

Global trends and predictions in ovarian cancer mortality

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Background: Over the last two decades, ovarian cancer mortality rates have levelled or declined. There are, however, persisting and substantial differences in ovarian cancer patterns and trends.

Patients and methods: We updated global trends in ovarian cancer mortality to 2012, and predicted trends in rates to 2020 using data from the World Health Organization database.

Results: In the EU, age-adjusted ovarian cancer mortality rates decreased 10% between 2002 and 2012, to 5.2/100 000. The decline was ~16% in the USA, to 4.9/100 000 in 2012. Latin American countries had lower rates, and declines were observed in Argentina and Chile. Likewise, modest declines (–2.1%) were observed in Japan, whose rate remained low (3.2/100 000 in 2012). Australia had a rate of 4.3/100 000 in 2012, and a 12% decline. The falls were larger in young women, than in middle or old age. Recent rates at age 20–49 were higher in Japan than in the EU and the USA. Predictions to 2020 indicate a further 15% decline in the USA and 10% in the EU and Japan.

Conclusions: The main reason for the favourable trends is the use of oral contraceptives (OCs), particularly, in the USA and countries of the EU where OCs were introduced earlier. Declines in menopausal hormone use may also have played a favourable role in elderly women, as well as improved diagnosis, management and treatment.

Key words: ovarian cancer, mortality, oral contraceptives, menopausal hormone replacement therapy, diet, treatment

Introduction

Over the last two decades, ovarian cancer mortality rates have tended to level off and decrease in several high-income European countries and North America, where rates were highest [1–4].

The falls were greater in young and middle-aged women than in the elderly, and earlier and larger in the USA, the UK and northern Europe [5]. These are the countries where oral contraceptives (OCs)—which have a long-term protective effect on ovarian cancer risk [6–8]—were introduced earlier and used more frequently. Advancement in diagnosis and treatment may also have influenced these trends, particularly in high-income countries [3, 4, 9].

However, persisting marked differences in ovarian cancer patterns and trends across various areas of the world [2] remain. To provide a comprehensive picture of recent patterns and trends in ovarian cancer mortality, we considered most recent global death certification rates available (up to 2012 in most countries), and provided predictions to 2020 [10] for selected larger countries or groups of countries.

Materials and methods

We obtained official death certification data for ovarian cancer from 1970 to 2012 or the most recent available year in each country, from the World Health Organization (WHO) database, available on electronic support [11]. Figures were derived for the EU as a whole (28 countries as of July 2013, minus Cyprus due to data unavailability), plus other 4 European countries, 11 American countries and 6 other countries worldwide. We excluded countries with <2 million inhabitants, or with <500 ovarian cancer deaths in 2005–2009. Further details are given in the supplementary Appendix, available at *Annals of Oncology* online.

During the calendar period considered, three different Revisions of the International Classification of Diseases (ICD) were used [12–14]. Ovarian cancer deaths were recorded according to the 10th Revision of the ICD (C56–C57.4).

From the matrices of certified deaths and resident population, we computed age-specific rates for each 5-year age group (from 0–4 to 85+ years, and from 0–4 to 80+ for the Americas) and calendar year or quinquennium. We then computed age-standardised mortality rates per 100 000 women using the direct method on the basis of the world standard population at all ages, and at ages 20–49, 50–69 and 70–79 years [15].

We used joinpoint regression models [16], allowing for up to three joinpoints, to identify significant changes in mortality trends for 19 major countries worldwide and the EU as a whole. For each of the trends identified by the joinpoint model, we computed the estimated annual per cent changes

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(APC) and the average annual per cent change (AAPC) over the whole period [17, 18].

For eight large countries (France, Germany, Italy, Poland, Spain, UK, the USA and Japan) and the EU, we predicted ovarian cancer deaths and rates for 2020 [10]. These were derived by fitting a joinpoint model to the number of certified deaths in each 5-year age group to identify the most recent trend segment. Subsequently, a linear regression was applied to the mortality data in each age group over the time period identified by the joinpoint model. We thus computed the predicted age-specific number of deaths, and the 95% prediction intervals (PIs). Predicted standardised mortality rates, and their 95% PIs, were computed using the projected populations from EUROSTAT, the USA Census Bureau, and the Japanese National Institute of Population and Social Security Research (IPSS) databases [19–21].

results

Table 1 shows mortality data from ovarian cancer at all ages and 20–49, 50–69 and 70–79 years from 31 European countries, the EU and selected countries worldwide around 2002 (2000–2004 quinquennium), 2007 (2005–2009 quinquennium) and 2012 (single year, or the closest available year when missing), along with per cent changes between 2012 and 2002.

