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Age-specific cancer mortality trends in 16 countries

Lee Liu · Kristen Liu

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Abstract

Objectives This study explored previously little-known cancer mortality trends with a focus on changes with age and sex differences in 16 countries.

Methods Time series age–sex-specific cancer mortality, deaths from all causes, and population data were used for statistical description.

Results The cancer mortality rate (CMR) peaked and declined with age in 11 countries. CMRs appeared to peak earlier and decline more dramatically in earlier time periods rather than later periods and for males rather than females. CMR peaking could have possibly been historically delayed. Moreover, "percentage of deaths from cancer" (PDC) in all 16 countries plunged after about age 60. Middle-aged women may have higher CMRs than men. Premenopausal women may have higher PDCs than postmenopausal women.

Conclusions The findings make significant contributions to the literature, though their interpretation and application have limitations due to data quality and availability. Future research should explore if and how the findings apply to other countries and time periods. Public health practitioners and policy makers should consider age–sex-specific strategies for more effective cancer control.

L. Liu (✉)
Geography Program, School of Environmental, Physical and Applied Sciences, University of Central Missouri, Humphreys 225, Warrensburg, MO 64093, USA
e-mail: laliu@ucmo.edu; liulee2007@hotmail.com

K. Liu
Independent Scholar, 1210 E. 54th St., Chicago, IL 60615, USA

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Introduction

Cancer is a leading cause of death and a major global public health problem, resulting in 8.2 million deaths in 2012 (Torre et al. 2015). Recent papers have examined global cancer mortality trends to enhance epidemiological advances (Althuis et al. 2005; Hirte et al. 2007; Leung et al. 2011), inform health policy (Coleman et al. 2011), provide a key insight into the overall effectiveness of the health system (Quaresma et al. 2014), and reduce cancer burden worldwide (Jemal et al. 2011; Siegel et al. 2015; Torre et al. 2015). Earlier studies suggest that cancer mortality rate (CMR) increases exponentially with age, but the increase may eventually decelerate (Finkel et al. 2007; Balducci and Ershler 2005; Andersen et al. 2005; Frank 2007; Yang et al. 2012). Smith (1996) reported that CMR peaked in populations aged 90 years based on the 1990 US data, while Harding et al. (2012) found CMR declines in the oldest old in 1998–2002 based on 9.5 % of the US population. Some studies have also found cancer mortality declines in terms of percent of deaths from cancer (PDC), as compared to deaths from all causes, among the very elderly in the United States (Stanta et al. 1997) and the Netherlands (de Rijke et al. 2001). However, researchers are still unable to determine if most countries experienced CMR declines with age (Harding et al. 2012). Ultimately, the intrinsic complexity of aging and cancer requires widening research to understand the links between the two (de Magalhães 2013).

Studies have also found that women are less likely than men to die of cancer (Cook et al. 2011; OuYang et al.

2015; Qu et al. 2015). The biological, environmental, and behavioral causes of such a "female advantage" are largely contested (Yang et al. 2012; OuYang et al. 2015). The controversial "estrogenic hypothesis" suggests that the female hormone enhances the survival of premenopausal women (OuYang et al. 2015; Qu et al. 2015). However, other researchers disagree and stress the lack of knowledge about the relationship between cancer mortality and population aging (Finkel et al. 2007). There is also disagreement on women's mortality advantage in female–male health-survival paradox (Van Oyen et al. 2013; Dix 2014). As cancer research has expanded, papers have also explored how cancer mortality is associated with social and environmental factors. For example, socioeconomic inequalities were found to be associated with cancer mortality (Jasilionis et al. 2015) while unemployment and government healthcare expenditure were associated with colorectal cancer mortality in the European Union (Maruthappu et al. 2016).

Despite the significant achievements reviewed above, the literature still lacks international studies on CMR declines with age (Harding et al. 2012). PDC has not been used often as a tool to explore cancer mortality changes with age in most countries. This study attempted to fill in the gaps by exploring previously little-known international trends in cancer mortality. It used data from 16 countries with attention to the oldest old and premenopausal women. Our specific research objectives were to explore in the 16 countries (1) what the similarities and differences were in CMR changes with age, (2) how PDCs, used as an indicator, could help further uncover cancer mortality changes with age, and (3) if premenopausal women in all age groups had an advantage in cancer mortality.

Methods

Criteria for inclusion of countries

The study intended to include as many countries as possible, while preferring larger populations and longer time series data to ensure trend regularities. Thus, the selection was limited by the unavailability of matching age–sex-specific population, death, and cancer mortality data capped above age 85 years. For example, no such data were available for some large populations such as China, India, or Indonesia. Canada and Australia appeared to be the only countries offering custom services for ordering unpublished data. Eventually, data for 16 countries were selected for the research, with Sweden as the smallest population (9.63 million in 2014).

Operational definitions

The study regards persons aged 85 years and over as the oldest old and persons aged 65–84 as the old, following the US Census Bureau (Ortman et al. 2014). Premenopausal women refers to women before age 45 and postmenopausal women are those aged 55 and over (OuYang et al. 2015). Death data were from death of all causes (ICD-10) while deaths under "age not stated" were excluded in the 5-year age-specific data. Cancer refers to malignant neoplasms (ICD C00–C97) in the cause of death statistics, with some variation for Australia and Japan. Australia uses all cancer combined (C00–C97, D45–D46, D47.1, and D47.3); separate C00–C97 data were unavailable. Though D45–D46, D47.1, and D47.3 cancers contribute to a small fraction of all cancer deaths, caution is still needed when comparing Australia with other countries. The ICD Code used for cancer in Japan was 140–205 for the years of 1958–1967, 140–209 for 1968–1978, 140–208 for 1979–1994, and C00–C97 for 1995–2013.

CMR was a crude rather than an age-standardized rate which was unavailable for age-specific data for the countries. The actual number of deaths was used to derive the PDCs. PDCs reflect the relationship between cancer mortality and deaths from all causes and help to highlight the relative importance of cancer mortality in public health. PDC as a cancer mortality indicator has been used in many cancer statistics reports, such as USCDC (2014a, c) and Cancer Research UK (2015), and papers on global or national cancer mortality trends, though different terms may have been used (e.g. Siegel et al. 2015). PDCs have also been used as an indicator of cancer mortality declines by Smith (1996), Stanta et al. (1997) and de Rijke et al. (2001). To measure sex differences, this study uses female-to-male CMR ratios (FMCMRRs) and female-to-male PDC ratios (FMPDCRs). A ratio value below 1 indicates a female advantage and a value above 1 suggests a female disadvantage as compared to male.

