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International Variation in Prostate Cancer Incidence and Mortality Rates

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Abstract

Context: Wide variation exists internationally for prostate cancer (PCa) rates due to differences in detection practices, treatment, and lifestyle and genetic factors.
Objective: We present contemporary variations in PCa incidence and mortality patterns across five continents using the most recent data from the International Agency for Research on Cancer.
Evidence acquisition: PCa incidence and mortality estimates for 2008 from GLOBOCAN are presented. We also examine recent trends in PCa incidence rates for 40 countries and mortality rates for 53 countries from 1985 and onward via join-point analyses using an augmented version of Cancer Incidence in Five Continents and the World Health Organization mortality database.
Evidence synthesis: Estimated PCa incidence rates remain most elevated in the highest resource counties worldwide including North America, Oceania, and western and northern Europe. Mortality rates tend to be higher in less developed regions of the world including parts of South America, the Caribbean, and sub-Saharan Africa. Increasing PCa incidence rates during the most recent decade were observed in 32 of the 40 countries examined, whereas trends tended to stabilize in 8 countries. In contrast, PCa mortality rates decreased in 27 of the 53 countries under study, whereas rates increased in 16 and remained stable in 10 countries.
Conclusions: PCa incidence rates increased in nearly all countries considered in this analysis except in a few high-income countries. In contrast, the increase in PCa mortality rates mainly occurred in lower resource settings, with declines largely confined to high-resource countries.

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1. Introduction

Prostate cancer (PCa) is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide with an estimated 899 000 new cases and 258 000 new deaths in 2008 [1]. The worldwide PCa burden is expected to grow to 1.7 million new cases and 499 000 new deaths by 2030 simply due to the growth and aging of the global population [1]. The only well-established risk factors for PCa are older age, black race/ethnicity, and a family history of the disease [2]. The wide variation in international PCa incidence rates and trends is in part due to the substantial differences worldwide in the diagnosis of latent cancers through prostate-specific antigen (PSA) testing of asymptomatic individuals as well as during prostate surgery. PCa mortality rates and trends are less

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affected by diagnostic practices but reflect differences in PCa treatment worldwide as well as underlying risk.

We present contemporary variations in PCa incidence and mortality patterns across five continents by examining the most up-to-date incidence rates as published for 40 countries based on 63 population-based cancer registries, as well as mortality rates for 53 selected countries obtained from the World Health Organization (WHO) mortality database. We discuss the time trends in PCa rates in relation to the varying patterns of PCa screening and treatment activities in different countries and their impact on the corresponding incidence and mortality rates worldwide.

2. Evidence acquisition

PCa incidence and mortality rates for 2008 for all countries worldwide were obtained via the estimates made at the International Agency for Research on Cancer (IARC), as compiled in GLOBOCAN 2008 [1]. The methods used to estimate the incidence and mortality rates for specific countries are described in detail elsewhere and depend on the availability and accuracy of cancer incidence and mortality data for each country [3].

PCa incidence rates and time trends by year were obtained for selected population-based cancer registries, either representing the entire country (Australia, Croatia, the Czech Republic, Ireland, Israel, the Netherlands, New Zealand, Slovakia, Slovenia, and the United Kingdom) or specific regions of a given country, as extracted from the Cancer Incidence in Five Continents (CI5) series [4] and supplemented with more recent published data where available [5–20]. Inclusion in CI5 provides a criterion indicative of each registry's data quality over time, given that the editorial process involves a detailed assessment of the comparability, completeness, and validity of the incidence data [21]. Data from regional registries were aggregated (where applicable) to serve as a proxy of the national PCa incidence rates. We restricted our temporal analyses to 40 countries derived from national or regional registries with long-term data series available from 1985 and thereafter.

Mortality data covering approximately 30% of the world population are abstracted from death certificates and compiled by IARC as part of the WHO mortality database [22]. The quality of mortality data in terms of coverage and completeness, as well as accuracy, tends to vary from country to country. We obtained annual age-standardized PCa mortality rates from the WHO mortality database for 53 countries with long-term data available from 1985 onward.

For cross-sectional analysis and display of the data, we averaged all available rates for each country for the years in the designated time periods 2000–2004 (incidence) and 2000–2006 (mortality). Therefore, the overall rate for a specific country may represent the average of 5 yr (incidence) or 7 yr (mortality) of data or less depending on that country's data availability.

We examined trends in PCa incidence and mortality rates using join-point regression analysis, which involves fitting a series of joined straight lines on a logarithmic scale to the trends in the annual rates. The direction and magnitude of the resulting trends are described by the annual percent change (APC), the linear slope, across each line segment between two join points. The method is described in detail elsewhere [23]. 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 last 10 yr of available data for each country. The AAPC is estimated as a geometric weighted average of the different APCs from the join-point trend analysis, with the weights equal to the lengths of each segment during the specified time interval [24]. In describing the change, the terms *increase* or *decrease* were used when the AAPC was statistically significant; otherwise the term *stable* was used.

All rates were age standardized to the world standard population [25,26] to compare data across countries and over time with different age compositions. PCa incidence data were categorized according to *International Classification of Diseases* (ICD), 10th revision, codes (C61), and mortality data were categorized by the ICD 9th and 10th revisions: ICD-9 (185) up to 1991 and ICD-10 (C61) thereafter.

3. Evidence synthesis

3.1. Geographic variation

Almost 899 000 PCa cases and 258 000 PCa deaths are estimated to have occurred in 2008 worldwide (Table 1), with 72% of the cases and 53% of the deaths in developed countries (all regions of Europe plus North America, Australia/New Zealand, and Japan), representing <20% of the world population. PCa incidence rates varied 24-fold worldwide in 2008 with the highest estimated rates in Australia/New Zealand, western Europe, North America, and the Caribbean and the lowest in south central Asia, northern Africa, and eastern Asia (Table 1; Fig. 1a). In contrast, estimated PCa mortality rates varied 10-fold with the highest rates in the Caribbean, but also in a number of countries in southern and western Africa, and in South America; the lowest rates were observed in most parts of Asia, northern Africa, as well as North America (Table 1; Fig. 1b). Although PCa is the most commonly diagnosed cancer among men in 2008 in many regions of the world (including all of Australia/New Zealand, North America, and South America, as well as most of western and northern Europe and parts of sub-Saharan Africa) (Fig. 2a), it is estimated as the most common cause of cancer deaths in only a handful of countries, located primarily in the Caribbean, South America, and sub-Saharan Africa (Fig. 2b).

