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Recent global trends in testicular cancer incidence and mortality

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Abstract

Testicular cancer (TCa) has a relatively rare incidence and mortality, but has not been thoroughly evaluated. We analyzed global variations and recent trends in TCa incidence and mortality.

Age-standardized rates (ASRs) of TCa incidence and mortality were retrieved from the GLOBOCAN 2012 database. Temporal patterns were assessed using data obtained from the Cancer Incidence in Five Continents (volumes I–X) and World Health Organization Mortality databases. The incidence and mortality trends over the last 10 years were analyzed using join point analysis.

Western and Northern Europe had the highest incidence of TCa (ASR = 8.7 and 7.2, respectively), with most countries showing an increase in incidence rates except for China, which had a stable incidence. Incidence rates were markedly increased in Southern European countries (average annual percent change of 6.8% in Croatia and 6.1% in Spain) but were attenuated in western Europe. The highest mortality rates were observed in western Asia (ASR = 0.7), with most countries showing a decrease in mortality.

While the incidence of TCa has increased, mortality from TCa has decreased in most countries. More socioeconomically developed countries had a higher incidence of TCa with lower mortality.

Abbreviations: AAPC = average annual percent change, ASRs = age-standardized rates, Lowess = locally weighted regression, TCa = testicular cancer.

Keywords: cancer trends, epidemiology, incidence, mortality, testicular cancer

1. Introduction

Testicular cancer (TCa) is a relatively rare cancer on a per-population basis, accounting for 1% to 2% of all neoplasms in men and boys[1,2] and over 52,000 new cases and almost 10,000 deaths worldwide in 2008.[3] However, TCa is the most common malignancy in young adult men (aged 15–40 years).[4] The natural course of TCa is metastasis that eventually results in death. Although there are no primary methods to prevent TCa at the present time, multimodal treatments, including surgery, chemotherapy, and radiation, have been developed, resulting in a high curative rate for TCa.

TCa incidence has been increasing over the last 30 to 40 years,[5,6] affecting mainly Caucasian populations. Incidence rates among young white men in Nordic countries are more than 10 times higher than those observed among black and Asian men.[6,7] The increase in TCa incidence is mainly driven by birth cohort effects, meaning that an individual's risk is largely a function of the era in which he is born.[8–10] Furthermore, several studies have noted that immigrants retain their original region's incidence of TCa, even after relocating to a different geographical region.[3,11,12]

Known risk factors for TCa are cryptorchidism, a previous diagnosis of TCa, a genetic predisposition, and maternal estrogen exposure.[13–16] However, we do not clearly understand why distinct geographic and temporal variations exist in the incidence of TCa. As TCa incidence and mortality have distinct geographic variations, with Northern and Western Europe having the highest incidence rates,[8] most epidemiological studies have focused on European, but not global, cohorts. Previous studies of global TCa incidence using the GLOBOCAN 2008 database reported the highest TCa incidence rates in Western and Northern Europe (7.8 cases and 6.7 cases per 100,000 man-years, respectively) and the lowest incidence rates in Asia and Africa (0.7 cases and 0.4 cases per 100,000 man-years, respectively).[17] This article provides the most recent overview of global variations in TCa incidence and mortality rates, with a comprehensive description and comparison of recent global TCa trends.

2. Materials and methods

2.1. Data sources

Estimated TCa incidence and mortality rates [International Classification of Diseases 10th revision (ICD-10) diagnosis code C62] were retrieved from the GLOBOCAN database for 184

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was not required for the purposes of this study, as the study was based on retrospective anonymous patient data and did not involve patient intervention or the use of human tissue samples.

None of the authors have any conflicts of interest to declare.

The author(s) of this work have nothing to disclose.