Data collection and management

We calculated CMRs and PDCs in the 16 countries based on age-specific data collected from national government offices and the World Health Organization (WHO) (Table 1). To examine CMR changes in the oldest old, we made special effort to obtain data capped at 100 years of age or as old as possible. The desire to use such data reduced data availability. As a result, country-specific data vary by number of calendar years. The time period ranged from 5 years for England and Wales to 56 years for Japan.

In addition to information presented in Table 1, some data require further explanation. For Australia, data on

Table 1 Data description, output, and sources for the 16 countries

Country	Data types, (capped age), years	Output: CMR, PDC, FMCMRR, FMPDCR	Source
Australia	All age ≥85 (100) 1968–2012	CMR 1971–2012; the others 1968–2012	AIHW (2015a)
Australia	Death (85) 1968–2012	PDC, FMPDCR	AIHW (2015b)
Australia	Cancer (85) 1968–2012	FMCMRR	AIHW (2015c)
Belgium	All (95) 1998–2012	All	WHO (2015)
Canada	All (90) 2000–2011	All	Statistics Canada (2015a)
Canada	All over age 89 (100) 2000–2011	All	Statistics Canada (2015b)
England and Wales, UK	All (95), 2009–2013	All	UKONS (2014)
France	Death (95), population (85), 2000–2011	All	WHO (2015)
Germany	All (95) 1998–2012	CMR 2010–2011; the others 1998–2012	WHO (2015)
Italy	Death (95) 2003, 2006–2010; population (95) 2003, 2006, 2008	CMR 2003, 2006, 2008; the others 2003, 2006–2010	WHO (2015)
Japan	Cancer (85) 1958–2013	CMR, FMCMRR	NCC, Japan (2015)
Japan	Death (85) 1958–2013	PDC, FMPDCR	PSOSJ (2015a)
Japan	Population (100) 2010–2012	CMR	Statistics Japan (2015)
Japan	Death (100) 2010–2012	CMR	PSOSJ (2015b)
Japan	All (95) 2005–2009	CMR	WHO (2015)
Poland	Death (95) 1999–2012; population (95) 2003–2006, 2010–2012	CMR 2003–2006, 2010–2012; the others 1999–2012	WHO (2015)
Portugal	Death (85), population (85), 2002–2003, 2007–2012	All	WHO (2015)
Romania	Death (95) 1999–2013; population (95) 2001–2010	CMR 2001–2010; the others 1999–2012	WHO (2015)
South Korea	Death (95) 1995–2012; population (95) 2000–2012	CMR 2000–2012; the others 1995–2012	WHO (2015)
Spain	All (95) 1999–2012	All	WHO (2015)
Sweden	Death (95) 1997–2012; population (95) 2001–2012	CMR 2001–2012; the others 1997–2012	WHO (2015)
The Netherlands	All (95) 2000–2012	All	WHO (2015)
The United States	Death (100) 2013	All	USCDC (2014a)
The United States	Population (100) 2013	All	US Census Bureau (2015)
The United States	Cancer (85) 1999–2011	All	USCDC (2014b)
The United States	Death (85) 1999–2011	All	USCDC (2014c)

Output: *CMR* cancer mortality rate, *PDC* percent of deaths from cancer, *FMCMRR* female-to-male cancer mortality rate ratio, *FMPDCR* female-to-male percent of deaths from cancer ratio

population and number of all deaths and cancer deaths for ages above 84 were purchased from the Australia Institute of Health and Welfare (AIHW) (2015a) for the years 1968–2012. However, the population data were capped at age 85 for the years 1968–1970. As a result, the 1971–2012 data capped at age 100 were used to study CMR declines while the 1968–2012 data were used for the other indicators. For England and Wales, each year's death data were downloaded from different tables in the source. The age–sex-specific data from the 2011 Population Census were used to calculate CMRs for 2009–2013. This was considered not ideal but acceptable since the census year was in the middle of the 5-year period. Population data capped over age 85 were unavailable from other sources. The same 2009–2013 data were used to derive the other indicators. For Germany, the 1999 population data were used to substitute for the missing 1998 population data to obtain the time series data on 1998–2012 rates. For the United States, the 2013 data were obtained from the USCDC (2014a). The death rate data were capped at age 85, while the number of death data were capped at age 100. Age-specific data for population aged 85 and over were obtained from US Census Bureau (2015). Using both data sources, CMRs in the oldest old were calculated. The 2013 CMR were used to show CMR decline. The 1999–2011 cancer data (capped at age 85) and death data were combined with the 2013 data to derive the other indicators.

Statistical analysis

In this study, statistical description was used for data analyses. Country time series data were analyzed to derive age–sex-specific means of CMRs, PDCs, FMCMRRs, and FMPDCRs. The means were examined to detect trends. Special attention was paid to peak levels and the declines afterwards. To explore CMR trends in the 16 countries, CMR means were first examined for the whole time period for which data were available. If no declines were present, additional analyses explored if declines were evident for individual years, certain time periods, or certain sex. Means of CMRs for multiple years were used instead of individual years to enhance data reliability due to possible CMR fluctuation, particularly for smaller populations. For Japan and Australia, data were available for over 40 years. Further analyses were done for different periods to explore if earlier years had trends different from later years. Furthermore, the data were graphed to enhance the description of trends.

Results

Cancer mortality rates declined with age in 11 of the 16 countries

Eleven of the 16 countries experienced substantial CMR declines with age for at least selective years and sex (Table 2). For Australia, the 19.3 % decline for 1971–2012 was lower than declines in each individual decade. This was because the peaked ages 95–99 for 1971–2012 CMRs were not the peaked ages for all individual decades. That consequently lowered the peak value at ages 95–99 for 1971–2012. No Japanese CMR declines with age were detected in the means for the whole period 1958–2013 (data capped at age 85). However, declines with age did happen in 1958–1984. Japan actually provided the earliest evidence of CMR decline with age. Individuals aged 85 and over were 29.5 % less likely to die of cancer than those aged 75–79 in the years 1958–1972 (Table 1).

