Global Trends of Prostate Cancer by Age, and Their Associations with Gross Domestic Product (GDP), Human Development Index (HDI), Smoking, and Alcohol Drinking

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Key points

Question: What are the global disease burden and trends of prostate cancer incidence and mortality by age, and their associations with gross domestic product (GDP), human development index (HDI), smoking, and alcohol drinking?

Findings: There was a wide variation in the burden of prostate cancer with the highest mortality found in low-income countries while the highest incidence was observed in high-income countries. We found moderate to high positive correlations for GDP, HDI, and alcohol drinking with prostate cancer incidence, whilst a low negative correlation was observed for smoking. Globally, there was an increasing incidence but decreasing mortality of prostate cancer, and such trends were particularly prominent in Europe. Notably, the incidence increase was also found in the younger population aged <50 years.

Meaning: The modifications on potentially related lifestyle risk factors, including smoking and alcohol drinking, could influence its incidence and mortality. As the incidence increase in prostate cancer is substantial in the young individuals aged less than 50 years, early action on possible preventive measures is needed to slow down this trend.

Abstract

Importance: Prostate cancer is the leading cause of urological malignancy and the second most common cancer in males.

Objective: We aimed to examine the global disease burden and trends of prostate cancer incidence and mortality by age, and their associations with gross domestic product (GDP), human development index (HDI), smoking, and alcohol drinking.

Design: Trend analysis of global and national cancer registries.

Setting: Population-based.

Data sources: We retrieved the Global Cancer Observatory (GLOBOCAN) database for the incidence and mortality of prostate cancer in 2020; the World Bank for GDP per capita; the United Nations for HDI; the WHO Global Health Observatory for prevalence of smoking and alcohol drinking; the Cancer Incidence in Five Continents (CI5), WHO mortality database, for trend analysis.

Main Outcome Measures: We presented the prostate cancer incidence and mortality using age-standardised rates (ASRs). We examined their associations with GDP, HDI, smoking, and alcohol drinking by Spearman's correlations and multivariable regression. We estimated the 10-year trend of incidence and mortality by joinpoint regression analysis with average annual percent change (AAPCs) with 95% confidence intervals (CI) in different age groups.

Results: There was a wide variation in the burden of prostate cancer with the highest mortality found in low-income countries while the highest incidence was observed in high-income countries. We found moderate to high positive correlations for GDP, HDI, and alcohol drinking with prostate cancer incidence, whilst a low negative correlation was observed for smoking. Globally, there was an increasing incidence but decreasing mortality of prostate cancer, and such trends were particularly prominent in Europe. Notably, the incidence increase was also found in the younger population aged <50 years.

Conclusions and Relevance: There was a global variation in the burden of prostate cancer associated with GDP, HDI, smoking, and alcohol drinking. Prostate cancer had an increasing incidence but decreasing mortality. The increasing incidence of prostate cancer in the younger population is worrying and calls for early action on possible preventive interventions.

Keywords

Prostate cancer; incidence; mortality; smoking, alcohol drinking; temporal trend.

Word count: main text 3,200 words + abstract 320 words

1. Introduction

Prostate cancer is the most common urological cancer, inducing a substantial health burden to the world particularly in the developed countries.[1] In 2020, prostate cancer contributed to 14.1% and 6.8% of all cancer cases and deaths among males.[2] Age, race/ethnicity, geography, family history and gene changes are well-established risk factors of prostate cancer, however, whether some preventable lifestyle factors such as smoking and alcohol drinking would increase the risk of prostate cancer remains controversial.[3,4] Whether lifestyle factors have any implications on prostate cancer mortality is also unknown. Since international guidelines recommend prostate cancer screening at the age of 50 years for average-risk men[5,6], it is important to understand the most updated global trends of prostate cancer for individual countries by different age groups (≥ 50 years vs. < 50 years).

We have previously conducted a study on the global trend of prostate incidence and mortality using figures from the Global Cancer Observatory (GLOBOCAN) database (2012), Cancer Incidence in Five Continents (CI5) (up to 2007), and the WHO mortality database (up to 2012) in 36 countries.[7] A more recent study conducted by Culp *et al.* reported the global pattern in prostate cancer incidence and mortality rate used data from GLOBOCAN database in 2018 and conducted the time trend analysis of incidence in 44 countries.[8] However, none of these studies had reported the trends of prostate cancer by age. In the current study, we investigated the global incidence and mortality trends of prostate cancer based on the most updated figures from the GLOBOCAN (2020). We further determined whether the temporal trends differ by different age groups using incidence and mortality data up to 2017 in 48 countries. We also investigated the associations between smoking, alcohol drinking and prostate cancer incidence and mortality. We believe the findings will inform the development of tailored preventive measures on prostate cancer for individual countries.