At all ages, EU mortality rates decreased from 5.8 to 5.2/100 000 (–9.9%) between 2002 and 2012. All European countries, except Bulgaria, showed downward trends. Across major European countries, the per cent changes varied between –8% in Poland and –24% in Sweden. The declines were larger in northern and most central Europe, where ovarian cancer rates were highest in the past. The declines in North America were greater than in the EU. The USA per cent change was –16%, and in 2012 overall mortality rates were ~4.9 in the USA and Canada. The pattern was inconsistent in Latin America, with a few declines (Argentina, Chile and Uruguay) and other upward trends. In 2012, overall rates were systematically lower in Latin America (between 2.8/100 000 in Brazil and 4.3 in Uruguay) than in North America or Europe.

Ovarian cancer rates declined moderately in Japan and Hong Kong, but not Korea, which however had the lowest rate (2.3/100 000) among the countries considered. The falls in Australia and New Zealand were ~12%, and rates in 2012 were similar to those in North America.

The declines in ovarian cancer mortality were systematically larger in the young (20–49 years). In the EU, the fall was from 2.0 to 1.6 (–21.7%). However, in Japan, rates in the young only decreased slightly, to 1.9/100 000 in 2012, i.e. a higher rate than in the EU and the USA (1.2/100 000). Australia and New Zealand had the lowest rates for young women in 2012. In middle-aged women (50–69 years), the EU ovarian cancer mortality rate was 20.3 in 2002 and 18.1 in 2012 (–10.7%). The decline was –12.1% in the USA.

In the EU, the rate for 70- to 79-year-old women only declined modestly from 39.6 in 2002 to 38.7 in 2012 (–2.2%). Denmark had the greatest decline (–30.9%), and an over 10% decline was registered in the UK, too. The USA had the greatest decline among major countries, with ovarian cancer mortality rates of 44.3 in 2002 and of 36.5 in 2012 (–17.6%). Argentina also had changes of about –16%.

Figure 1 displays all ages ovarian cancer mortality rates in 2012 from largest to smallest. Lithuania and Ireland had the highest rates (7.1). Other northern, central and eastern European countries

also had high rates, between 5 and 7/100 000. France, Italy, Spain and Greece had lower rates (4.5–3.5/100 000). The EU overall had a higher ovarian cancer mortality rate (5.2) than the USA, Canada (4.9) and Australia (4.3). Most Latin American countries had rates below 4/100 000, similarly to Japan (3.2/100 000) and other Asian countries. Further country-specific comments are given in the supplementary Appendix, available at *Annals of Oncology* online.

Figure 2 and supplementary Appendix Table SA2, available at *Annals of Oncology* online, display the joinpoint analysis results for ovarian cancer mortality trends at all ages in 20 selected larger countries worldwide between 1970 and 2012. The EU shows an unfavourable significant trend (+0.9 APC) up to the 1990s, and a descending significant trend thereafter (–1.1 APC). Figure 3 gives the results for joinpoint analysis on rates for the four considered age groups (all ages, 20–49, 50–69 and 70–79 years) in the EU, the USA and Japan. US rates were downwards throughout the studied period with the exception of the 70–79 age group showing a rising trend (1.3 APC) between 1979 and 1992, and a subsequent decline.

Figure 4 gives the overall ovarian cancer mortality predicted to 2020 for selected major countries. All of these, except Spain, which however had one of the lowest rates, showed favourable predicted trends. The overall predicted decline is ~15% in the USA, to 3.9/100 000, 10% in Japan to 2.9/100 000 and ~10% in the EU, to 4.8/100 000. Within Europe, the predicted decline is larger in the UK, and similar across other countries, except Spain.

discussion

The present global report shows the persistence of falls in ovarian cancer mortality over the last decade in Europe and North America. The falls were larger at young and middle age, while death rates were approximately stable in the old in Europe, but declined in North America. Still, in 2012, there was an over twofold difference between the high mortality areas of central and northern Europe—with overall ovarian cancer rates over 6/100 000—and the low mortality ones—around or below 3/100 000—in Asia and South America. In young women (20–49), however, ovarian cancer rates were higher in Japan than in the EU and USA. For some of these countries, problems with death certification coverage and validity may partly account for their low rates, but this cannot explain the low rates in Korea, Japan or Argentina, whose death certification is considered reasonably valid [22, 23].

In the late 1990s, there was an about threefold variation in ovarian cancer rates across Europe (from 3.6 in Portugal to 9.3 in Denmark) [5], which has reduced over recent years. The largest western European countries have rates between 3.7 and 5.9/100 000. The recent favourable trends in ovarian cancer mortality in North America and Europe can be partly or largely attributed to the long-term protection of OC on ovarian cancer risk and recent declines in menopausal hormonal therapy use [6, 7, 24]. Indeed, the falls are larger in countries of northern Europe and in the USA, where OC use was earlier and more widespread [6, 25]. In the USA and UK, rates were appreciably downwards in 70–79 years old women as well [26]. These women born in 1930s and early 1940s were the first generation to use OCs frequently.

