Atomic Energy Agency (IAEA) has estimated that there is a shortage of at least 5,000 radiotherapy machines in developing countries (62). There are also social barriers such as fatalistic beliefs, reluctance or refusal to have one's breasts examined by a male doctor, and the stigma associated with breast cancer and its treatment (63). Cancer fatalism has been documented in Latin American, Arabic, and Ethiopian populations (64–66). In some societies, a woman may avoid revealing that she has breast cancer out of fear that she will be rejected by her family and community or that her daughter's potential for future marriage may be adversely affected. For these reasons, cancer education regarding the importance of early detection is fundamental to a successful breast cancer control program in lower- and middle-income countries.

This study is a comprehensive and up-to-date analysis of breast cancer incidence and mortality trends in the most recent time period using cancer incidence and mortality data from IARC and WHO (4, 7). It should be noted that the 2012 regional estimates presented from GLOBOCAN 2012 are aggregated from those for 184 countries and territories that are variable in accuracy, depending on the extent and validity of available data. Country estimates range from real and valid counts of cases and deaths to estimates based on samples or neighboring country rates. In addition, breast cancer is increasingly understood as a heterogeneous disease made up of a number of histologic and molecular subtypes that are distinct in etiology, presentation, and outcomes (67); however, information on breast cancer subtypes is not available in GLOBOCAN. Despite these limitations, GLOBOCAN 2012 represents the best estimates available and is useful for establishing

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priorities for cancer control in many low and middle-income countries where information for cancer cases and deaths are lacking or limited. Another limitation is that our presentation of overall rates for countries may obscure the breast cancer burden in specific racial and ethnic populations within countries. Breast cancer trends were also likely to be influenced by demographic changes within countries and regions, such as the immigration of low-risk populations in to high-risk countries (68). Finally, the reporting of trends was limited by the number of countries with sufficient historical data and by the variation in the range of most recent years of available data.

Conclusions

Breast cancer incidence and mortality rates are increasing in some parts of the world, particularly in low- and middle-income countries. This trend largely reflects the adoption of a Western lifestyle, including changes in diet, physical activity, and reproductive patterns. The growth and ageing of the population are predicted to further drive increases in the global burden of breast cancer, particularly in low and middle-income countries. In low resource settings, down staging of symptomatic disease is considered more beneficial and cost-effective than screening for asymptomatic disease. However, misconceptions about the nature or curability of breast cancer are still prevalent in many communities. Thus, it is necessary to increase awareness about breast cancer and the benefits of early detection, most notably in transitioning countries, to successfully implement breast cancer control programs, as well as to improve access to treatment.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: C.E. DeSantis, A. Jemal
Development of methodology: C.E. DeSantis, A. Jemal
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C.E. DeSantis, J. Ferlay
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): C.E. DeSantis, F. Bray, J. Ferlay, J. Lortet-Tieulent, B.O. Anderson, A. Jemal
Writing, review, and/or revision of the manuscript: C.E. DeSantis, F. Bray, J. Ferlay, J. Lortet-Tieulent, B.O. Anderson, A. Jemal
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