2. Methods

2.1. Source of data

We retrieved GLOBOCAN database for the most updated incidence and mortality of prostate cancer in 2020.[2] We extracted data on gross domestic products (GDP) per capita from the World Bank. We used the human development index (HDI) for each country from the United Nations, where HDI of <0.550, 0.550-0.699, 0.700-0.799, and ≥0.800 were considered as Low, Medium, High, and Very High HDI, respectively.[9] We searched the WHO Global Health Observatory data repository for age-adjusted prevalence of current smoking and total amount of alcohol drinking in 2010 for each country. Smoking was defined as the prevalence of current use of any smoked tobacco product. Alcohol drinking is defined as the total amount of alcohol consumed per person per year. As for the incidence trend analysis for prostate cancer, we searched the Cancer Incidence in Five Continents (CI5) volumes I-XI.[10] The CI5 had wide coverage of the global population with cancer registries of high quality. The CI5 contained global, regional and national cancer registries, and presents incidence data by validating the occurrence of each new cancer case reported within a specific time frame. Cancer incidence-related figures were available in the database, including the proportion of cases registered, the rate of cases microscopically reported, and incidence by age primary tumour site, region, and year. In terms of mortality trend analysis for prostate cancer, we employed the WHO mortality database to obtain mortality figures for each country.[11] The cancer mortality figures were collected from the national civil cancer registering system. The registering system recorded clinically certified cancer deaths and their causes at a local level and national level and reported to WHO annually. To ensure the comprehensiveness and accuracy of the mortality data, the WHO mortality database only published figures with a quality level of medium or above.[12] We also searched Surveillance, Epidemiology, and End Results (SEER) Programme and the Nordic Cancer Registries (NORDCAN) for the most updated cancer incidence for the United States

(US) and Northern European nations.[13-15] All cancer incidence and mortality figures were standardized by age using the Segi–Doll world reference population for different countries to calculate age-standardized rate (ASR).[16]

ASR is a weighted average of the age-specific rates per 100 000 persons, where the weights are the proportions of persons in the corresponding age groups of the standard population. Details regarding the data sources for analysis are presented in the **Appendix**.

2.2. Statistical analysis

We first presented the incidence and mortality of prostate cancer in 2020 in a descriptive manner. The correlations between the HDI, GDP, smoking, and alcohol drinking and prostate cancer incidence and mortality, were examined using Spearman's correlation coefficient. Further multivariable regression analysis was conducted to confirm their associations. We performed the joinpoint regression to examine the temporal trend in incidence and mortality of prostate cancer for the recent past decade in each country.[17] We had previously used this approach to examine the epidemiologic trends of incidence and mortality for other types of cancer.[18-20] We calculated the Average Annual Percent Change (AAPC) with its 95 % confidence interval (CI) in regression. We conducted a logarithmic transformation on the incidence and mortality data, and a binomial approximation on the corresponding standard errors. We apportioned weights equivalent to each segment's length for the specified timeframe.[21] We excluded countries with "missing" or "zero" values in any year of the recent past ten years for the trend analysis. We adopted a maximum of one joinpoint in the analysis as recommended by the analysis guidelines. We calculated the AAPCs as an average of Annual Percent Changes (APCs) by geometric weighting in subgroups of different ages (aged ≥ 50 years, aged < 50 years) and regions. All p values less than 0.05 were considered significant in the statistical tests.