PCa incidence rates (per 100 000) for 2000–2004 from selected registries worldwide vary markedly, with rates ranging from <10 in the Republic of Korea, Thailand (two registries), and Chennai, India, to >100 in the United States and New Zealand (Fig. 3). By far the highest PCa mortality rates (deaths per 100 000) over the period 2000–2006 were observed in Trinidad and Tobago, for which the rate of 53.6 was twice that of the second highest rate (22.6) in Cuba and

Table 1 – Estimated number of new prostate cancer cases and deaths by world area, 2008

Area	Population	Cases		Deaths	
	size	*n*	ASR	*n*	ASR
Africa	492 133 000	39 600	17.5	28 000	12.5
Eastern Africa	154 048 000	9 100	14.5	7300	11.7
Middle Africa	60 745 000	4 200	16.4	3400	13.4
Northern Africa	103 340 000	5 200	8.1	4000	6.2
Southern Africa	28 021 000	7 800	53.9	2600	19.3
Western Africa	145 979 000	13 300	22.2	10 700	18.3
Asia	2 097 629 000	133 200	7.2	59 700	3.1
Eastern Asia	808 216 000	82 700	8.2	26 800	2.5
South-central Asia	888 237 000	23 400	4.1	16 700	2.8
Southeast Asia	286 388 000	17 700	8.3	11 000	5.1
Western Asia	114 788 000	9400	13.8	5200	7.5
America	454 826 000	334 300	66.7	76 500	12.9
Caribbean	20 622 000	16 000	71.1	6500	26.3
Central America	73 669 000	20 500	34.8	8100	12.6
South America	190 301 000	84 100	50.2	29 300	16.2
North America	170 234 000	213 700	85.6	32 600	9.9
Europe	325 514 000	370 700	59.3	89 600	12.0
Central and eastern Europe	137 707 000	58 400	29.1	23 100	10.9
Northern Europe	47 987 000	64 900	73.1	17 400	15.4
Southern Europe	74 964 000	79 500	50.0	20 400	10.4
Western Europe	91 856 000	167 900	93.1	28 700	12.4
Oceania	17 456 000	21 400	94.5	4300	15.3
Australia/New Zealand	12 563 000	21 000	104.2	4000	15.4
Melanesia	4 278 000	300	15.8	200	12.4
Micronesia/Polynesia	615 000	160	39.9	50	13.0
World	3 402 841 000	899 100	27.9	258 100	7.4

ASR = Age standardized rate per 100 000.
Source: GLOBOCAN 2008 [1].
Numbers are rounded to the nearest 10 or 100 and may not sum up to total.

nearly 25 times higher than the lowest rate (1.6) observed in Uzbekistan (Fig. 4). Other countries with high PCa mortality rates (per 100 000) include Norway (21.3) and Sweden (21.1). The Republic of Korea (3.9), Kyrgyzstan (3.4), and Tajikistan (2.0) were observed to have among the lowest mortality rates worldwide (Fig. 4).

3.2. *Incidence and mortality trends*

Increasing PCa incidence rates were observed in 32 of the 40 countries included in the analysis with the estimated AAPC ranging from 2% to 3% in Sweden, the United Kingdom, and Thailand (two registries) to 12–16% in China (two registries), the Republic of Korea, and Lithuania (Table 2). PCa incidence trends stabilized in the remaining eight countries including the United States, Canada (except Quebec), Australia, and New Zealand as well as in a number of countries in South America, northern Europe, and Asia (Table 2); rates did not significantly decrease in any of these countries.

In contrast, PCa mortality rates decreased in 27 of the 53 countries included in the analysis, increased in 16, and remained stable in the remaining 10 countries (Table 3). The decreasing trends were mainly observed in North America, Oceania, western Europe, and parts of northern Europe; the increasing trend generally occurred in countries located in central and eastern Europe, parts of Asia, and Africa (Table 3; Fig. 5). The largest average increases in PCa mortality rates were estimated to have occurred in the Republic of Korea, Moldova, and Trinidad and Tobago (7.8%, 6.5%, and 4.5% per year, respectively); the largest decreases were seen in the United States, Austria, and Israel with average declines of 4.3%, 4.0%, and 3.7% per year, respectively (Table 3). Next we expand on the country- or region-specific trends within each area as defined by the United Nations.

3.2.1. *North America*

Both the United States and Canada (except Quebec) have among the highest PCa incidence rates worldwide, although incidence trends have been stabilizing over the last 10 yr (Fig. 6). Mortality rates are intermediate (Fig. 4) and have been decreasing by 4.3% in the United States and 3.1% in Canada over the last decade for which data are available (Table 3).

3.2.2. *Central and South America*

Incidence data from Central and South America suggest increasing PCa trends in Colombia (Cali), Costa Rica, and Ecuador (Quito) from 1993 to 2002. Incidence rates in Brazil (Goiania) are relatively high in the region, but they have remained rather stable in more recent years following an increase in the 1990s (Fig. 6). Mortality trends in this region are variable; rates are increasing in Brazil, Colombia, and Ecuador, decreasing in Argentina, Costa Rica, and Chile, and rather stable in Mexico (Fig. 6). Trinidad and Tobago and Cuba have among the highest mortality rates worldwide (Fig. 4), and their rates over the last decade have been increasing by 4.5% and 1.4% per year on average, respectively (Table 3).

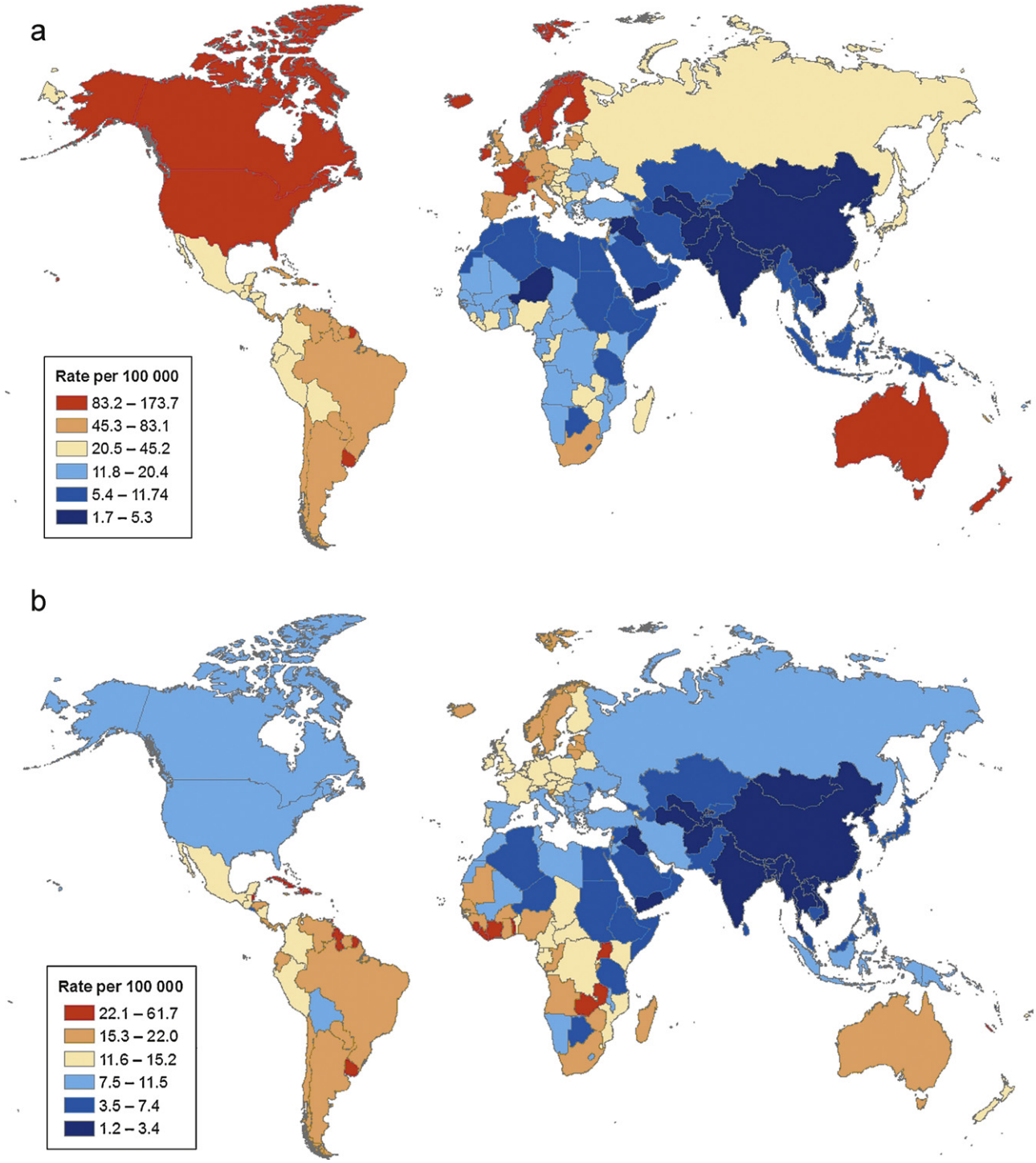

Fig. 1 – (a) International variation in age-standardized prostate cancer incidence rates; (b) international variation in age-standardized prostate cancer mortality rates. Source: GLOBOCAN 2008 [1].