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countries in 2012.[18] GLOBOCAN provides national estimates of incidence, mortality, and prevalence from the best available data sources in each country.[18] More developed regions include Europe, North America, Australia/New Zealand, and Japan. Less developed regions include Africa, Asia (excluding Japan), Latin America, and the Caribbean, Melanesia, Micronesia, and Polynesia, as defined in GLOBOCAN.[18]

Incidence data were derived from population-based cancer registries, using the Cancer Incidence in Five Continents (CI5) database, volumes I–X.[19] CI5, the main source of global cancer incidence data provided by population-based cancer registries worldwide, has the highest level of validity, completeness, and comparability because of its rigorous editorial processes.[20] Mortality data were extracted from the World Health Organization Mortality database.[21] The quality of incidence and mortality data, in terms of coverage and completeness, is known to vary greatly by country.[21]

2.2. Data analysis

Age-standardized rates (ASRs) for TCa incidence and mortality were computed by year/period and region/country using the standard world population.[22] Locally weighted regression (Lowess) curves were used for the graphically presented smoothed trend lines.[23] To evaluate incidence and mortality variations in the rates over time, joinpoint regression analyses were used,[24] which include fitting a series of joined, straight lines to the ASR trend.[24] Logarithmic transformation of the rates, the standard error (calculated using a binomial approximation), and a maximum number of 3 joinpoints were specified as options in the analyses. To estimate the magnitude and direction of the most recent trends, the average annual percent change (AAPC) and the corresponding 95% confidence intervals for the last available 10 years of incidence and mortality data for each country were calculated. AAPC is a geometrically weighted average of various APC values from the regression analyses using joinpoint trend analysis software, with weights equivalent to the lengths of each segment during the specified time intervals.[25]

3. Results

3.1. Incidence and mortality according to geographical location

According to the GLOBOCAN estimates, about 55,300 new TCa cases and 10,400 TCa-related deaths occurred in 2012 (Table 1). TCa incidence rates varied more than 44-fold worldwide in 2012. The highest rates were observed in Western Europe (ASR 8.7 per 100,000), Northern Europe (7.2), and Australia/New Zealand (6.8), and the lowest rates were observed in Middle Africa (0.2) (Table 1 and Fig. 1A). The regions with the most prominent incidence data compared with other regions in the same continent

Table 1

Estimated incidence and mortality of testicular cancer in 2012 by region*.

World region	Male population (thousands)	TCa incidence		TCa mortality	
		n	ASR	n	ASR
Africa	551,385	1529	0.4	864	0.3
Eastern Africa	182,067	409	0.3	250	0.2
Middle Africa	69,644	97	0.2	64	0.2
Northern Africa	106,527	570	0.6	290	0.3
Southern Africa	29,775	161	0.6	71	0.3
Western Africa	163,372	292	0.3	189	0.2
Asia	2,193,088	15,053	0.7	5849	0.3
East Asia	824,745	4346	0.5	1004	0.1
Southeastern Asia	306,015	2571	0.9	1236	0.5
South-Central Asia	935,661	5881	0.6	2813	0.3
Western Asia	126,667	2255	1.7	796	0.7
Europe	356,519	21,548	5.6	1612	0.4
Central and Eastern Europe	138,209	4913	3.2	901	0.5
Northern Europe	49,921	3635	7.2	119	0.2
Southern Europe	75,142	4783	5.9	265	0.3
Western Europe	93,247	8217	8.7	327	0.3
Central and South America and Caribbean	302,545	7197	2.2	1504	0.5
Caribbean	20,981	222	1	46	0.2
Central America	82,115	1951	2.3	511	0.6
South America	199,449	5024	2.4	947	0.4
North America	172,234	8965	5	484	0.2
Oceania	18,952	974	5	38	0.2
Australia/New Zealand	13,595	953	6.8	27	0.2
Melanesia	4762	18	0.4	11	0.3
Micronesia	256	3	0.5	0	0
Polynesia	339	3	0.8	0	0
More developed regions†	605,134	32,740	5.2	2209	0.3
Less developed regions‡	2,989,588	22,526	0.7	8142	0.3
World	3,594,722	55,266	1.5	10,351	0.3

ASR = age-standardized rate per 100,000 individuals, TCa = testicular cancer.

* Population size data were retrieved from the Department of Economic and Social Affairs, Population Division, United Nations (http://esa.un.org/unpd/wpp/Download/Standard/Population). [1]

† Europe, Northern America, Australia/New Zealand, and Japan.