Table 1. Age-standardised (world population) mortality rates per 100 000 women from ovarian cancer at all ages and at ages 20–49, 50–69 and 70–79 in 46 selected countries worldwide and the EU as a whole around 2002 (2000–2004), 2007 (2005–2009) and in 2012 (unless indicated in parentheses), and corresponding change in rates

	All ages				20–49 years				50–69 years				70–79 years			
	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)
Europe																
EU (28) (2011)	5.76	5.40	5.19	–9.9	2.03	1.76	1.59	–21.7	20.26	18.94	18.09	–10.7	39.55	38.59	38.69	–2.2
Austria	5.98	5.24	4.89	–18.2	1.66	1.32	1.32	–20.5	19.39	17.26	15.04	–22.4	49.17	43.06	45.42	–7.6
Belgium	5.90	5.38	4.66	–21.0	1.59	1.50	1.04	–34.6	20.01	17.82	14.80	–26.0	45.26	43.14	40.56	–10.4
Bulgaria	4.77	5.79	6.09	27.7	2.71	3.25	3.22	18.8	16.72	20.38	21.56	28.9	26.30	32.07	32.23	22.5
Croatia	6.45	6.42	6.14	–4.8	3.41	3.11	2.66	–22.0	20.32	21.59	20.82	2.5	45.90	40.70	40.07	–12.7
Czech Republic	7.75	6.85	6.29	–18.8	3.04	2.49	1.39	–54.3	27.12	24.58	23.73	–12.5	51.22	45.27	48.75	–4.8
Denmark	8.37	6.85	6.31	–24.6	2.42	1.50	1.41	–41.7	29.84	24.82	22.79	–23.6	66.62	55.63	46.05	–30.9
Estonia	7.95	7.01	5.67	–28.7	3.44	2.82	2.01	–41.6	29.62	22.88	20.15	–32.0	42.09	50.91	39.85	–5.3
Finland	5.49	5.31	5.30	–3.5	1.78	1.33	1.37	–23.0	19.30	18.47	16.25	–15.8	39.20	42.61	53.53	36.6
France (2011)	5.15	4.72	4.47	–13.2	1.57	1.28	1.12	–28.7	18.06	16.29	15.07	–16.6	36.93	36.22	36.69	–0.6
Germany	5.90	5.33	5.07	–14.1	1.68	1.48	1.47	–12.5	19.94	17.78	16.34	–18.1	46.05	43.12	43.22	–6.1
Greece	3.94	4.10	3.50	–11.2	1.57	1.57	1.26	–19.7	13.27	13.69	12.47	–6.0	26.32	27.43	22.09	–16.1
Hungary	6.25	5.90	6.21	–0.6	2.61	2.26	2.73	4.6	21.85	20.81	21.30	–2.5	38.83	39.90	41.79	7.6
Ireland	8.17	7.77	7.09	–13.2	2.15	1.95	1.87	–13.0	28.94	27.71	22.45	–22.4	64.77	62.98	59.10	–8.8
Italy	4.43	4.42	4.25	–4.1	1.68	1.56	1.53	–8.9	15.45	15.45	14.56	–5.8	29.18	30.39	30.46	4.4
Latvia	7.61	8.13	6.64	–12.7	3.34	3.67	2.47	–26.0	27.66	29.84	22.49	–18.7	45.05	44.37	48.07	6.7
Lithuania	8.21	7.64	7.10	–13.5	4.08	3.63	2.82	–30.9	28.15	27.36	26.82	–4.7	49.24	43.21	39.86	–19.0
The Netherlands	5.99	5.74	5.54	–7.5	1.61	1.55	1.37	–14.9	20.56	19.57	17.92	–12.8	46.28	44.06	52.36	13.1
Poland	6.98	7.11	6.45	–7.6	3.33	2.97	2.55	–23.4	25.81	26.40	23.66	–8.3	38.59	42.74	41.22	6.8
Portugal	3.35	3.14	3.03	–9.6	1.50	1.14	1.19	–20.7	11.21	10.68	10.07	–10.2	22.61	23.01	21.56	–4.6
Romania	5.16	5.11	4.77	–7.6	2.92	2.59	1.90	–34.9	18.47	18.68	17.82	–3.5	27.67	28.04	29.01	4.8
Slovakia	6.68	6.36	6.10	–8.7	2.91	2.88	2.08	–28.5	24.31	22.23	20.46	–15.8	41.11	39.38	47.85	16.4
Slovenia (2010)	6.58	6.56	6.19	–5.9	2.28	1.99	2.39	4.8	24.19	22.91	19.58	–19.1	42.76	52.07	42.96	0.5
Spain	4.16	3.92	3.69	–11.3	1.71	1.48	1.57	–8.2	14.61	13.72	12.48	–14.6	26.50	26.80	24.40	–7.9
Sweden	6.93	6.11	5.30	–23.5	1.97	1.78	1.38	–29.9	25.63	21.52	18.15	–29.2	51.06	46.76	43.38	–15.0
UK	7.51	6.63	5.86	–22.0	2.00	1.64	1.63	–18.5	27.69	23.55	19.52	–29.5	54.60	52.43	48.35	–11.4
Israel	5.60	4.98	5.21	–7.0	1.82	1.47	1.26	–30.8	19.54	16.96	18.22	–6.8	40.11	38.14	43.54	8.6
Belarus (2011)	5.95	5.18	4.62	–22.4	3.09	2.80	2.43	–21.4	22.31	19.16	17.05	–23.6	30.94	27.73	25.47	–17.7
Norway	7.21	6.92	6.35	–11.9	1.94	1.84	1.57	–19.1	26.96	25.80	21.91	–18.7	50.59	46.32	47.18	–6.7
Russian Federation (2011)	5.86	5.77	5.51	–6.0	3.12	3.00	2.93	–6.1	21.43	21.22	20.03	–6.5	31.11	30.39	29.97	–3.7
Switzerland	5.34	5.10	4.28	–19.9	1.35	1.08	0.85	–37.0	17.50	17.49	13.34	–23.8	45.79	44.58	40.91	–10.7
Ukraine	.	5.71	5.60	.	.	3.61	3.22	.	.	21.20	20.83	.	.	24.13	27.83	.
Americas																
Canada (2011)	5.42	5.03	4.95	–8.7	1.58	1.34	1.32	–16.5	18.41	17.44	17.60	–4.4	41.94	38.43	35.02	–16.5
USA	5.76	5.29	4.85	–15.8	1.72	1.44	1.23	–28.5	19.68	18.14	17.30	–12.1	44.30	41.68	36.51	–17.6
Argentina	4.07	4.08	3.79	–6.9	1.78	1.82	1.75	–1.7	13.93	14.13	13.01	–6.6	27.03	25.20	22.63	–16.3
Brazil	2.65	2.77	2.80	5.7	1.20	1.27	1.33	10.8	8.90	9.03	9.32	4.7	17.18	18.28	16.81	–2.2