3.2.3. *Western Europe*

Incidence rates have increased by about 4–5% per year since the mid-1990s in Austria (Tyrol), France (six registries), and Switzerland (two registries); rates were stable in the Netherlands from 1999 to 2008 (Table 2; Fig. 6). In contrast, PCa mortality rates decreased in all six western European countries examined, with the declines ranging from 2.3% per year in Germany and the Netherlands to 4.0% per year in Austria (Table 3).

3.2.4. *Northern Europe*

PCa incidence rates increased in four of the five (Denmark, Iceland, Norway, and Sweden) Nordic countries in the last decades, with the greatest average increase (8.2% per year)

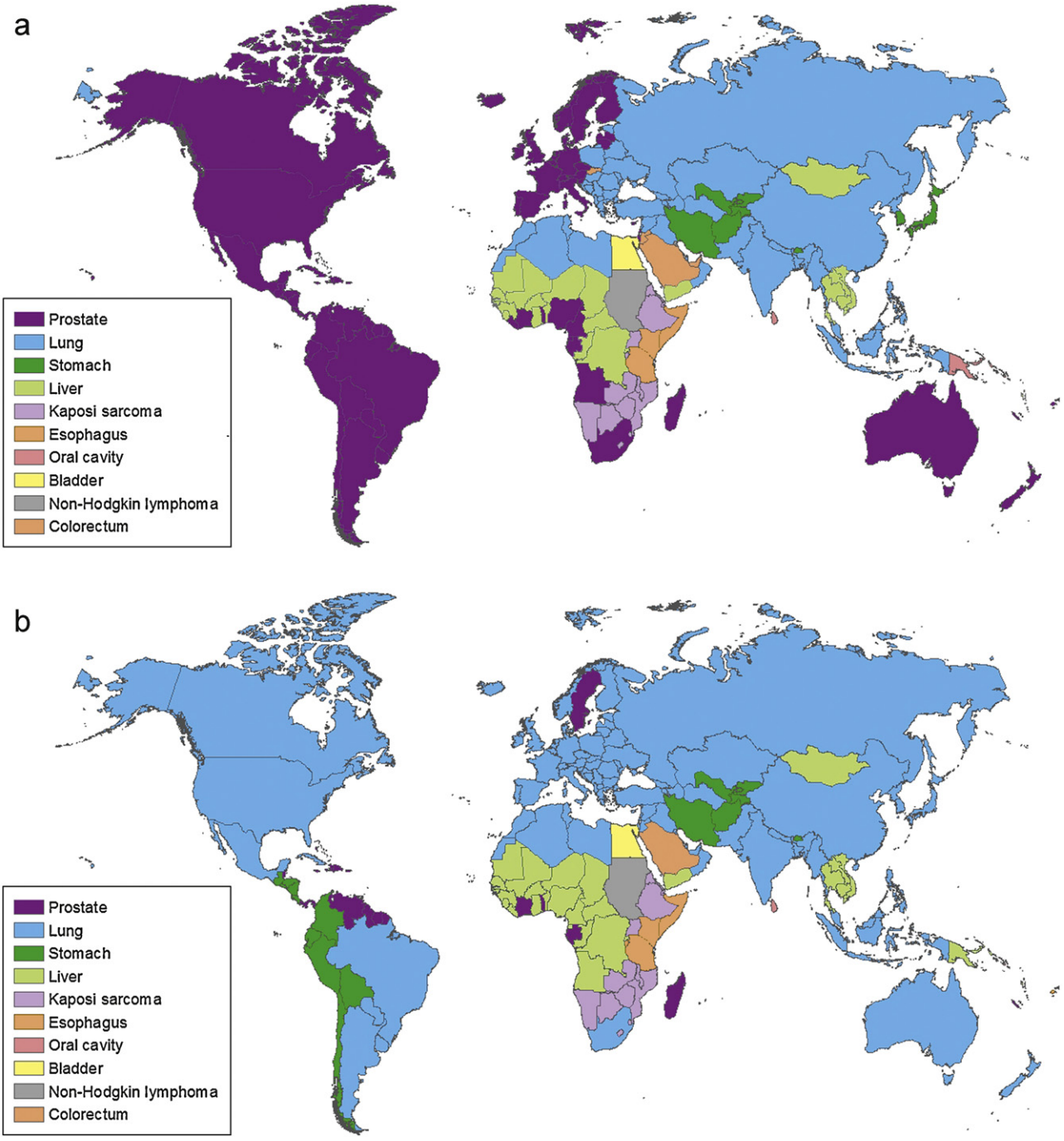

Fig. 2 – (a) Most commonly diagnosed cancer among men worldwide, 2008; (b) leading cause of cancer deaths among men worldwide, 2008. Source: GLOBOCAN 2008 [1].

observed in Denmark from 1999 to 2008 (Table 2). In Finland, incidence rates remained stable during the most recent time period; mortality rates have decreased 3.1% per year since 2000. Significant mortality declines were also observed in Norway and Sweden, whereas mortality trends were more stable in Denmark and Iceland (Table 3). In the United Kingdom and Ireland, increasing incidence trends and decreasing mortality trends were seen for the last 10 yr of available data (Fig. 5). The Baltic countries of Latvia and Lithuania exhibit a slightly different pattern than seen in the rest of northern Europe: very steep average increases in incidence (10.9% and 16.4% per year, respectively) coupled with rather stable mortality rates during the last decade (Tables 2 and 3).

3.2.5. *Southern Europe*

PCa incidence trends increased in all southern European registries examined, with Croatia exhibiting the largest