3. Results

3.1. Incidence and mortality rates of prostate cancer in 2020

There were a total of 1,414,259 new cases of prostate cancer and 375,304 related deaths reported in 2020. The global ASR of incidence was 30.7 per 100,000 persons and a thirteen-fold variation was observed between regions (**Figure 1**). The highest incidence was reported in Northern Europe (ASR 83.4), Western Europe (ASR 77.6), Caribbean (ASR 75.8), Australia and New Zealand (ASR 75.8) and Northern America (ASR 73.0); and high-income countries (ASR 65.4). The global ASR of mortality was 7.7 per 100,000 , a nine-fold variation was found between regions. The highest mortality was reported in the Caribbean (ASR 27.9), Middle Africa (ASR 24.8), Southern Africa (ASR 22.0), Polynesia (ASR 20.5), and Western Africa (ASR 20.2); and low-income countries (ASR 11.6). Detailed figures on regional incidence and mortality of prostate cancer can be found in **Appendix.**

3.2. Association with GDP, HDI, smoking, and alcohol drinking.

Moderate to high positive correlations were observed for GDP (*r* 0.53), HDI (*r* 0.50), and alcohol drinking (*r* 0.61) with prostate cancer incidence, whilst a low negative correlation was observed for smoking (*r* -0.30, **Figure 2**). As for mortality, very low to low negative correlations were observed for GDP (*r* -0.17), HDI (*r* -0.22), and smoking (*r* -0.25), whilst a low positive correlation was observed for alcohol drinking (*r* 0.30). In the regression analysis, a higher HDI and amount of alcohol drinking were positively associated with a higher incidence of prostate cancer, whilst the association was inverse for prevalence of smoking. For the mortality of prostate cancer, there was a positive association of the amount of alcohol drinking, whilst there was a negative association for the level of HDI and prevalence of smoking (**Appendix**).

3.3. Temporal trends of prostate cancer

The incidence and mortality trends of each age group and country and the corresponding results from the joinpoint regression analysis are presented in **Appendix**. The AAPC of prostate cancer incidence and mortality are discussed as follows.

3.3.1. Incidence trend

Most countries studied showed an increasing trend in incidence of prostate cancer (**Figure 3**). Among the 20 countries having a significant increase in incidence, 12 of them were from Europe. The increase was most evident in Belarus (AAPC 9.68, 95% CI 8.47 to 10.91), Bulgaria (AAPC 8.66, 95% CI 4.89 to 12.57), Japan (AAPC 7.98, 95% CI 5.81 to 10.20), Estonia (AAPC 7.78, 95% CI 5.28 to 10.34), and Korea (AAPC 7.16, 95% CI 4.75 to 9.62). Only seven countries showed a significant decrease in incidence, with Austria (AAPC -4.88, 95% CI -5.55 to -4.21), the US (AAPC -4.15, 95% CI -6.88 to -1.34), and Iceland (AAPC -3.83, 95% CI -6.03 to -1.58) presenting the most significant decrease.

3.3.2. Mortality trend

Unlike incidence, the majority of the countries showed a decreasing trend in the mortality of prostate (**Figure 4**). Among the 23 countries having a significant decrease in mortality, 15 of them were from Europe. The decrease was most evident in France (AAPC -4.01, 95% CI -4.30 to -3.73), Ireland (AAPC -3.46, 95% CI -4.35 to -2.56), and Italy (AAPC -3.40, 95% CI -3.70 to -3.09). However, five countries showing a significant increase in mortality, including the Philippines (AAPC 11.52, 95% CI 9.22 to 13.86), Thailand (AAPC 6.67, 95% CI 5.58 to 7.78), Belarus (AAPC 3.13, 95% CI 2.01 to 4.26), Russia (AAPC 2.26, 95% CI 1.88 to 2.65) and Bulgaria (AAPC 1.46, 95% CI 0.14 to 2.80).

3.3.3. Incidence of prostate cancer in younger versus older individuals

Regardless of age (≥50 years versus <50 years), the majority of the countries had an increasing incidence of prostate cancer globally. For the men aged ≥50 years, 19 countries had a significant increase in incidence, and 12 of them were from Europe. The increase was most evident in Belarus (AAPC 9.69, 95% CI 8.50 to 10.89), Slovakia (AAPC 6.63, 95% CI 5.84 to 7.43), Japan (AAPC 7.89, 95% CI 5.70 to 10.13, Bulgaria (AAPC 8.78, 95% CI 5.20 to 12.49), and Estonia (AAPC 7.70, 95% CI 5.11 to 10.35). Eight countries showed a significant decrease in incidence, with the US (AAPC -4.02, 95% CI -6.76 to -1.20), Iceland (AAPC -3.73, 95% CI -6.00 to -1.41), and Austria (AAPC -4.91, 95% CI -5.59 to -4.23) presenting the most significant decrease.