Continued

Table 1. Continued

	All ages				20–49 years				50–69 years				70–79 years			
	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)	2002	2007	2012	% change (2012/2002)
Chile	3.73	3.40	3.33	−10.7	1.75	1.58	1.19	−32.0	13.18	11.89	12.48	−5.3	21.50	20.21	20.27	−5.7
Colombia	2.98	3.33	3.27	9.7	1.49	1.55	1.45	−2.7	10.19	11.08	10.86	6.6	17.25	22.52	21.51	24.7
Cuba	2.82	2.93	3.07	8.9	1.61	1.69	1.78	10.6	9.78	9.68	9.55	−2.4	13.88	15.48	18.16	30.8
Mexico	3.17	3.21	3.28	3.5	1.69	1.76	1.93	14.2	10.54	10.52	10.99	4.3	18.07	18.78	16.99	−6.0
Uruguay	4.39	4.36	4.30	−2.1	1.87	2.21	1.37	−26.7	15.29	14.48	15.75	3.0	28.74	27.92	29.24	1.7
Venezuela	3.24	3.34	3.42	5.6	1.77	1.81	1.58	−10.7	10.37	10.93	11.37	9.6	18.18	18.68	20.27	11.5
Asia, Australia and Oceania																
Hong Kong SAR	2.64	2.53	2.46	−6.8	1.51	1.49	1.66	9.9	8.24	8.43	6.75	−18.1	17.29	12.81	16.86	−2.5
Japan	3.30	3.28	3.23	−2.1	1.98	1.87	1.91	−3.5	11.41	11.64	11.63	1.9	14.81	14.49	12.94	−12.6
Republic of Korea	2.13	2.31	2.26	6.1	1.08	1.18	1.22	13.0	7.15	7.61	7.58	6.0	12.52	13.95	11.75	−6.2
Australia (2011)	4.84	4.34	4.27	−11.8	1.35	1.15	1.09	−19.3	16.44	14.58	14.29	−13.1	38.19	33.81	34.25	−10.3
New Zealand (2011)	5.61	5.53	4.93	−12.1	1.52	1.48	1.12	−26.3	19.68	19.07	16.70	−15.1	42.13	41.93	42.04	−0.2