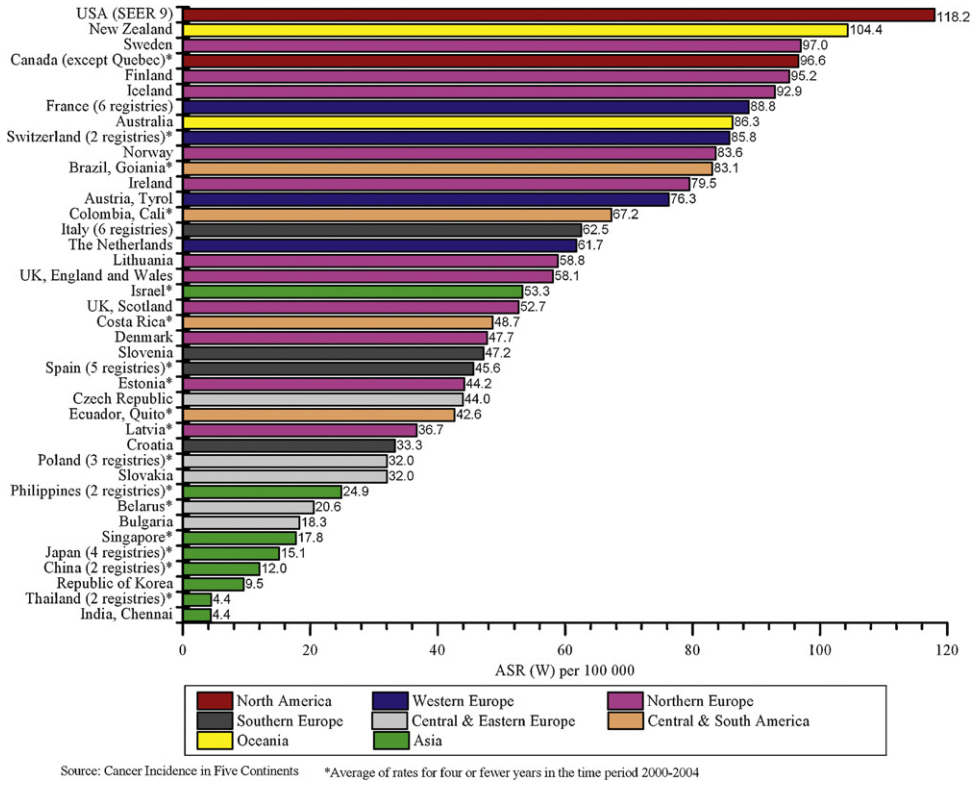

Fig. 3 – Prostate cancer incidence rates for select registries, 2000–2004. Source: Cancer Incidence in Five Continents [4].
ASR (W) = age-standardized rate (world); SEER = Surveillance Epidemiology and End Results.
***Average of rates for ≤4 yr in the time period 2000–2004.**

increase (8.5% per year) from 1998 to 2007 (Table 2). Mortality trends were more variable with rates increasing in both Croatia and Slovenia, and declining in Italy, Malta, and Spain (Table 3).

3.2.6. *Central and eastern Europe*

Incidence rates for PCa increased rapidly in all of the central and eastern European countries considered in this analysis, ranging from 4% to 8% with the greatest rise of 7.7% per year in three registries representing Poland (Table 2). Mortality rates in most countries within the region also increased, with only the Czech Republic and Hungary exhibiting declining trends of around 2.5% per year from 2000 to 2009 (Table 3).

3.2.7. *Asia*

PCa incidence rates in Asia are among the lowest worldwide (Fig. 3); however, rates increased in almost all countries examined, with the increases varying from 3.1% per year on average in the Philippines (based on two registries) and Thailand (also two registries) to 13.8% per year in the Republic of Korea (Table 2). Mortality rates were more variable with increasing trends observed in China (Hong Kong), Kazakhstan, and the Republic of Korea, decreasing trends seen in Israel, Japan, Kyrgyzstan, and Uzbekistan, and with rather stable trends in Singapore and Tajikistan (Table 3).

3.2.8. *Africa*

Long-term trends in incidence and mortality data are not available from Africa, except for mortality for the island nation of Mauritius, which exhibited an increase in PCa mortality rate of 2.2% per year from 2000 to 2009 (Table 3).

3.2.9. *Oceania*

Similar to the profile in North America, trends in PCa incidence rates were stable in both Australia and New Zealand, whereas mortality rates decreased by 2.3% and 2.8% per year on average, respectively, over the last 10 yr of observation (Tables 2 and 3).

3.3. *Discussion*

The highest estimated PCa incidence rates generally remain in the highest resource areas of the world that include North America, Australia and New Zealand, and western and northern Europe. However, the highest estimated PCa mortality rates tend to be seen elsewhere, mainly in the low- to medium-resource areas of South America, the Caribbean, and sub-Saharan Africa [1]. PCa incidence rates increased in 32 of the 40 countries included in this study and stabilized in 8 countries. The rising incidence trends observed in a number of countries were seemingly observed irrespective of geographic location and level of underlying

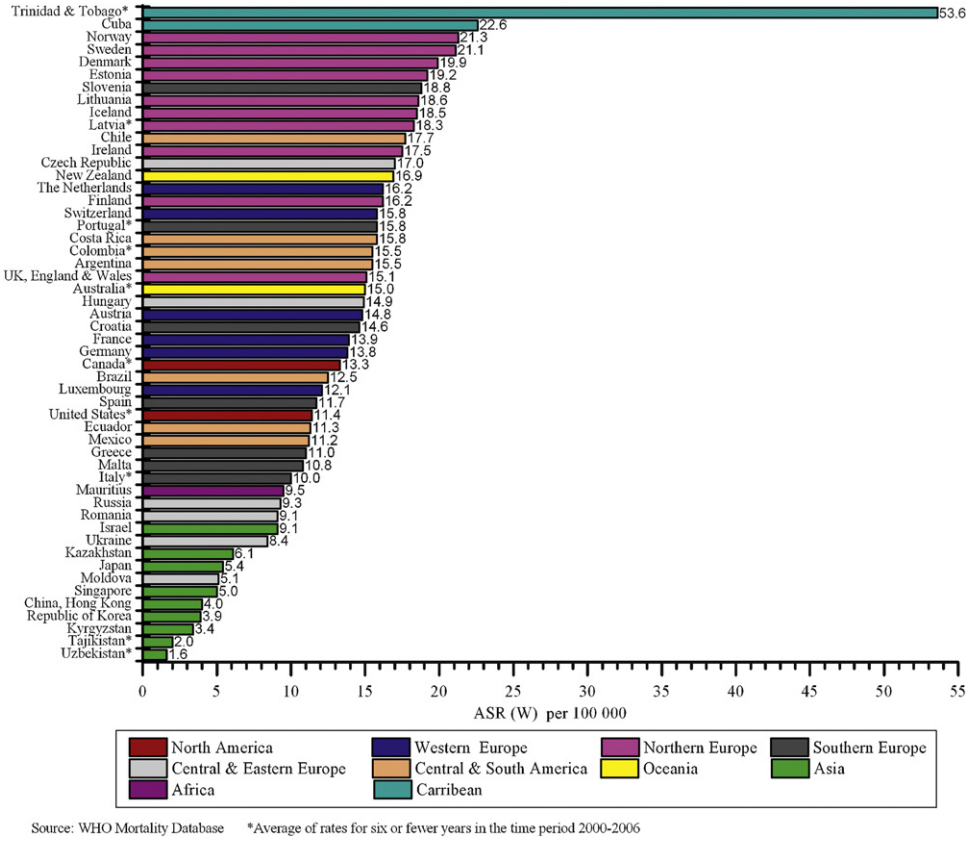

Fig. 4 – Prostate cancer mortality rates for select countries, 2000–2006. *Average of rates for ≤6 yr in the time period 2000–2006. Source: World Health Organization mortality database [22].
ASR (W) = age-standardized rate (world).

incidence. However, some of the largest increases in PCa incidence rates were observed in countries that showed stable or increasing mortality rates including the Republic of Korea, Lithuania, China (Hong Kong), Croatia, and Latvia. In contrast, in countries where incidence trends have stabilized, decreasing mortality rates are commonly observed (the United States, Finland, Canada, New Zealand, Australia, and the Netherlands).