‡ All regions of Africa, Asia (except Japan), Latin America, and the Caribbean, plus Melanesia, Micronesia, and Polynesia.

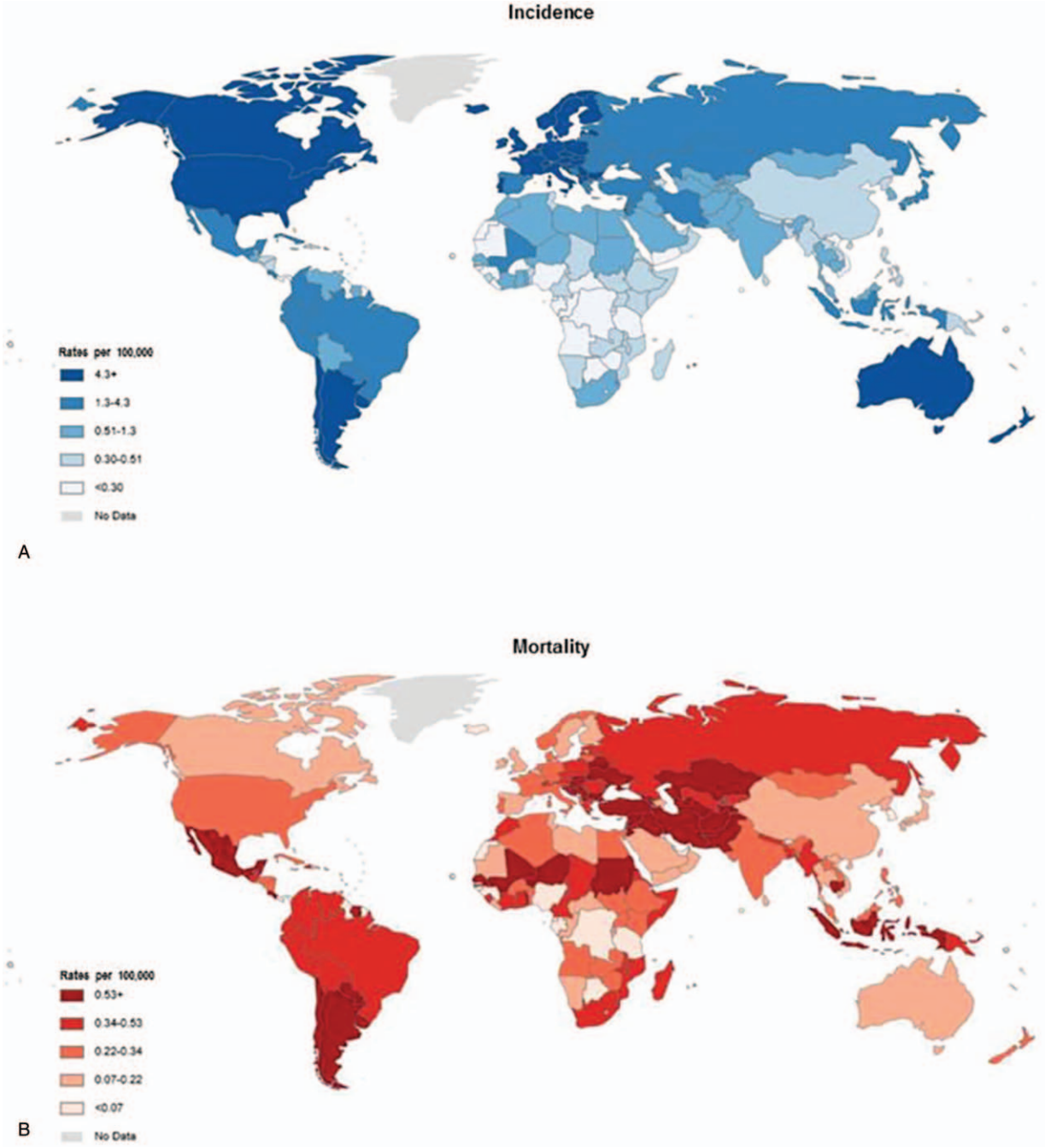

Figure 1. International variations in estimates of national age-standardized incidence (A) and mortality rates (B) of testicular cancer in all age groups. [18]

included Western Asia (1.7), Western Europe (8.7), and Australia/New Zealand (6.8) (Table 1 and Fig. 1A). When compared with the incidence data estimated in 2008,[17] the sharpest rise was observed in Southern Europe (4.2 in 2008 vs 5.9 in 2012).