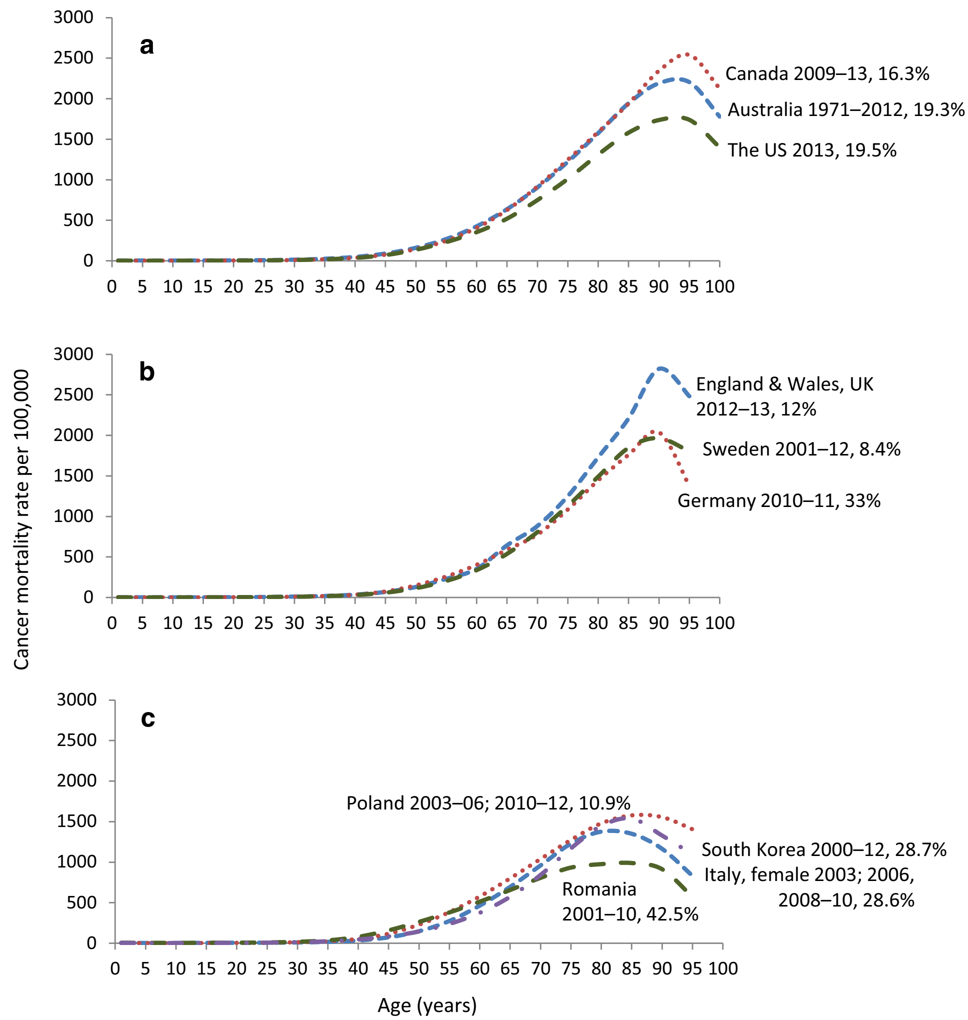
Cancer mortality rate declines with age differed by countries, time periods, and sexes

CMR trends varied among the 11 countries and multiple periods for Australia and Japan (Table 1). The CMRs peaked from 75–79 years old for Japan during 1958–1972 to 95–99 years old in some other cases. The largest CMR decline was 36.6 % from ages 90–94 to ages 100 and over in the years 1971–1980 in Australia. Figure 1 further illustrates the CMR declines in ten of the 11 countries, which were grouped by their geographic location, culture, and CMR peaking ages. CMRs among the countries were similar before age 40 but increasingly varied as the ages increased. Australia, Canada, and the United States all had their CMR peak at ages 95–99 with declines at similar rates, though their CMRs varied (Table 2; Fig. 1a). CMRs in England and Wales, Germany, and Sweden all peaked at ages 90–94 (Table 2; Fig. 1b). The peak years ranged from

Table 2 Cancer mortality rates (CMRs), peaks, and declines in the old population in 11 countries

Country	Period	Peak age group	Oldest age group	Peak CMR	Oldest age group CMR	Decline %
Australia	1971–2012	95–99	100+	2204	1780	19.3
Australia	2001–2012	95–99	100+	2442	1922	21.3
Australia	1991–2000	90–94	100+	2195	1717	21.8
Australia	1981–1990	90–94	100+	1971	1543	21.7
Australia	1971–1980	90–94	100+	1794	1137	36.6
Canada	2009–2013	95–99	100+	2541	2127	16.3
England and Wales, UK	2012–2013	90–94	95+	2820	2483	12
Germany	2010–2011	90–94	95+	2039	1374	33
Italy	2003, 2006, 2008–2010	80–84	95+	1377	832	28.6
Japan	2010–2012	95–99	100+	2425	2162	10.9
Japan	2005–2009	90–94	95+	2095	2054	2
Japan	1973–1984	80–84	85+	1261	1132	10.2
Japan	1958–1972	75–79	85+	978	689	29.5
Poland	2003–2006, 2010–2012	85–89	95+	1578	1406	10.9
Romania	2001–2010	85–89	95+	990	569	42.5
South Korea	2000–2012	85–89	95+	1538	1097	28.7
Sweden	2001–2012	90–94	95+	1966	1800	8.4
United States	2013	95–99	100+	1740	1400	19.5

Fig. 1 Trends in ten countries where cancer mortality rates (CMR) eventually declined with age. The ages shown represent the starting years of each 5-year age group. The labels show country names, data years, and the associated CMR declines from peaks in percentages. Countries with the largest declines from peak years include 42.5 % in Romania, 33 % in Germany, and 28.7 % in South Korea. Romanians 95 years and over had a lower CMR than those aged 65–69 (color figure online)



ages 80–84 among Italian women to ages 85–89 in South Korea, Romania, and Poland (Table 2; Fig. 1c), where CMRs were lower at the peak and in the oldest age groups, as compared to the other countries (Fig. 1a, b).