Overall, PCa mortality rates decreased in 27 of the 53 countries included in the study, increased in 16 countries, and stabilized in 10 countries. Although no consistent geographic variation was observed with respect to the direction and magnitude of the recent mortality trends, decreasing rates were observed primarily in the highest resource areas, whereas increasing mortality was seen in lower resource settings with high underlying rates such as Trinidad and Tobago, Estonia, and Latvia or in areas with lower rates including Asia (Republic of Korea and China [Hong Kong]) and eastern Europe (Moldova, Ukraine, and Russia).

International differences in PCa diagnostic practices are most likely the greatest contributor to the variation in PCa incidence rates worldwide. PSA testing, which was introduced in many high-income countries between the mid-1980s and early 1990s (including the Nordic countries [27], the United States, Canada, and Australia [28,29]), has been shown to increase PCa detection by 81% compared with digital rectal examination alone [30], and it detects indolent cancers that may otherwise go undiagnosed during a man's lifetime (overdiagnosis). Before the introduction of PSA testing, PCa detection increased as an incidental finding of transurethral resection of the prostate (TURP) for the treatment of benign prostate hyperplasia [31]. High PCa rates in the most developed areas over the past 20 yr are thus likely due in part to the increasing prospect of PCa diagnoses resulting from TURP and PSA testing in countries where such use has been common as well as advances in technology such as improvements in imaging and biopsy techniques. It has been estimated that 23–42% of PCa cases in Europe and the United States result from overdiagnosis due to PSA testing [32,33]. Detection of indolent cancer by PSA testing causes lead time bias in survival proportions, a phenomenon that occurs when PCa is detected in an earlier phase before clinical manifestation without changing the actual time of death. This makes international comparisons of survival difficult. However, differences in PSA testing and surgical procedures cannot fully explain the international variations in PCa incidence because a nearly 50-fold difference in rates worldwide was already observed in the 1980s before the introduction of PSA testing [4]. Therefore, other factors,

Table 2 – Trends in prostate cancer incidence rates in selected registries

	Join-point analyses									
	Trend 1		Trend 2		Trend 3		Trend 4		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Last 10 yr	
North America										
Canada (except Quebec)	1985–1989	3.0	1989–1993	12.5*	1993–1996	−5.0	1996–2002	4.0*	1993–2002	0.9
United States (SEER 9)	1985–1989	7.2*	1989–1992	19.8*	1992–1995	−6.9	1995–2008	0.1	1999–2008	0.1
Central and South America										
Brazil, Goiania	1988–1993	−0.3	1993–1996	45.7	1996–2002	−2.1			1993–2002	11.8
Colombia, Cali	1985–2002	6.6*							1993–2002	6.6*
Costa Rica	1985–2002	8.0*							1993–2002	8.0*
Ecuador, Quito	1985–2002	4.5*							1993–2002	4.5*
Western Europe										
Austria, Tyrol	1990–2004	5.4*							1995–2004	5.4*
France (6 registries)	1985–1989	10.6*	1989–1998	2.8*	1998–2002	11.3*	2002–2004	−1.9	1995–2004	5.4*
Switzerland (2 registries)	1985–2002	4.3*							1993–2002	4.3*
The Netherlands	1989–1995	7.7*	1995–2001	−0.2	2001–2004	7.7	2004–2008	−1.0	1999–2008	2.0
Northern Europe										
Denmark	1985–1995	−0.3	1995–2002	5.9*	2002–2005	13.3*	2005–2008	5.5*	1999–2008	8.2*
Estonia	1985–1989	−5.0	1989–1993	18.6*	1993–2003	2.9*			1994–2003	2.9*
Finland	1985–1990	0.7	1990–1995	10.2*	1995–2005	5.8*	2005–2008	−11.2*	1999–2008	−0.2
Iceland	1985–2008	3.0*							1999–2008	3.0*
Ireland	1994–2005	8.1*							1996–2005	8.1*
Latvia	1985–1994	1.6	1994–2003	11.0*					1994–2003	10.9*
Lithuania	1985–2000	5.3*	2000–2006	22.4*					1997–2006	16.4*
Norway	1985–2008	4.3*							1999–2008	4.3*
Sweden	1985–1996	2.2*	1996–2004	7.5*	2004–2008	−3.7*			1999–2008	2.3*
UK, England and Wales	1985–2004	5.3*	2004–2007	0.8					1998–2007	3.8*
UK, Scotland	1985–2005	3.9*							1996–2005	3.9*
Southern Europe										
Croatia	1988–1998	1.5	1998–2001	16.6	2001–2007	4.6*			1998–2007	8.5*
Italy (6 registries)	1991–1993	14.8*	1993–2000	6.8*	2000–2003	10.9*	2003–2005	−3.5	1996–2005	5.7*
Slovenia	1983–1988	−0.01	1988–2007	6.4*					1998–2007	6.4*
Spain (5 registries)	1985–2000	6.8*							1991–2000	6.8*
Central and Eastern Europe										
Belarus	1985–2002	5.1*							1993–2002	5.1*
Bulgaria	1993–2008	4.0*							1999–2008	4.0*
Czech Republic	1986–1998	5.5*	1998–2001	1.0	2001–2005	10.7*	2005–2007	0.7	1998–2007	5.1*
Poland (3 registries)	1988–2002	7.7*							1993–2002	7.7*
Slovakia	1985–1993	1.5	1993–2006	4.2*					1997–2006	4.2*
Asia										
China (2 registries)	1988–1994	2.1	1994–2002	13.4*					1993–2002	12.1*
India, Chennai	1985–1995	10.1*	1995–2005	−0.5					1996–2005	−0.5
Israel	1985–2002	7.1*							1993–2002	7.1*
Japan (4 registries)	1985–1992	0.1	1992–1995	12.5*	1995–1999	2.6	1999–2002	10.0*	1993–2002	7.2*
Philippines (2 registries)	1985–2002	3.1*							1993–2002	3.1*
Republic of Korea†	1999–2007	13.8*							1999–2007	13.8*
Singapore	1985–2002	4.6*							1993–2002	4.6*
Thailand (2 registries)	1988–2002	3.1*							1993–2002	3.1*
Oceania										
Australia	1985–1991	4.9*	1991–1994	24.8*	1994–1998	−10.4*	1998–2004	5.9*	1995–2004	0.1
New Zealand	1985–1991	0.7	1991–1995	27.5*	1995–2001	2.5	2001–2005	−5.7*	1996–2005	−1.2

SEER = Surveillance Epidemiology and End Results [study]; APC = annual percent change; AAPC = average annual percent change.
* The APC or AAPC is statistically different from zero.
† The AAPC for Korea represents 9 yr of data.
Source: Cancer Incidence in Five Continents [4].

particularly a westernization of diet, a more sedentary lifestyle, and greater levels of obesity may also play roles in the wide variations in PCa incidence rates worldwide [34–36], although few, if any, specific risk determinants have been clearly identified thus far.