The highest mortality rate was observed in Western Asia (0.7), whereas the lowest rates (0.2) were found for most regions of Oceania (Table 1 and Fig. 1B).

3.2. Age-standardized rates for incidence

The overall incidence trends showed volatile curves, while the recent 10 years of incidence trends showed persistent increases in most countries worldwide, except in Japan, Switzerland, and China, which had stable incidences (Figs. 2 and 3A). Although AAPCs were lowest or insignificant in Asian populations, except for Israel at 3%, significant but modest increases were observed in Oceania and North America. Of the 3 Latin America and Caribbean registries contributing data, Costa Rica showed a significant increase in incidence (AAPC of 4.6%) (Figs. 2 and 3A).

Significant increases were observed in most European countries, especially in Southern Europe, with AAPCs of 6.8% in Croatia and 6.1% in Spain. A stabilization of the incidence was noted within the last decade in Denmark (AAPC of 0.1%), Switzerland (AAPC of 0.7%), Malta (AAPC of 2.5%), Japan

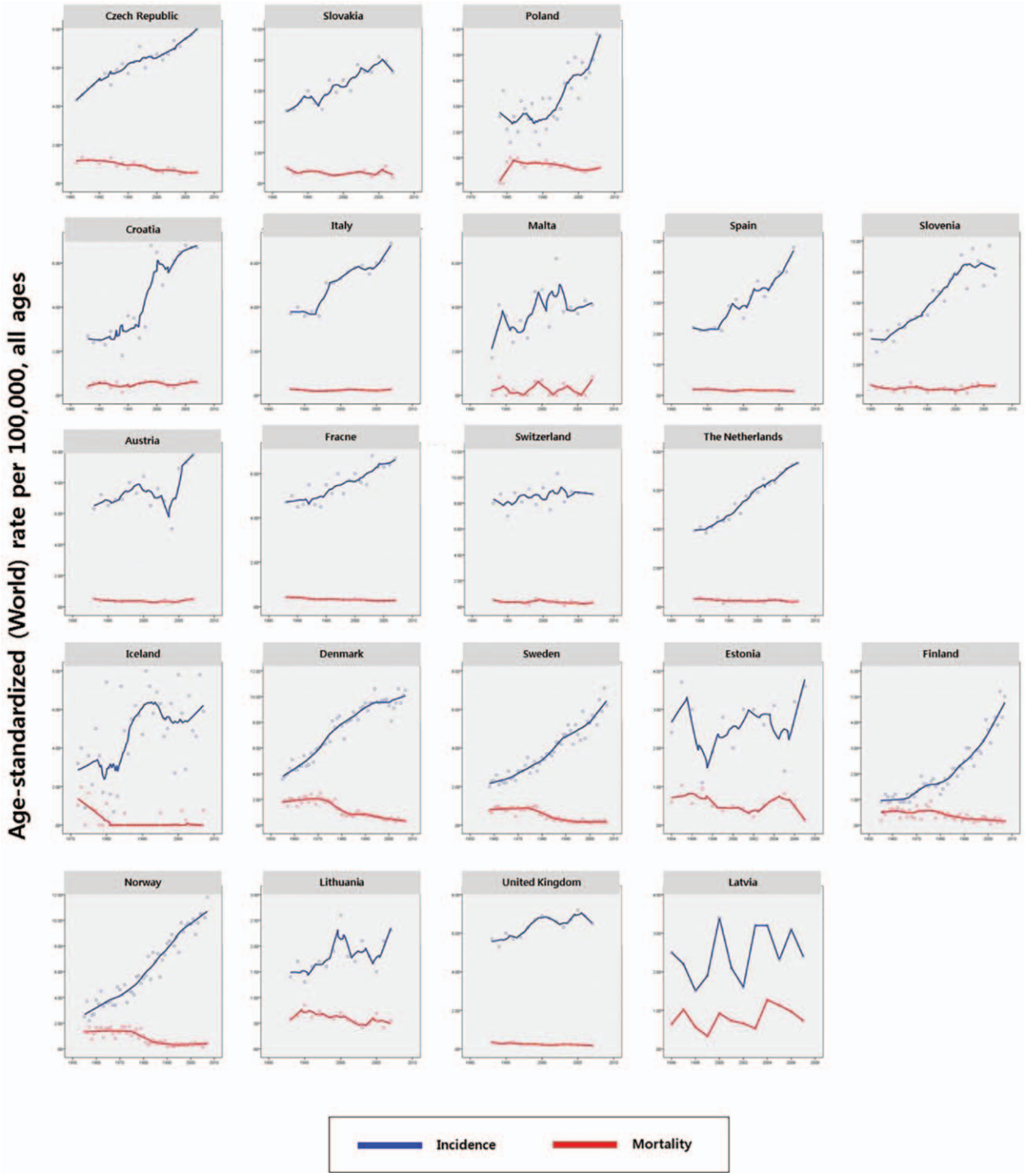

Figure 2. Trends in age-standardized (world) incidence and mortality rates of testicular cancer in all age groups. Dots are observed values; solid lines are locally weighted regression curves (30% of the data were used in smoothing each point). [19,21]

(AAPC of 0.6%), China (AAPC of -0.3%), the Philippines (AAPC of 0.5%), and Brazil (AAPC of 2.9%).

3.3. Age-standardized rates for mortality

Most countries showed decreased mortality, except in Croatia and Brazil, which had increasing mortality (AAPCs of 1.7% and 1.8%, respectively) (Figs. 2 and 3B). Most Asian countries showed significant decreases in mortality, especially China, which had a significant decrease in mortality (AAPC of -6.1%).

4. Discussion

This paper comprehensively analyzed the epidemiology of worldwide TCa incidence and mortality using recent, high-quality data. Continuous increases in global TCa incidence rates in most countries were noted. Compared with an incidence in