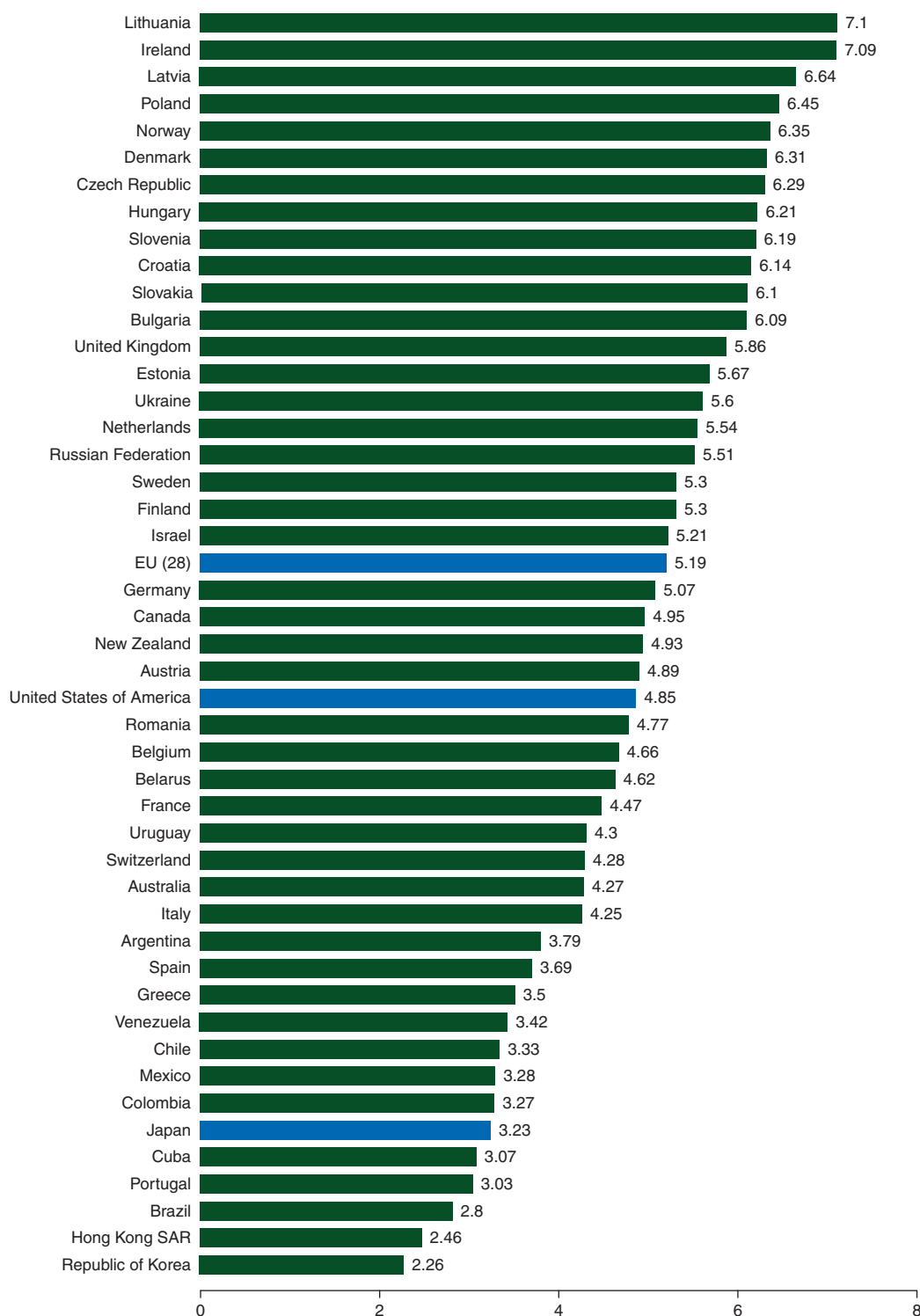


Figure 1. Age-standardised (world population) death certification rates from ovarian cancer from 46 selected countries worldwide and the EU as a whole, 2012.

A recent decrease in menopause hormone use—a recognised risk factor [25, 27–30]—after the Women’s Health Initiative report in 2002 [31] may also partly explain the fall in rates for middle aged and elderly women in countries like Germany, the UK or the USA, where the use of menopausal hormones was more common [24, 28, 31]. Part of the falls in these countries

may be due to the fact that they had the highest ovarian cancer rates in the past and—as for breast [32], or colorectal [33] cancer—mortality rates tend to level off across Europe.