In addition, CMRs appeared to peak earlier and lower while declining more dramatically for earlier years than later years for the two countries with the longest time series data (Table 2; Fig. 2). Japanese peak ages increased from 75–74 in 1973–1984 to 95–99 in 2010–2012. Peak rates increased over 150 % from 1973–1984 to 2010–2012 (Table 2; Fig. 2a). Japanese individual year data demonstrate a similar trend (Table 3). While CMRs peaked at ages 75–79 every year in 1958–1972, the declines became smaller from 39.2 % in 1958 to 17.2 % in 1972. Similarly, the declines shrank from 19.6 % in 1973 to 1.7 % in 1984, when CMRs peaked at ages 80–84. For Australia, CMRs declined considerably in each decade (Table 2; Fig. 2b).

Large sex differences were also present in cancer mortality trends. Men's CMRs all peaked higher, often over 100 % higher, than women's (Table 4). The highest peak was 4498/100,000 for men in England and Wales. Men's CMRs in the oldest age groups were also higher than women's, except in Germany. In the oldest age group, Canadian men had the highest CMR at 4315/100,000. CMRs also appeared to peak earlier and decline more dramatically for males than females, which was true in 12 out of the 17 cases in Table 4. The largest declines in male CMRs included 61 % in Germany, 56.5 % in Romania, and around 50 % in 1971–1990 Australia. For women, the largest declines were around 30 % in Romania and 1971–1980 Australia and a little over 20 % in South Korea and 1958–1972 Japan.

On the other hand, CMR peaks and declines were not found in the remaining five countries (Fig. 3). For Belgium, Spain, and the Netherlands, the exponential growth of CMRs eventually leveled off (Fig. 3a). However, no such leveling-off could be detected in France and Portugal, which shared a similar growth pattern in CMRs (Fig. 3b).

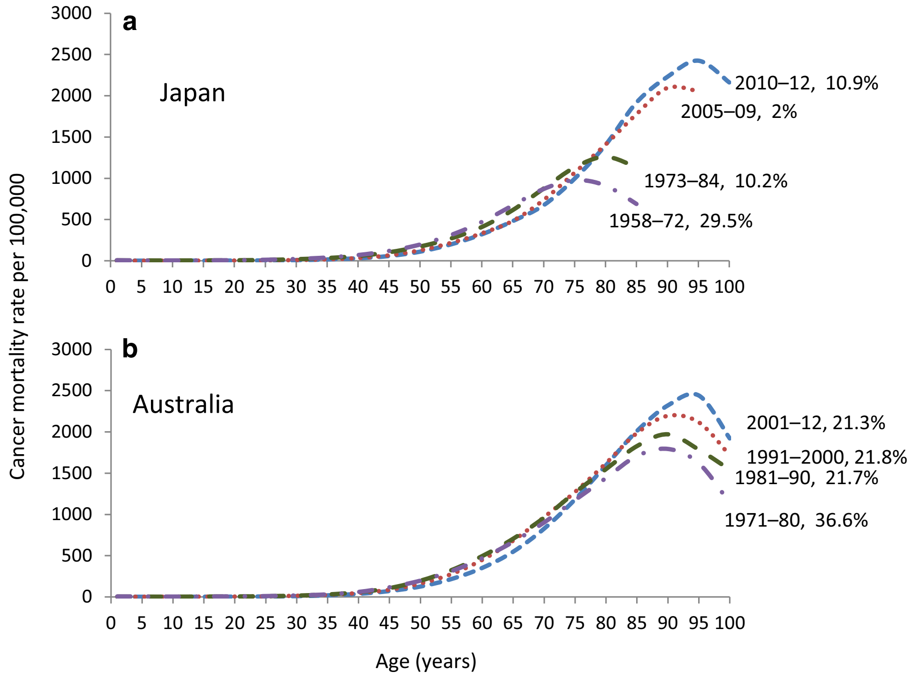


Fig. 2 Trends in **a** Japan and **b** Australia where cancer mortality rates (CMR) eventually declined with age in different time periods. The ages shown represent the starting years of each 5-year age group. The labels show data years and the associated rate declines from peaks in percentages. Japanese aged 85 years and over were less likely to die of cancer than those aged 70–74 in 1958–1972. There appears to be a historically delayed peaking in both countries (color figure online)

Table 3 Cancer mortality rate declines from peak years (ages 75–79 in 1958–1972 and ages 80–84 in 1973–1984) to the oldest age group (age ≥85), Japan

Year	From ages 75–79 to ≥85 (%)	Year	From ages 80–84 to ≥85 (%)
1958	39.2	1973	19.6
1959	36.4	1974	18.6
1960	31.1	1975	18.1
1961	36	1976	19.6
1962	33.2	1977	15.8
1963	32.2	1978	14
1964	33.4	1979	13.5
1965	34.2	1980	11.8
1966	32.6	1981	5.4
1967	31.2	1982	5.6
1968	29.6	1983	3.7
1969	27.9	1984	1.7
1970	27		
1971	24.1		
1972	17.2		

Percent of deaths from cancer provided a new perspective to cancer mortality trends

All 16 countries under study experienced a sharp decline in PDCs (Fig. 4a–d). They also shared a common trend: a small hill around ages 5–9 and peak between ages 55–69. Southern and Western Europeans and Canadians all had high PDC peaks (Fig. 4a–c). The highest peaks were in Italy, Spain, the Netherlands, France, and Canada, where half of all deaths were from cancer for population at the peaked ages. The US, Australia, the two East Asian and two Eastern European Countries appeared to have low peaks (Fig. 4c, d). Romania not only had the lowest peak PDC (31 %) but also the largest decline (93.5 %) to about 2 % in population aged 95 and over. South Korea, Canada, and Poland also experienced about 90 % PDC declines. PDCs in the capped age groups were also below 4.5 % in South Korea, Poland, and Australia. The smallest PDC decline was 56.4 % in the United States. These sharp PDC declines provide clear evidence of the diminishing contribution of cancer as a major cause of death starting around ages 60–74, depending on the country.

Premenopausal women did not have an advantage in cancer mortality rates

The trends of the FMCMRRs indicated an advantage for women (with a ratio below 1) in most age groups, particularly for postmenopausal women, as compared to men (Fig. 5a–d). However, premenopausal women did not have an advantage in all age groups and may be less advantageous than postmenopausal women. Middle-aged women in all 16 countries were disadvantageous in two–six age-groups from ages 25–29 up to the 40s and even 50s (with a ratio above 1). The highest ratios were found in Sweden and the Netherlands at 1.54 females to 1 male, and Canada at 1.46–1 (Fig. 5b, c). The lowest peaks were found in Portugal, in South Korea, Poland, and Spain (Fig. 5a, d).