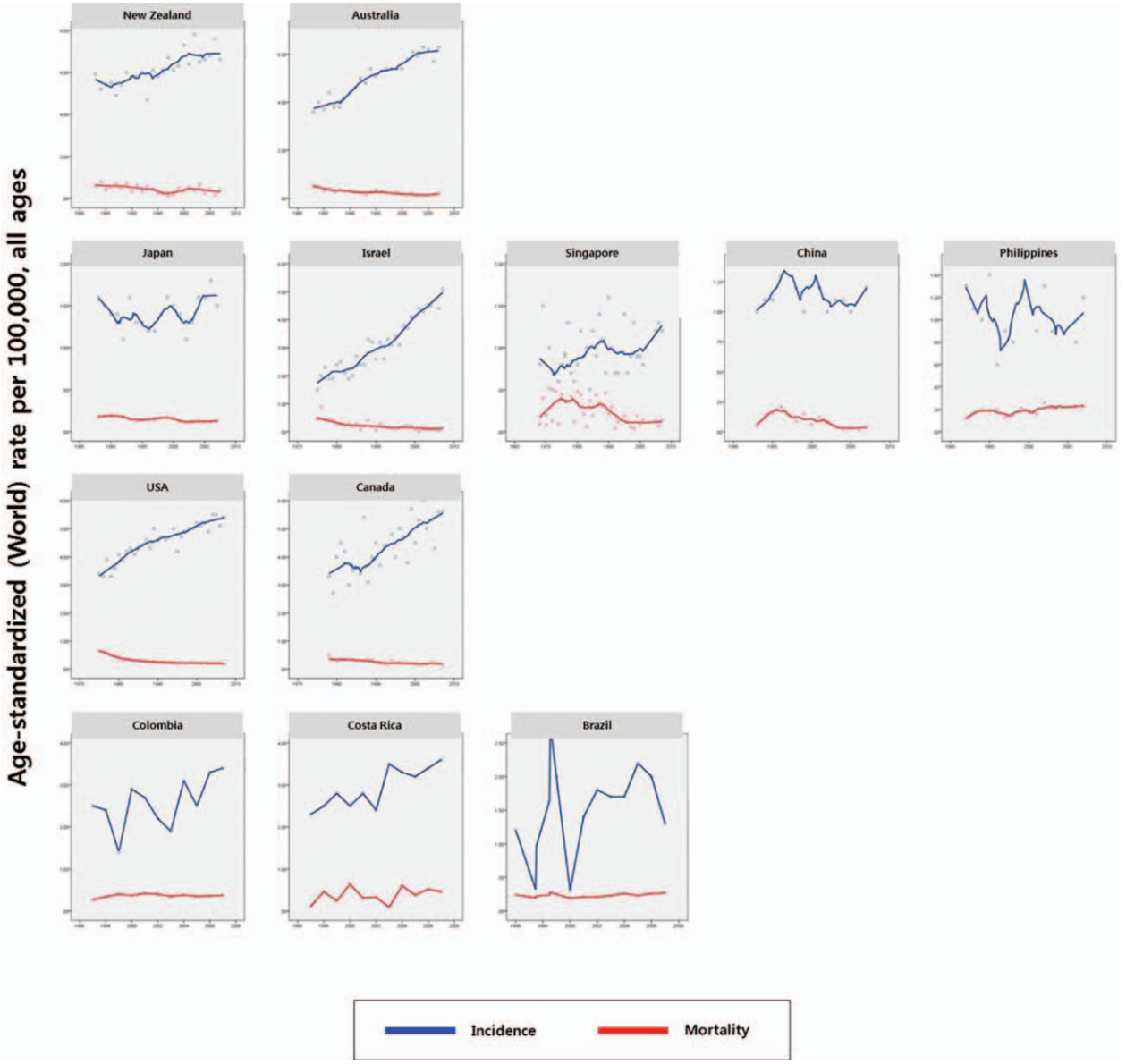

Figure 2. Continued

2008 of 52,322, an incidence of 55,266 was found in 2012, a slight increase. The mortality rate was 10,351 in 2012 compared with 9874 in 2008, and the incidence-mortality ratio of 2012 was 18.7%, which is lower than that found in 2008 (18.9%), suggesting beneficial effects of improvements in both the diagnosis and treatment of TCa.

Although incidence rates varied greatly by geographical region, Western Europe, Northern Europe, and Australia/New Zealand had the highest incidence of TCa, whereas Middle Africa had the lowest. Although a high incidence was noted in Western and Northern Europe, the mortality rate was relatively low, suggesting beneficial effects of a prompt diagnosis followed by effective multimodal treatment and surveillance. However, whereas the overall incidence of TCa was low in Africa and Asia, mortality rates roughly equaled incidence rates, likely because of the lack of effective tools for diagnosis and treatment.[26] A previous study reported that in patients with nonseminomatous germ cell tumors, diagnostic delays were associated with advanced stage at the time of diagnosis and reduced 5-year survival.[27]

In addition to the stabilization of TCa incidence in Denmark, the UK, and Ireland both showed a leveling off of the incidence of TCa over time. However, an increased TCa incidence was noted in the UK in 2012. The steepest increase in incidence was first observed in Southern Europe in 2008, and similar trends have continued. Compared with incidence estimates in 2008, AAPC trends were similar in Asian populations that had the lowest or insignificant AAPCs, except in Israel. China showed a stabilization of incidence compared with an increase in 2008; this finding suggests beneficial effects of improvements in TCa diagnosis and treatment in China. Stabilization of trends was observed in areas where the highest incidence levels were historically observed; in countries such as Asia and Africa, in which TCa incidence has been historically low, incidence began to increase, with TCa becoming an important cause of morbidity and mortality. These findings are consistent with global cancer rates,[28] but an