Reasons for the extremely high PCa rates in black men in the United States [37] and some Caribbean countries such as Trinidad and Tobago and Jamaica [38,39] are not fully understood but may be due to inherent genetic factors. In the United States, for example, PCa incidence rates for African American men were 1.6 times higher (230.0 vs 143.8 per 100 000) and mortality rates 2.3 times higher (54.2 vs 22.8 per 100 000) compared with US whites during the period 2003–2007 [40]. Genetic differences such as variants in alleles on chromosomes including (but not limited to) 8q24 and 17q21 may be specific to men of African descent [41–43] in the United States and elsewhere, suggesting that the PCa disparity by race may partly be due to variations in genetic

Table 3 – Trends in prostate cancer mortality rates for selected countries

	Join-point analyses									
	Trend 1		Trend 2		Trend 3		Trend 4		AAPC	
	Years	APC	Years	APC	Years	APC	Years	APC	Last 10 yr	
North America										
Canada	1985–1994	0.6*	1994–2004	3.1*					1995–2004	−3.1*
United States	1985–1992	2.0*	1992–1995	−2.4	1995–2000	−5.1*	2000–2005	−3.6*	1996–2005	−4.3*
Central and South America										
Argentina	1985–1987	6.1*	1987–1992	0.7	1992–1998	3.1*	1998–2008	−0.9*	1999–2008	−0.9*
Brazil	1985–1993	2.9*	1993–1997	5.2*	1997–2000	−0.2	2000–2008	2.2*	1999–2008	1.9*
Chile	1985–1993	2.8*	1993–1996	8.7*	1996–2007	−1.0*			1998–2007	−1.0*
Colombia	1985–2002	3.4*							1993–2002	3.4*
Costa Rica	1985–2000	3.4*	2000–2009	−2.0*					2000–2009	−2.0*
Ecuador	1985–2009	1.3*							2000–2009	1.3*
Mexico	1985–1995	2.6*	1995–2003	0.9*	2003–2008	−1.8*			1999–2008	−0.6
Caribbean										
Cuba	1985–1990	5.5*	1990–2008	1.4*					1999–2008	1.4*
Trinidad and Tobago	1985–2002	4.5*							1993–2002	4.5*
Western Europe										
Austria	1985–1991	2.3*	1991–2000	−0.9	2000–2009	−4.0*			2000–2009	−4.0*
France	1985–1990	0.9*	1990–2003	−1.8*	2003–2008	−3.6*			1999–2008	−2.8*
Germany	1985–1994	1.5*	1994–2006	−2.3*					1997–2006	−2.3*
Luxembourg	1985–2008	−2.5*							1999–2008	−2.5*
Switzerland	1985–1992	−0.1	1992–2007	−3.2*					1998–2007	−3.2*
The Netherlands	1985–1995	1.4*	1995–2009	−2.3*					2000–2009	−2.3*
Northern Europe										
Denmark	1985–1993	2.1*	1993–2006	−0.1					1997–2006	−0.1
Estonia	1985–2009	2.9*							2000–2009	2.9*
Finland	1985–1998	0.9*	1998–2009	−3.1*					2000–2009	−3.1*
Iceland	1985–2009	−0.7							2000–2009	−0.7
Ireland	1985–1996	2.0*	1996–2009	−2.2*					2000–2009	−2.2*
Latvia	1985–1998	1.7*	1998–2006	6.5*	2006–2009	−4.2			2000–2009	2.8
Lithuania	1985–2007	3.3*	2007–2009	−7.1					2000–2009	0.9
Norway	1985–1997	1.3*	1997–2009	−2.1*					2000–2009	−2.1*
Sweden	1985–1998	1.4*	1998–2008	−1.6*					1999–2008	−1.6*
UK, England and Wales	1985–1992	2.4*	1992–2000	−1.8*	2000–2003	0.9	2003–2007	−2.9*	1998–2007	−1.4*
Southern Europe										
Croatia	1985–1989	6.1*	1989–1995	−3.3	1995–2009	1.8*			2000–2009	1.8*
Greece	1985–1988	−1.6	1988–2007	1.9*	2007–2009	−6.2			2000–2009	0.0
Italy	1985–2003	−0.8*							1994–2003	−0.8*
Malta	1985–1993	7.8*	1993–2008	−2.7*					1999–2008	−2.7*
Portugal	1985–1998	2.7*	1998–2003	−2.1					1994–2003	0.0
Slovenia	1985–2009	1.5*							2000–2009	1.5*
Spain	1985–1998	0.7*	1998–2008	−3.3*					1999–2008	−3.3*
Central and eastern Europe										
Bulgaria	1985–2008	1.5*							1999–2008	1.5*
Czech Republic	1986–2004	1.1*	2004–2009	−5.3*					2000–2009	−2.5*
Hungary	1985–1997	1.0*	1997–2009	−2.6*					2000–2009	−2.5*
Moldova	1985–1994	4.7*	1994–1999	−7.6	1999–2009	6.5*			2000–2009	6.5*
Romania	1985–1989	−2.8	1989–1996	3.1*	1996–2006	0.9*			1997–2006	0.9*
Russia	1985–2006	2.6*							1997–2006	2.6*
Ukraine	1985–1990	4.8*	1990–1998	0.9	1998–2006	2.9*			1997–2006	2.6*
Asia										
China (Hong Kong)	1985–2009	1.8*							2000–2009	1.8*
Israel	1985–1995	4.4*	1995–2008	−3.7*					1999–2008	−3.7*
Japan	1985–1993	2.3*	1993–1996	8.7*	1996–2004	0.4	2004–2009	−1.6*	2000–2009	−0.7*
Kazakhstan	1985–2008	1.2*							1999–2008	1.2*
Kyrgyzstan	1985–2009	−1.0*							2000–2009	−1.0*
Republic of Korea	1985–2002	13.4*	2002–2006	1.3					1997–2006	7.8*
Singapore	1985–2000	3.5*	2000–2006	−7.0					1997–2006	−3.6
Tajikistan	1985–1991	13.3*	1991–1995	−21.1	1995–2005	4.1			1996–2005	4.1
Uzbekistan	1985–2005	−1.8*							1996–2005	−1.8*
Africa										
Mauritius	1985–2009	2.2*							2000–2009	2.2*
Oceania										
Australia	1985–1994	2.2*	1994–1997	−5.5	1997–2004	−1.3*			1995–2004	−2.3*
New Zealand	1985–2000	0.3	2000–2007	−3.7*					1998–2007	−2.8*

APC = annual percent change; AAPC = average annual percent change.
* The APC or AAPC is statistically different from zero.
Source: World Health Organization mortality database [22].