For the male population aged <50 years, 18 countries had a significant increase in incidence, and 11 of them were from Europe (**Figure 5**). The increase was most evident in Japan (AAPC 25.93, 95% CI 8.61 to 46.02), Estonia (AAPC 25.69, 95% CI 7.42 to 47.08), Ecuador (AAPC 20.16, 95% CI 10.14 to 31.08), Lithuania (AAPC 16.52, 95% CI 1.85 to 33.30), and Czech (AAPC 15.51, 95% CI 8.93 to 22.49). The AAPCs were generally higher than those in the older population. Only two countries showed a significant decrease in incidence, including the US (AAPC -7.89, 95% CI -9.27 to -6.49) and Austria (AAPC -3.99, 95% CI -5.90 to -2.03).

4. Discussion

We performed an up-to-date analysis on global burden of prostate cancer, as well as its temporal pattern among different age groups in using high-quality cancer registries data for individual countries. We also investigated their associations between GDP, HDI, smoking, and alcohol drinking. We discussed the major findings as follows.

4.1. Variation in disease burden and its associated factors

4.1.1. Disease distribution and GDP/HDI

In 2020, the highest incidence of prostate cancer was reported primally in high-income region, such as Northern Europe, Western Europe, Australia and New Zealand, and Northern America. Countries with higher incidence of prostate cancer also had higher GDP and HDI. Several factors may have contributed to this phenomenon observed. Countries with high GDP and HDI usually had higher availability of screening and diagnostic ascertainment, prevalence of related risk factors, and capacity of cancer registries for prostate cancer.[7] In addition, ethnic genetics may also play a role as prostate cancer occurs more often in non-Hispanic whites than in Asian-American and Hispanic/Latino.[3,4] However, for mortality, the highest rate was mainly found in low-income regions, such as the Caribbean, Middle Africa, Southern Africa, and Western Africa. We found in the analysis that the mortality of prostate cancer was inversely associated with GDP and HDI. Possible explanations include higher stage of disease or more metastatic disease upon diagnosis due to the limited access to facilities of screening and the lack of treatment options, including radical prostatectomy, hormonal therapy, and radiation therapy in low-income countries.[22] According to a recent study, the participation rate of prostate cancer screening was only 5% in Kenya.[23] The low level of awareness and the existence of misconceptions which predominantly associated prostate cancer with sexual behaviours were also reported in the study.[23]

4.1.2. Smoking

Previous findings of the effect of smoking on the risk of prostate cancer have been inconsistent.[3,4] The results of current studies showed the prevalence of smoking was associated with a decreased risk of prostate cancer, which was also reported by previous studies.[24,25] Possible explanation was more developed countries usually had a lower prevalence of smoking and also provided better cancer screening services. At individual level, the non-smokers tend to be with greater health consciousness and participating in PSA screening. For instance, in a study of 37,325 males from the US, the uptake rate of screening was lower among the smokers (46.1%) than the non-smokers (60.8%).[26] However, there was evidence showing that smoking was associated with an increased risk of advanced prostate cancer.[24,25] Smoking may increase the level of serum oestrogen metabolites, which have been postulated to induce a more advanced prostate cancer.[27]

4.1.3. Alcohol Consumption

The association between alcohol drinking and risk of prostate cancer has been controversial. A meta-analysis of 47 studies reported a positive association between alcohol drinking and the risk of prostate cancer (RR: 1.16, 95% CI: 1.06–1.26).[28] However, another meta-analysis indicated no evidence of any substantial effect of alcohol drinking and risk of prostate cancer. The current analysis shows countries with a larger amount of alcohol consumption had higher incidence and mortality of prostate cancer, which was also supported by evidence that there was an association between alcohol drinking and the risk of advanced or fatal prostate cancer.[29,30] Another study also found Liquor, but not wine or beer, consumption was positively associated with prostate cancer.[31] Alcohol drinking may increase the risk of prostate cancer by producing the carcinogen, ethanol or acetaldehyde, causing damage to DNA.[32,33] The effect of alcohol on prostate cancer was also mediated by increasing the level of oestrogens and decreasing androgens and sex hormone-biding globulin.[34,35]