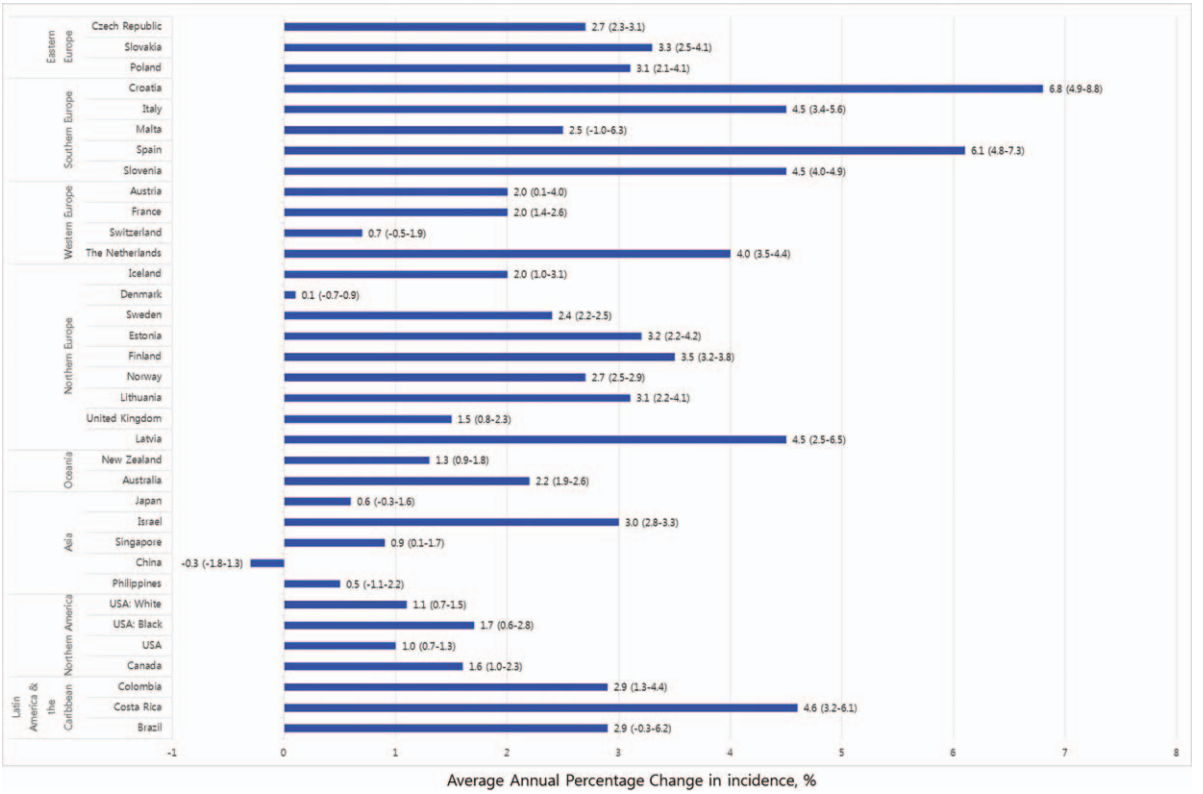

Figure 3. Average annual percent change in testicular cancer (A) incidence and (B) mortality rates for the last 10 years of available data by region in all age groups.