Table 4 Sex differences in cancer mortality trends in ten countries

Country	Years	Sex	Peak age group	Oldest age group	Peak CMR	Oldest age group CMR	CMR decline %
Australia	1971–2012	Male	95–99	100+	3560	2322	34.8
Australia	1971–2012	Female	95–99	100+	1814	1640	9.6
Australia	2001–2012	Male	95–99	100+	4079	2555	37.4
Australia	2001–2012	Female	95–99	100+	1951	1759	9.86
Australia	1991–2000	Male	90–94	100+	3596	2506	30.31
Australia	1991–2000	Female	90–94	100+	1769	1530	13.53
Australia	1981–1990	Male	90–94	100+	3161	2478	51.07
Australia	1981–1990	Female	90–94	100+	1607	1599	4.05
Australia	1971–1980	Male	90–94	100+	2536	2304	48.94
Australia	1971–1980	Female	90–94	100+	1524	1415	29.26
Canada	2009–2013	Male	95–99	100+	4341	4315	0.58
Canada	2009–2013	Female	95–99	100+	2083	1786	14.25
England and Wales, UK	2012–2013	Male	90–94	95+	4498	4164	7.42
England and Wales, UK	2012–2013	Female	90–94	95+	2156	2041	5.35
Germany	2010–2011	Male	90–94	95+	2990	1167	61
Germany	2010–2011	Female	90–94	95+	1742	1464	16
Japan	2010–2012	Male	95–99	100+	4047	3931	2.9
Japan	2010–2012	Female	95–99	100+	2050	1890	7.8
Japan	1973–1984	Male	80–84	85+	1784	1637	8.2
Japan	1973–1984	Female	80–84	85+	939	892	5
Japan	1958–1972	Male	75–79	85+	1304	1225	27.7
Japan	1958–1972	Female	75–79	85+	751	735	22.4
Poland	2003–2006, 2010–2012	Male	8589	95+	2456	2412	10.6
Poland	2003–2006, 2010–2012	Female	85–89	95+	1288	1201	3.9
Romania	2001–2010	Male	85–89	95+	1367	1226	56.5
Romania	2001–2010	Female	85–89	95+	799	757	30.6
South Korea	2000–2012	Male	85–89	95+	2720	2490	18.8
South Korea	2000–2012	Female	85–89	95+	1108	1007	20.2
United States	2013	Male	95–99	100+	2665	2225	16.5
United States	2013	Female	95–99	100+	1442	1216	15.7

Peaking was between ages 30 and 39 for all countries except for England and Wales which peaked at ages 40–44 (Fig. 5c). After peaking, FMCMRRs declined to below 0.5 by age 60 in most countries. Men's CMRs for population aged 60 or over were higher than women's in all 16 countries, as illustrated with ratios below 1. On the other hand, the declines were not necessarily linear. Only Sweden, the United States, and Canada had the lowest FMCMRRs in the capped age groups (Fig. 5b, c).

Premenopausal women were disadvantageous in percent of deaths from cancer

FMPDCRs demonstrated greater risks in cancer mortality for women than FMCMRRs did (Fig. 6). Women were more likely than men to die of cancer as compared to other causes of death. This disadvantage existed from youth to the late 50s in South Korea, the 60s in Japan, Spain, Portugal, Romania, France, Italy, Belgium, the Netherlands, and Poland, and even the 70s in the US, Canada, England and Wales, Australia, and Sweden. The trends were very similar in the four Southern European countries (Fig. 6a) and the four English speaking countries (Fig. 6c). The peaks of FMPDCRs were 3.79 females to 1 male in Poland, 3.16–1 in Romania, and 2.97–1 in Portugal, indicating that women had about three times the risk that men had at the peak ages. The lowest peak values were found in Japan, the Netherlands, and South Korea. In the capped age groups, PDC ratios for all countries were below 0.75–1, indicating an advantage for older women.

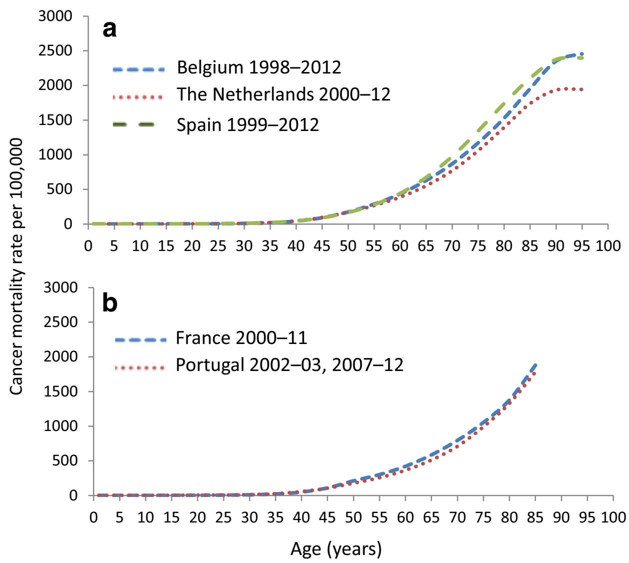


Fig. 3 Trends in countries where cancer mortality rates (CMRs) did not decline with age. The ages shown represent the starting years of each 5-year age group. The labels show country names and data years. **a** The three countries with eventual leveling-off in CMRs, with data capped at age 95. **b** The two countries with continued exponential growth with age, with data capped at age 85 (color figure online)

Discussion

Contributions to the literature

This is the first time that such CMR peaks and declines have been found in these countries, except for in the United States. Our US findings generally support earlier papers by Smith (1996) and Harding et al. (2012). Similar to de Rijke et al. (2001), we did not detect CMR declines in the Netherlands based on recent data. Furthermore, we identified differences in CMR trends by countries, time periods, and sexes. CMRs tended to peak in younger age groups in earlier time periods in Japan and Australia. Men's CMRs all peaked higher than women's.