4.2. Global trend of incidence and mortality

Although there was a wide variation in the burden of prostate cancer across regions, we observed an overall increasing trend of the incidence but decreasing mortality of prostate cancer for the past decade. The substantial increase in the incidence of prostate cancer, especially among the developed countries, maybe a reflection of the increasing use of prostate-specific antigen (PSA) blood tests for screening and transurethral resection of the prostate.[36] Since, the approval of PSA test for monitoring disease progression, and later for prostate cancer screening among the average-risk males, the incidence of prostate cancer has been increasing in Western counties.[37,38] Although screening could be the key driver to the increasing incidence of prostate cancer, other related factors may include the increasing prevalence of environmental risk, unhealthy lifestyle habits, and metabolic diseases. The explanations for decreasing mortality trends may include early detection of prostate cancer by the extensive use of PSA screening and advances in treatment and surveillance for prostate cancer these years.[39] However, although it is well-established that PSA screening tests can reduce the mortality of prostate cancer mortality rate[40,41], there has been a discussion on overdiagnosis and overtreatment.[42-44] As a result, the US Preventive Services Task Force (USPSTF) did not recommend PSA screening in 2008 and 2012.[45,46] However, a recent study shows reductions in PSA screening were responsible for the recent increase in metastatic prostate cancer at diagnosis in the US, which needs attention on revisiting the screening policies of prostate cancer.[47]

4.3. Increasing incidence in the younger population

We expected an increasing incidence of prostate cancer among the population aged 50 years and older, however, a notable finding of this study is the incidence increase was also observed in the younger population aged < 50 years (among whom the PSA screening test was not recommended) in a substantial number of countries. The increasing incidence of prostate cancer in the younger population may be attributable to the increasing prevalence of risk factors related to prostate cancer among the younger population. Previous literature has identified alcohol consumption[48], obesity[49], central obesity[50], and metabolic syndrome[51] as potential risk factors for prostate cancer. The 2017 National Survey on Drug Use and Health in the US shown 55.9% of those aged 18 to 25 years reported drinking alcohol during the four weeks.[52] The WHO reported the global prevalence of childhood obesity has increased from 4% to 18% during 1975-2016.[53] We have previously identified a more drastic rise in the prevalence of central obesity (16.3 to 33.9% vs. 43.6 to 57.9%) and metabolic syndrome (7.6% to 16.5% vs. 33.0% to 35.2%) in young adults aged 15-40 years than those among the older population aged > 40 years from 1985 to 2015.[54, 55] It is postulated that all these factors may have contributed to the recent prominent rise in incidence of prostate cancer among younger individuals.

4.4. Strengths and limitations

We provided the most up-to-date analysis on the worldwide incidence and mortality of prostate cancer, as well as their temporal pattern by age for individual countries. We collected the incidence and mortality data from international and national cancer registries of high quality. However, we admitted there existed some limitations in the study. Firstly, there could be variations in reporting cancer cases between high-income regions and low-income regions. The increased use of screening may also have identified more asymptomatic prostate cancers predominantly in developed countries while the cancer incidence could have been underestimated in developing countries. Secondly, the data regarding some other risk factors, such as dietary risk factors and obesity, were not available for the association analysis with incidence and mortality of prostate cancer. Thirdly, the comparability between different countries may be limited by the variation in cancer reporting systems by different countries and periods. Lastly, we were unable to analyse the temporal trend of prostate cancer by tumour grading and staging, which is important in clinical practice.

4.5. Implications

The incidence of prostate cancer remained high and increasing especially among western countries in the recent past ten years. With the increased use of PSA screening tests and the growth of ageing population, the incidence of prostate cancer is expected to increase further, especially for countries with ongoing population-based screening programmes for prostate cancer. The modifications on potentially related lifestyle risk factors, including smoking and alcohol drinking, could influence its incidence and mortality. As the incidence increase in prostate cancer is substantial in the young individuals aged less than 50 years, early action on possible preventive measures is needed to slow down this trend.

5. Conclusions

There was a global variation of incidence and mortality of prostate cancer in 2020. The highest incidence was reported in high-income countries whilst the highest mortality was observed in low-income countries. There were varying associations between GDP, HDI, smoking, and alcohol drinking, and incidence and mortality of prostate cancer. We found an increasing incidence but decreasing mortality of prostate cancer globally, and such trends were particularly prominent in Europe. We need to pay extra attention to the increasing incidence of prostate cancer in the younger population. More extensive preventive measures for prostate cancer are warranted in these populations.

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Table and Figure Legends

Figure 1 - The global burden of prostate cancer in 2020, males, all ages.