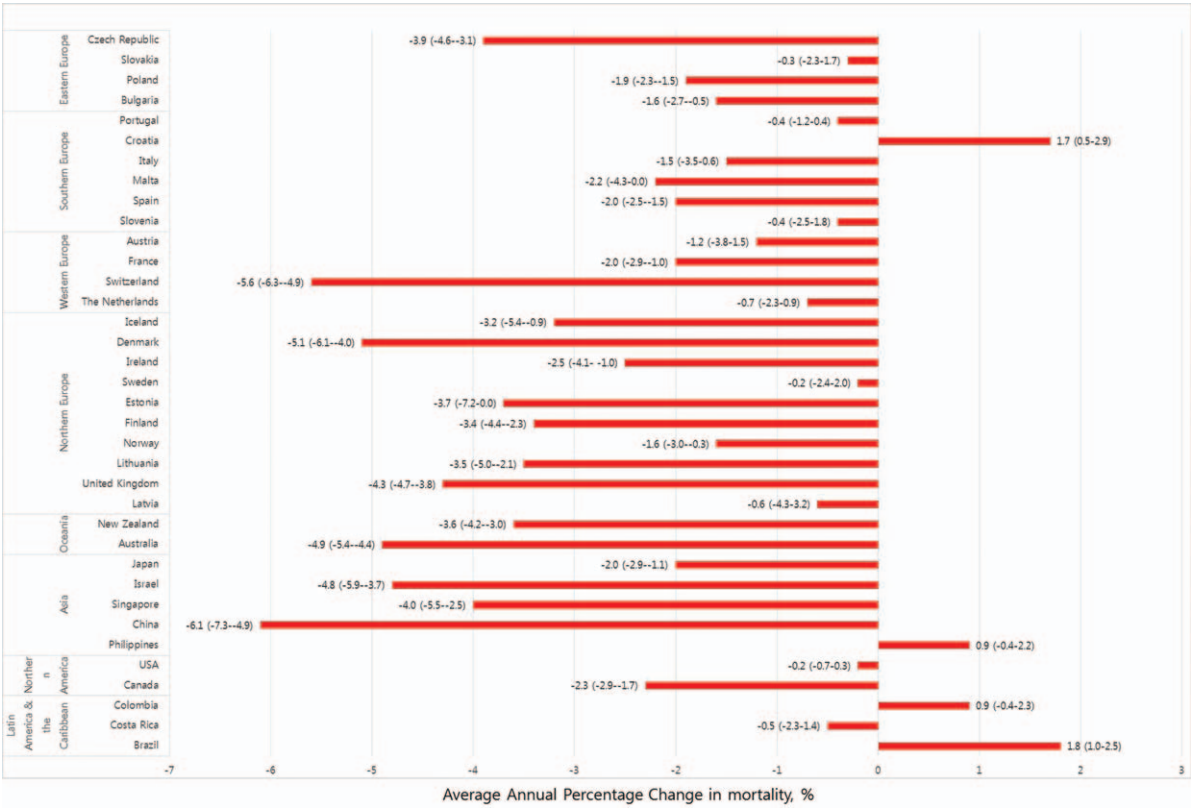

Figure 3. Continued

accurate interpretation of the observed geographical and temporal variations is difficult, and the underlying causative mechanisms are absent.

The introduction of cisplatin-based therapies in the late 1970s brought about a decrease in mortality rates, with survival rates reaching 95%. This decline in mortality rates began in Northern and Western Europe, the United States, and Canada in the 1970s; these rates have now been stabilized, resulting in very low mortality levels of approximately 0.2 per 100,000.[29] However, significant declines were also noted in the United States, Canada, and most of Northern and Western Europe in 2008. Although there have been significant decreases in mortality in Canada, this trend has not continued in the United States or in some Northern and Western European countries.

Although data from GLOBOCAN, assembled from the best sources available, have been used to quantify the incidence and mortality rates of TCa worldwide, the quality and consistency of these data sources may not accurately represent the international profile of TCa cases; this remains a limitation of the present study.

5. Conclusion

TCa incidence rates increased in most countries examined in this study, whereas TCa morality rates declined in most countries, especially in more developed countries. Absolute TCa incidence is likely to increase, as suggested by our data. Mortality rates in highly developed and affluent countries are comparatively low compared with other regions. The latest estimates show that TCa survival is almost 95% in affluent regions; however, of 10,351 TCa deaths, about 80% occurred in Africa, Asia, Central and South America, and the Caribbean. This finding suggests that prompt global actions are needed to expand and improve high-quality diagnosis and treatment resources for cases of TCa to reduce morbidity and mortality, specifically in more resource-deprived countries. Future studies are needed to analyze these epidemiological trends in association with other socioeconomic factors as well as with TCa incidence and mortality data.

Author contributions

Conceptualization: Jee Soo Park, Won Sik Ham.
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Supervision: Won Sik Ham.
Validation: Jongchan Kim, Ahmed Elghiaty.
Writing – original draft: Jee Soo Park.
Writing – review & editing: Jee Soo Park, Won Sik Ham.

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