Delays in the adoption of recent advancements in diagnosis and management may have unfavourably affected mortality in central and eastern European countries in ovarian as other

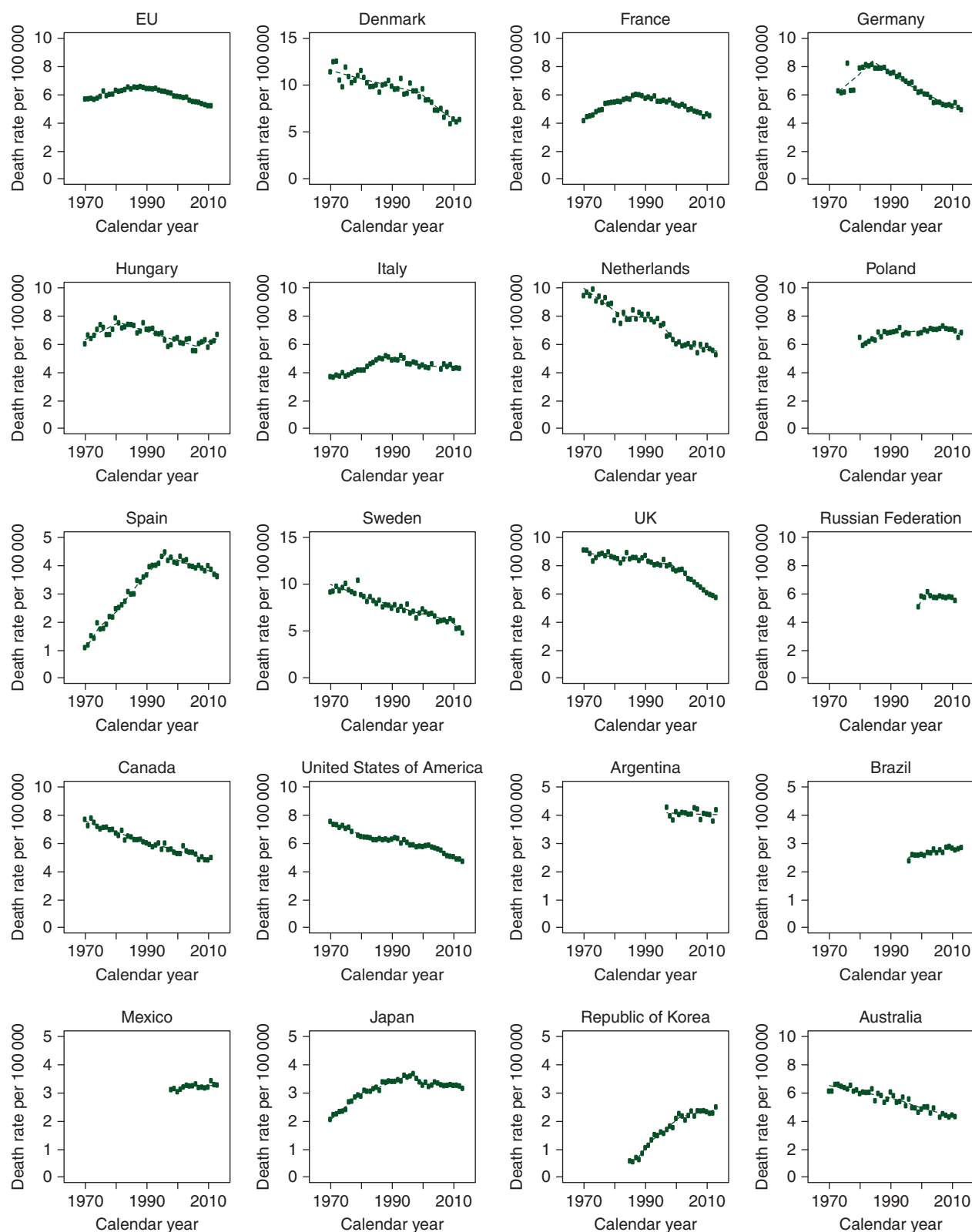


Figure 2. Joinpoint analysis for all ages ovarian cancer mortality in 19 selected countries and the EU as a whole, 1970–2013.

cancers [9]. Recent improvements in ovarian cancer management are however likely limited, apart from advancements in the treatment of ovarian germ cell tumours, which account for

<10% of all ovarian cancers [34]. It is difficult, to explain the persisting high rates in central and eastern Europe. Fertility has been relatively low in that area over the last decades, and parity