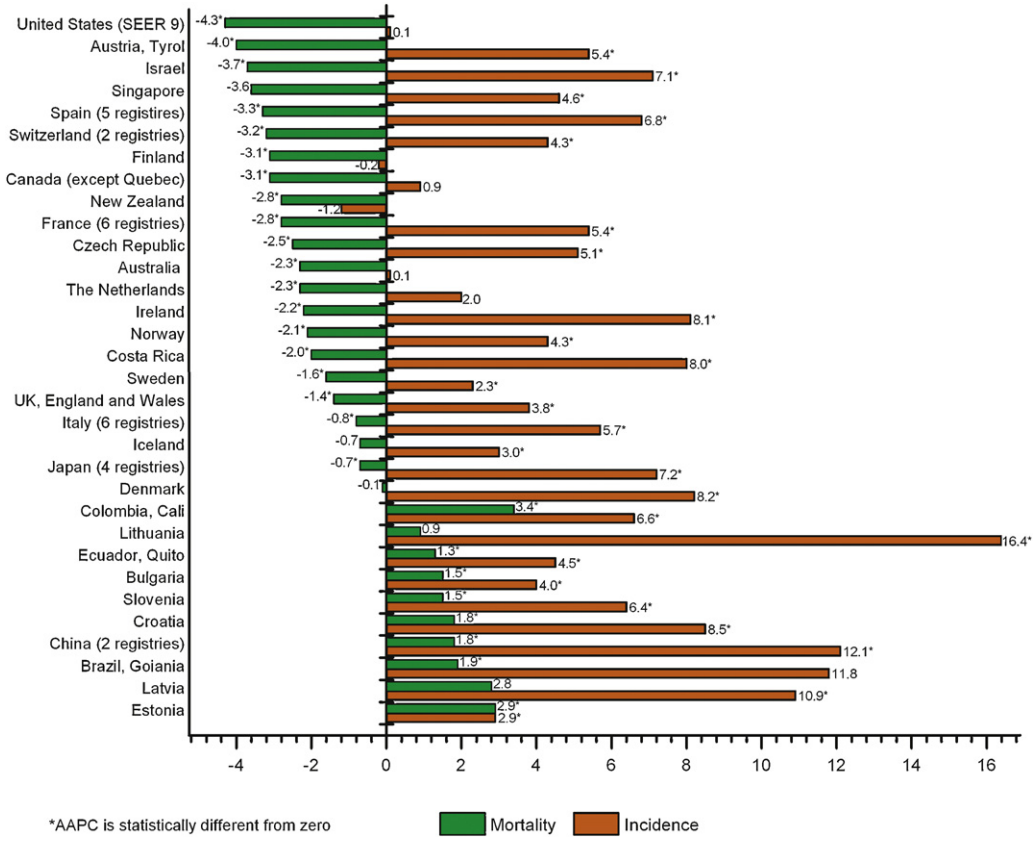

Fig. 5 – Average annual percent change (AAPC) in incidence and mortality rates for the last 10 yr of available data.
SEER = Surveillance Epidemiology and End Results.
***AAPC is statistically different from zero.**

susceptibility, although further studies are needed to confirm this possibility and determine the underlying biologic mechanisms involved. Additionally, African Americans have higher odds of an advanced Gleason score, a marker of PCa severity, relative to whites [44].

Stabilizing PCa incidence trends were primarily observed in countries with higher rates of PSA testing including the United States, Canada (except Quebec), and Australia. Although the AAPC for the last 10 yr of observation shows a stable incidence trend for each of these countries, dramatic increases followed by sharp reductions in PCa incidence in the late 1980s and early 1990s were observed in each as a result of the widespread introduction of PSA testing [28,33]. In other high-resource settings, including many in northern and western Europe, gradually increasing PCa incidence trends have yet to yield a dramatic peak (although Finland is a notable exception) [45]. This could be due in part to the later introduction and more gradual adoption of PSA testing as well as greater awareness of PCa screening [46]. Increases in PCa incidence rates were also observed in Asia including Japan (four registries), Singapore, and Thailand (two registries) where PSA testing remains relatively uncommon. Some researchers have suggested a possible role of a westernization of lifestyle in explaining such trends [47]. In addition, Parkin and colleagues reported that PCa incidence increased in Kampala, Uganda, by 4.5% per year on average from 1991 to 2006, with the rise occurring predominantly among men >65 yr of age [48]. This increase in PCa, which is not attributed to screening, may be related to increases in PCa awareness, prostatectomy among elderly men, and histologic examinations of biopsies [48].

In contrast to incidence, PCa mortality rates have decreased in most high-resource settings examined including North America, Oceania, alongside northern and western Europe. Reasons for the declining rates are multifold for which the main factors may be improved treatment and/or early detection [49,50]. Improvements in treatments in the 1990s for early stage PCa including radical prostatectomy [51], radiation therapy [52], and hormone therapy coupled with an increased detection of early stage disease as a result of PSA testing appear to be reasonable explanations for the declining mortality trends observed in many high-resource countries [53]. However, the specific role of PSA testing in explaining the favorable recent declines in PCa mortality continues to be debated, particularly given downward trends observed in countries where the prevalence of PSA testing is reasonably low (such as in the United Kingdom) [54]. In addition, recent results from a randomized PCa screening trial in the United States failed to show a benefit from screening related to PCa mortality, whereas a trial in Europe found a PCa mortality reduction of 20% attributable to screening [55,56]. However, methodological issues such as

differences in statistical power and variability between the study arms could provide possible reasons for differences in the trial outcomes [57]. Etzioni et al. used models to project disease mortality in the absence and presence of PSA testing and found that 45–70% of the observed decline in PCa in the United States could be attributed to a stage shift induced by screening [50]. Even if PSA testing and subsequent treatment does contribute to declining mortality, the ratio of benefits to risks remains uncertain due to the significant morbidity associated with treatment.

Although mortality rates have decreased in many high-resource countries over the last 10 yr, the rates increased in many countries studied in central and eastern Europe, Asia, and Africa. Reasons for the increasing trends are not well known but may be related to an increased prevalence of risk factors associated with economic development such as obesity, increased consumption of dietary fat, and decreased physical activity [58]. They may also reflect improved data collection.

Our study is strengthened by the comprehensive quantification and comparison of PCa incidence and mortality trends using the high-quality cancer registry data from IARC and mortality data from the WHO mortality database [4,22]. However, IARC incidence data and WHO mortality data are limited in geographic coverage and often unavailable for the lowest resource countries. In addition, PCa incidence and mortality estimates obtained from GLOBOCAN 2008 vary in accuracy, depending on the extent and the validity of available data by country, ranging from real and valid counts of cases and deaths, to estimates based on samples, to those based on rates in neighboring countries [3]. When available, local registry data were aggregated and used as proxies of the national profile; however, the untested nature of this assumption should be taken into consideration when interpreting the results. Delays in reporting in some registries in the most recent years of data availability may also affect overall trends by possibly attenuating increasing PCa trends and strengthening decreasing trends [59]. Finally, interpretation of our results is difficult given that it is unclear as to the extent to which the increasing trends in PCa incidence in low- and middle-income countries are indicative of a truly changing risk or represent increased detection of latent disease. Also uncertain is the extent to which the declines in mortality in high-income countries are the result of early diagnosis through PSA testing and subsequent biopsy, or the result from curative treatment because both came into existence at a similar time period.