Our findings indicate that the literature is incomplete on the exponential growth of CMRs and the eventual leveling-off of the growth. In a complete process, the exponential growth tends to be followed by a leveling-off, a peak, and then decline. We believe the availability of data on the oldest old was to blame for the incompleteness. Declining CMRs in the oldest old may usually be hidden when data are capped at age 85, which is a common practice. For example, if all data in Figs. 1 and 2 had been capped at age 85, we would not have detected declines in Germany, England and Wales, Australia (1971–2000), or Sweden. Australian (1971–2012), Canadian, and US declines would also have been concealed if data had been capped at age 95 (Fig. 1a). Harding et al. (2012) were unable to determine if CMRs peaked in most nations because the data were capped at age 85. In these situations, PDC could be used as an alternative or additional indicator of cancer mortality trends. PDCs for all ages are currently used to describe the burden of cancer, such as 24 % in the United States (Siegel et al. 2015) or 29 % in the UK (Cancer Research UK 2015). However, it is important to go beyond the conventional approach to measure age-specific PDCs.

Our PDC findings expand the studies by Stanta et al. (1997) and de Rijke et al. (2001). Additionally, we found that PDCs in the Netherlands declined to 6.72 % in the age 95+ years group. This is lower than what de Rijke et al. (2001) reported (11 % for men and 7 % for women). Moreover, it has been reported that the US censuses tend to overstate the population of the very elderly, potentially leading to CMR underestimation for this population group (Harding et al. 2012). Similar problems related to the availability and reliability of population data may be avoided by using PDCs as a cancer mortality indicator, since PDCs do not have to be based on population.

Unlike earlier reports, we demonstrated that middle-aged women had a disadvantage in CMRs, which persisted in two–six age-groups starting from age 25. Meanwhile, a female advantage in CMR existed in other age groups but was greatest in postmenopausal rather than premenopausal women. Furthermore, women were two to three times more disadvantageous than men in PDCs from youth to the late 50s or even the 70s, depending on the country. These findings contradict the literature on female advantage theory and the estrogenic hypothesis.

Limitations

The research was limited by the lack of data for many large populations and variable data periods for 16 large populations. Thus caution is needed when applying the findings to countries that the research did not cover. In addition, the data used in the research were obtained from different sources (Table 1) which may have used different data collection methods such as mortality registrations, censuses, and estimates. There were changes in coding over time in Japan and different coding of all cancers between Australia and other countries. Data collection methods may also have changed over time in the same country. This may have resulted in improved data quality and availability but led to uncertainties in cross-period comparisons. It was possible that the very elderly population in other countries had also been overstated, as reported in the US (Harding et al. 2012). Therefore, it should be emphasized that the data might be variable in quality. Precautions need to be undertaken when making cross-country and cross-period comparisons.

Despite these limitations, the data were the best available. Data for most of the countries were from the WHO, which employs different methods to enhance data

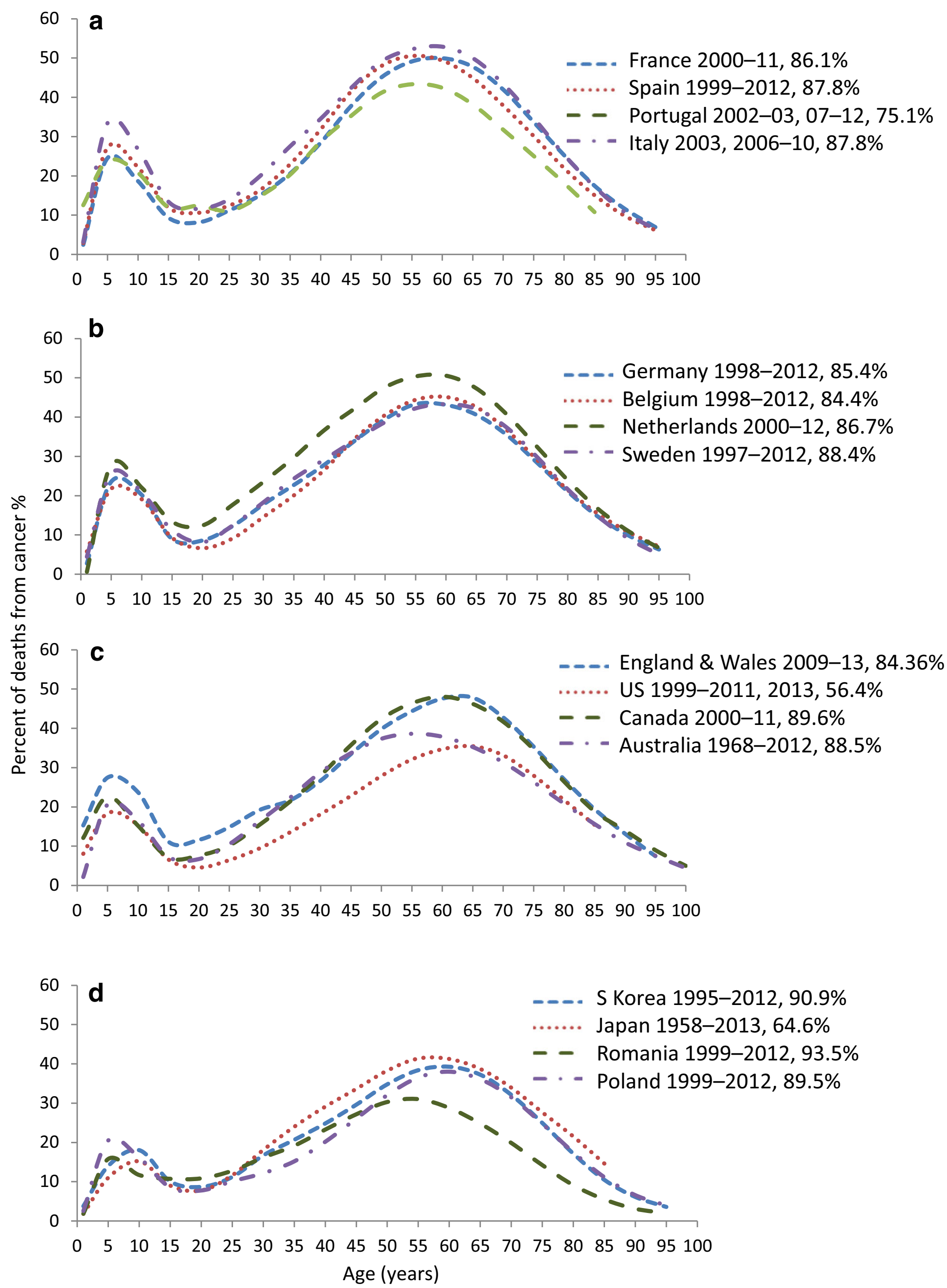


Fig. 4 Trends of age-specific percent of deaths from cancer in 16 countries. The ages shown represent the starting years of each 5-year age group. The labels show country names, data years, and the associated rate declines from peaks in percentages (color figure online)

accuracy, completeness, and comparability across countries in the published datasets (Bray et al. 2015). In addition, we mainly used means of time series data for individual countries to further enhance data accuracy and comparability. The results based on the data should provide a legitimate basis for further research and policy considerations for public health.