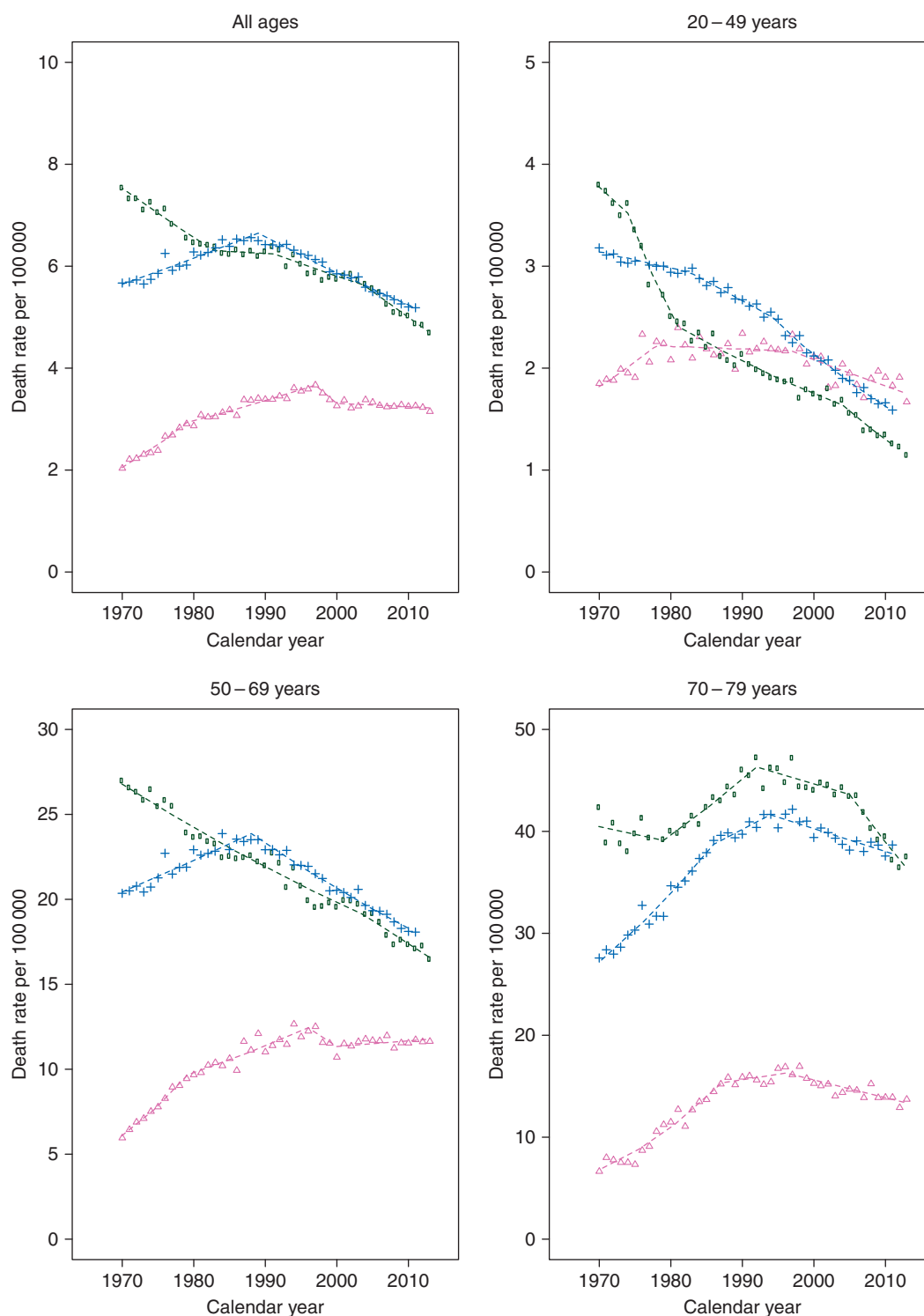


Figure 3. Joinpoint analysis for ovarian cancer mortality in the USA (circles), EU (crosses) and Japan (triangles) for the all ages, 20–49, 50–69 and 70–79 years age groups, in the 1970–2013 period.

and breastfeeding are protective on ovarian cancer risk [8, 35, 36]. However, differences in fertility across Europe [37] hardly explain the substantial differences.

Other environmental factors, including obesity [38] and diet [39], have been related to ovarian cancer risk. The quantification of their effect on national mortality rates remains undefined.