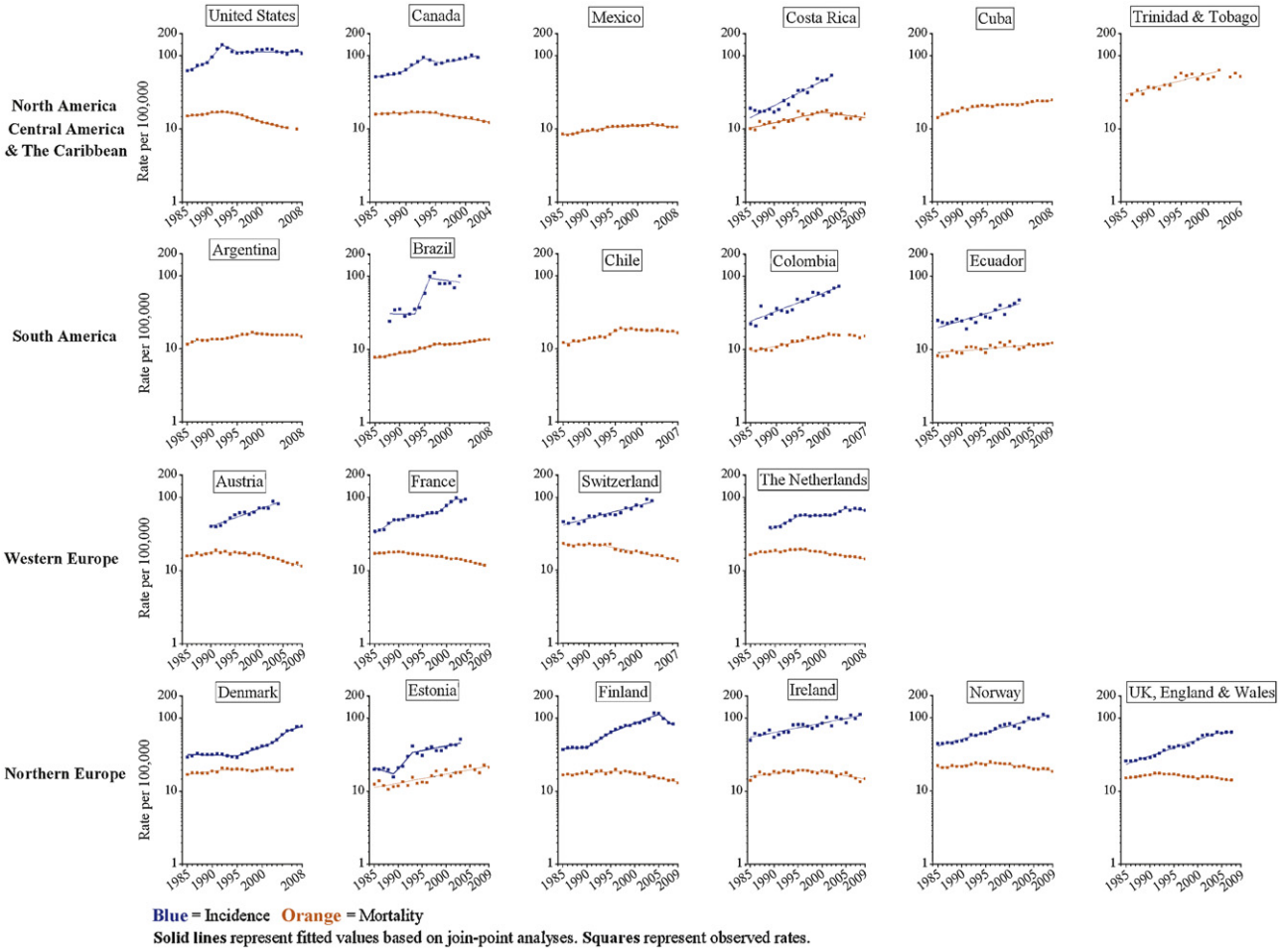

Fig. 6 – Trends in prostate cancer incidence and mortality rates, select countries. Sources: incidence: Cancer Incidence in Five Continents [4]; mortality: World Health Organization (WHO) mortality database [22].

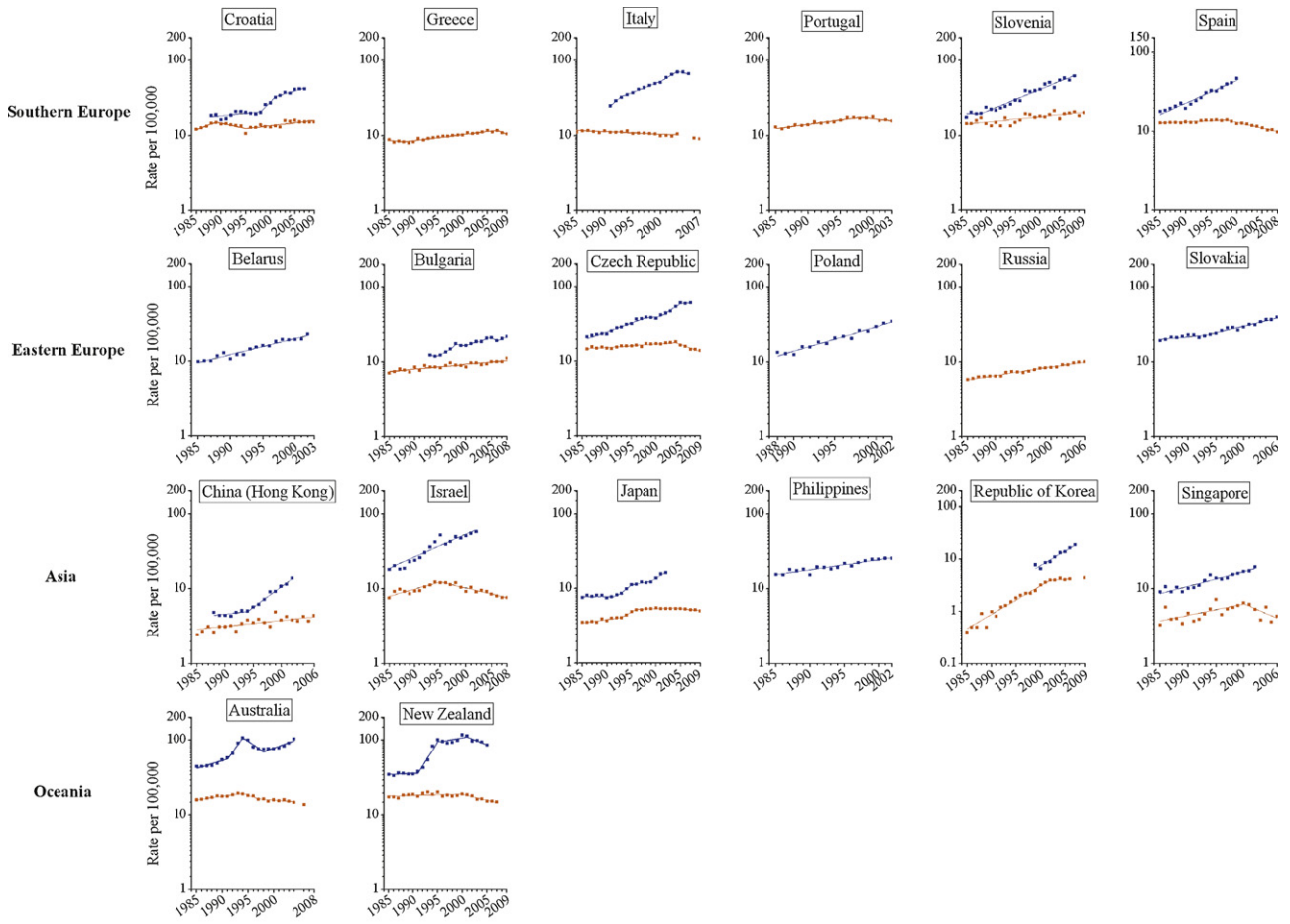

Fig. 6 (*Continued*).

4. Conclusions

Estimated PCa incidence rates remain highest in the highest income regions of the world including North America, Oceania, and western and northern Europe, whereas mortality rates tend to be highest in low- to middle-income settings including parts of South America, the Caribbean, and sub-Saharan Africa. For the vast majority of countries examined, PCa incidence rates increased over the last 10 yr of observation. Although no examples of declining incidence trends were observed in our study, most of the registries exhibiting stabilizing incidence trends covered high-resource catchment populations for which declines in mortality trends were observed at the national level. In contrast, the greatest increases in incidence rates occurred in less resourced countries with stable or increasing mortality trends.

Author contributions: Ahmedin Jemal had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Center, Jemal, Bray, Ward, Brawley.
Acquisition of data: Lortet-Tieulent, Ferlay, Center.
Analysis and interpretation of data: Center, Jemal, Bray.
Drafting of the manuscript: Center, Jemal, Bray.
Critical revision of the manuscript for important intellectual content: Center, Jemal, Bray, Lortet-Tieulent, Ferlay, Ward, Brawley.
Statistical analysis: Center.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: None.
Other (specify): None.

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