Future research

Important questions remain to be answered. Based on our findings, we would like to propose a hypothesis that other large populations have also experienced CMR peaks and declines with age and similar trends in PDCs, FMCMRRs, and FMPDCRs. Future research should test this hypothesis when data become available. PDCs should be used in further studies as an additional measurement of age-specific cancer mortality trends. FMCMRRs and FMPDCRs should also continue to be used to assess sex differences in age-specific cancer mortality. This paper should also encourage future research to explore the possible biological, environmental, and social causes for these trends. The results could also help further evaluate women's cancer mortality (dis)advantage.

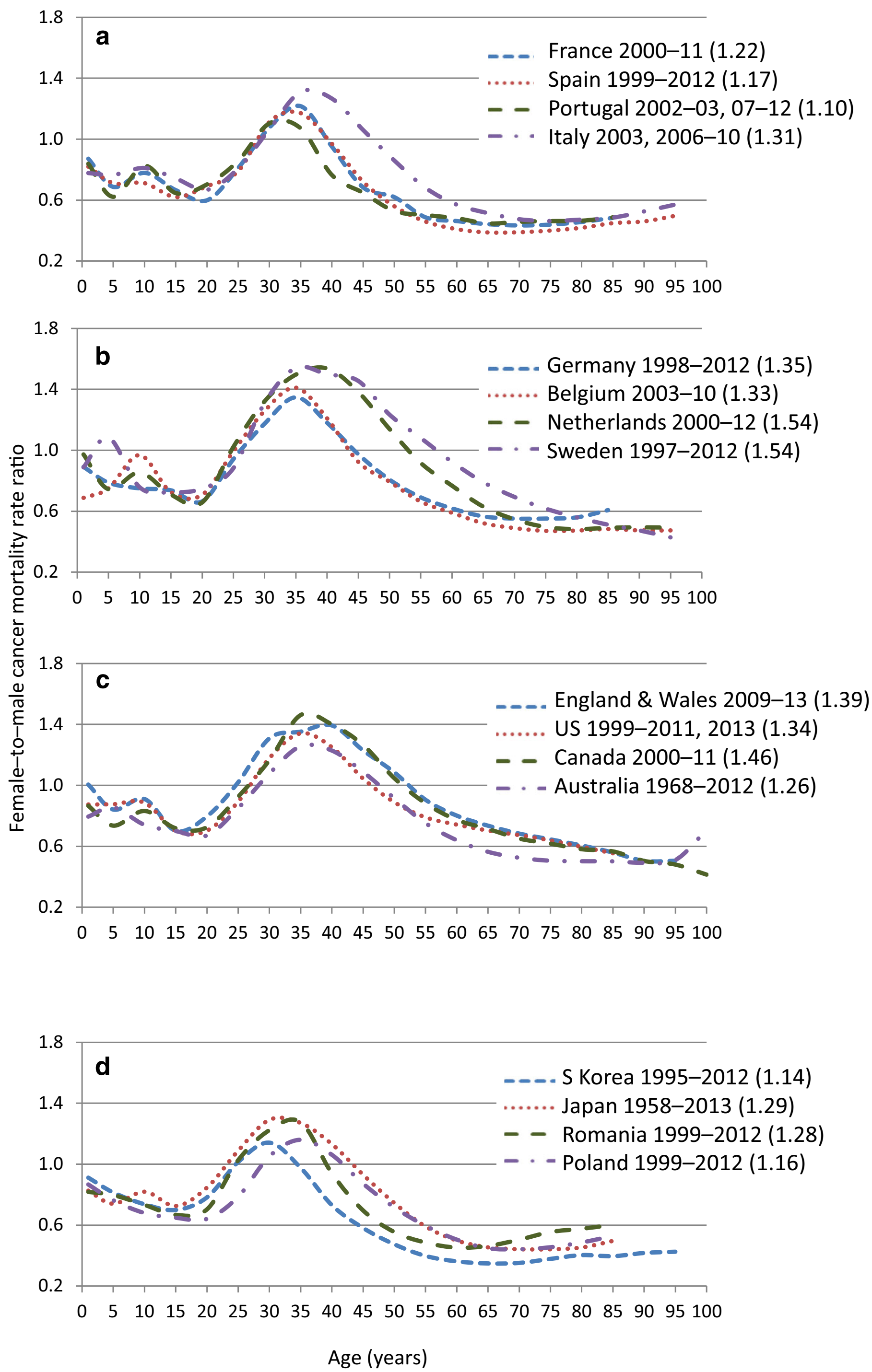


Fig. 5 Trends of age-specific female-to-male cancer mortality rate ratios in 16 countries. The ages shown represent the starting years of each 5-year age group. The labels show country names, data years, and the associated peak ratios in *brackets*. A ratio above 1 (as marked) means higher value for women than men, a female disadvantage. The disadvantage began at ages 25–29 in England and Wales, Japan, South Korea, and Romania, and at ages 30–34 in the other countries. It lasted for 10 years in France, South Korea, and Spain; 15 years in Germany, Belgium, Romania, and Poland; 20 years in Australia, Italy, Japan, and the United States; 25 years in Canada and the Netherlands; and 30 years in England and Wales and Sweden. The top three peak ratios were 1.56 female to 1 male in the Netherlands, 1.5 to 1 in Sweden, and 1.46 to 1 in Canada (color figure online)

Practical and policy implications

The research findings should inspire public health practitioners and policy makers to consider age–sex-specific strategies. In particular, such professionals need to consider the declines in CMRs in the oldest old. Cancer as compared to all causes of deaths may be the most threatening to people in their 50s and 60s. Since PDCs may range from 2 to over 50 % in different age groups, age-specific approaches may enhance the overall effectiveness of the health system. Health care resources should also be allocated to cancer control with consideration toward age and sex differences. Individual countries and the WHO should now publish age-specific data capped at age 100 instead of ages 85–95 due to increases in the oldest old population. Such data are commonly collected by death registries worldwide.