It is also difficult to explain the low rates in Japan and Korea. Diet and leanness in the past [38, 39] may partly account for them, but parity and OC use were relatively low in those countries. Thus, hormonal and reproductive features cannot account for their low rates. Recent trends in these countries have not been declining appreciably, suggesting a future global levelling of ovarian

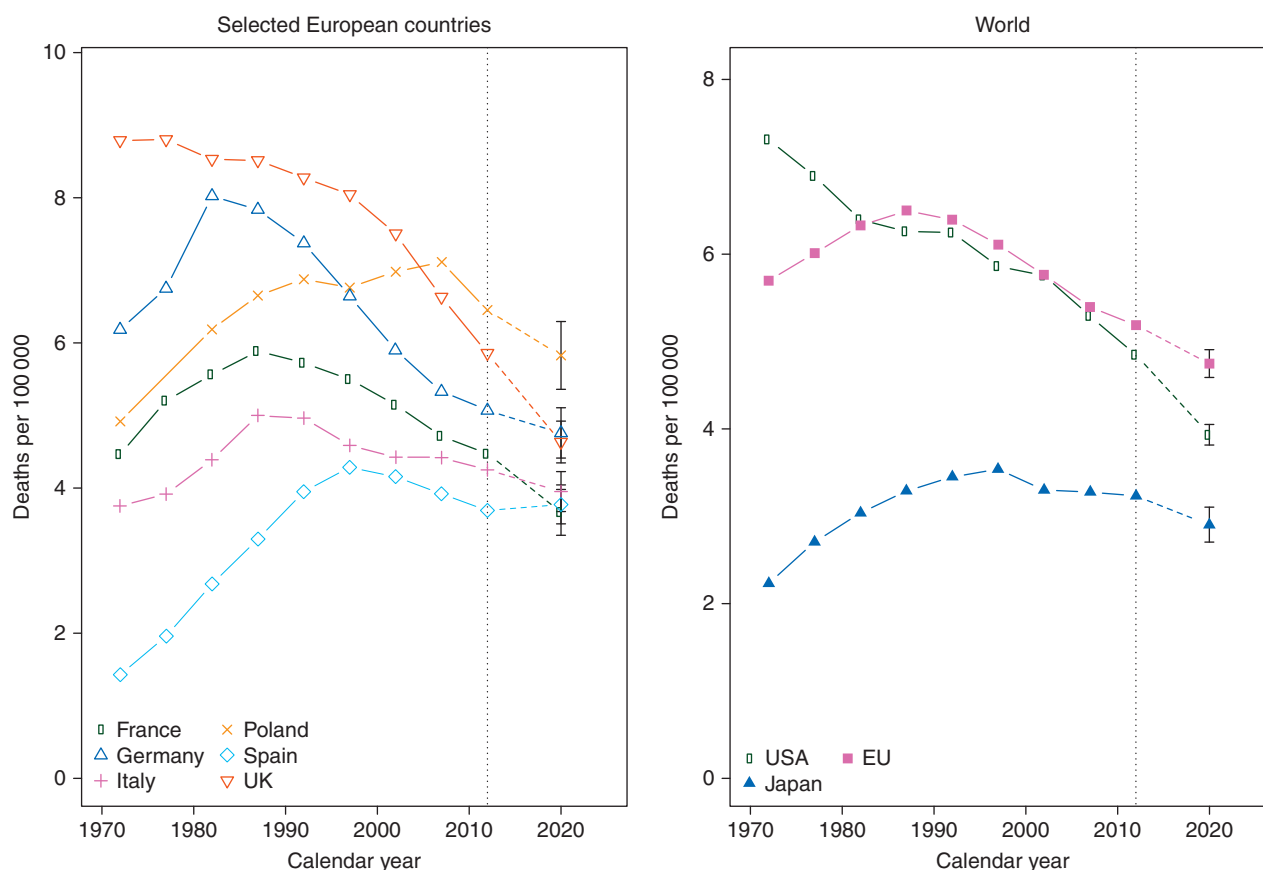


Figure 4. Age-standardised (world population) quinquennial ovarian cancer death rates in eight countries worldwide and the EU as a whole in 1972–2012, and predicted rates to 2020.

cancer mortality, as confirmed by the recent rates higher in young Japanese women compared with western countries.

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disclosure

The authors have declared no conflicts of interest.

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No 'cure' within 12 years of diagnosis among breast cancer patients who are diagnosed via mammographic screening: women diagnosed in the West Midlands region of England 1989–2011

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Background: We have previously reported that there is little evidence of population 'cure' among two populations of women diagnosed with invasive breast cancer. 'Cure' has not yet been examined in the context of screen-detection.

Patients and methods: We examined cancer registry data on 19 800 women aged 50–70, diagnosed with a primary, invasive, non-metastatic breast cancer between 1 April 1989 and 31 March 2011 in the West Midlands region of England, linked to Hospital Episode Statistics (HES) and the National Breast Screening Service (NBSS). Follow-up was complete on all women up to 31 July 2012. Analyses were stratified by screening status, age, tumour stage, deprivation and

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