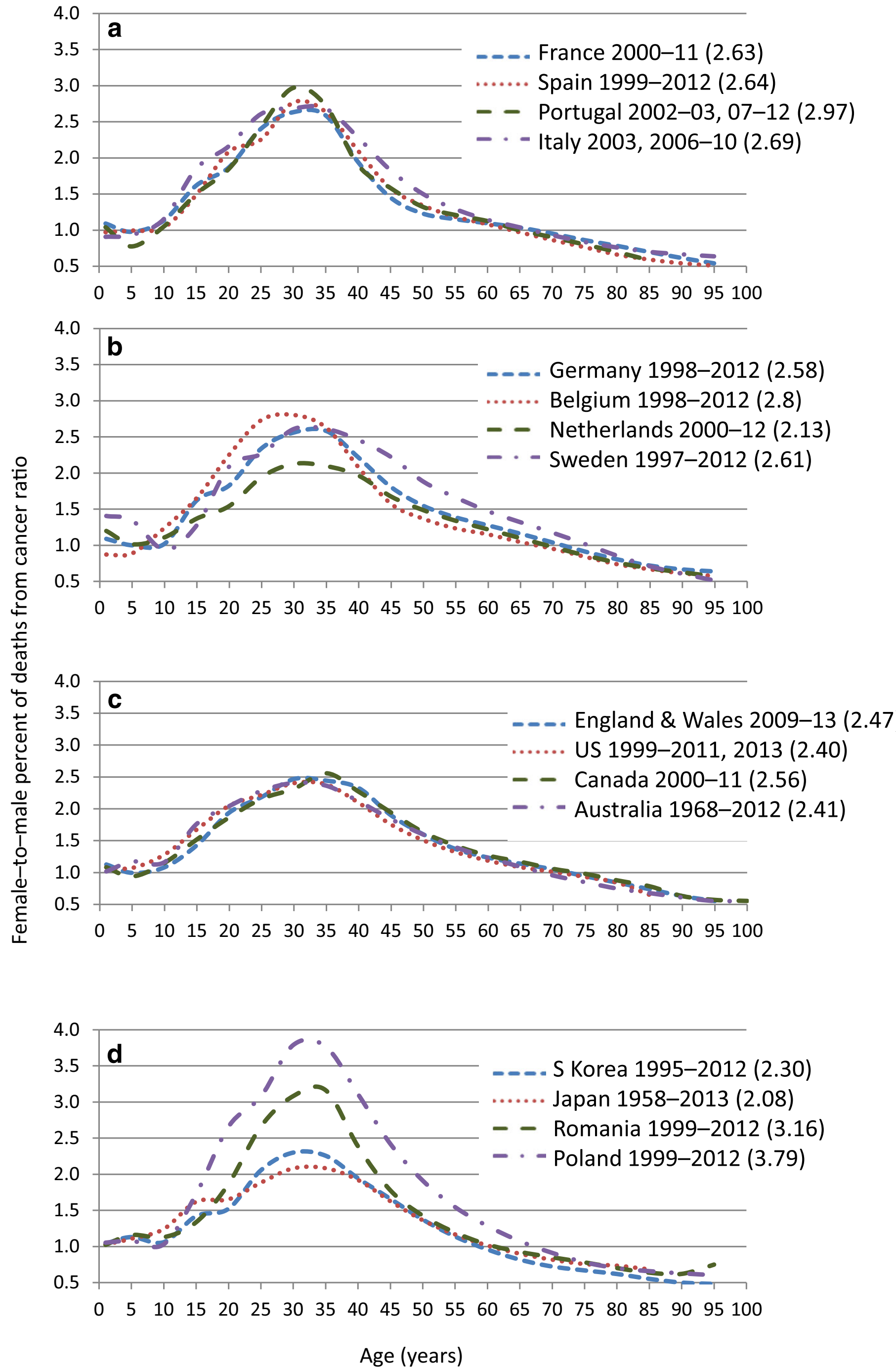


Fig. 6 Trends of age-specific female-to-male percent of deaths from cancer ratios in 16 countries. The ages shown represent the starting years of each 5-year age group. The labels show country names, data years, and the associated peak ratios in brackets. A ratio above 1 (as *marked*) means higher value for women than men, a female disadvantage. The top three peak ratios were 3.79 female to 1 male in Poland, 3.16 to 1 in Romania, and 3–1 in Portugal (color figure online)

Making them available would not require much effort but could make a difference in future research in the oldest old. For example, all eight cases with data capped at age 100 had a decline in CMRs for at least 10.9 % (Table 2).

Conclusions

We have attempted to explore the international trends in age–sex-specific cancer mortality in order to inspire debates in public health, with attention to the oldest old and premenopausal women. Our findings provided indications of substantial declines with age in CMRs in 11 of the 16 countries studied, which has been previously unknown except for in the US. CMRs peaked at ages as early as 75–79 and declined by as much as 39 %. There were indications that CMRs could have peaked earlier and declined more dramatically for earlier rather than later time periods and for males rather than females. On the other hand, no declines were found in 5 of the 16 countries, possibly due to lack of data capped at age 100. Compared to CMR, PDC as an indicator of cancer mortality helped reveal earlier and more dramatic cancer mortality declines with age in all countries. These declines were not confined to the oldest old as CMR declines tended to be, but could happen starting at ages as young as 60 and decline by as much as over 90 %. Additionally, FMCMRRs and FMPDCRs helped uncover trends in cancer mortality in terms of sex differences. Women actually had higher CMRs than men for ten or more years starting from age 25. Their PDCs were two to three times as high as men's. An advantage in PDCs could only be detected in post-menopausal women. Data limitations meant that the research was explorative in nature. However, the novel findings should provide a basis for future research and policy considerations in public health.

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Compliance with ethical standards

Funding This study received no funding from any source.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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