Figure 2 - Correlations with GDP, HDI, smoking, and alcohol drinking.

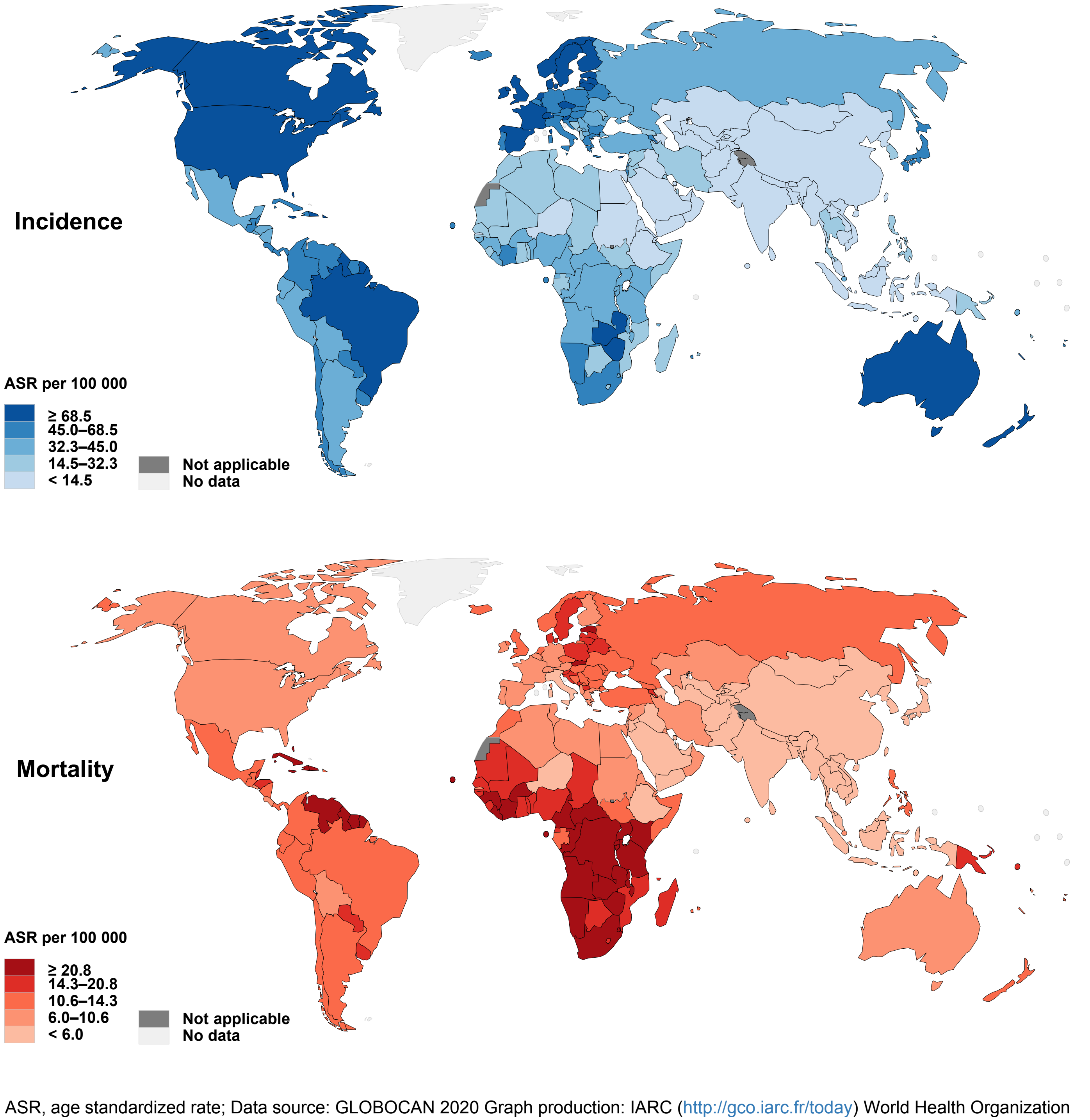
Figure 3 - The AAPC of the incidence of prostate cancer in males aged 0-85+ years.

Figure 4 - The AAPC of the mortality of prostate cancer in males aged 0-85+ years.

Figure 5 - The AAPC of the incidence of prostate cancer in males aged < 50 years.

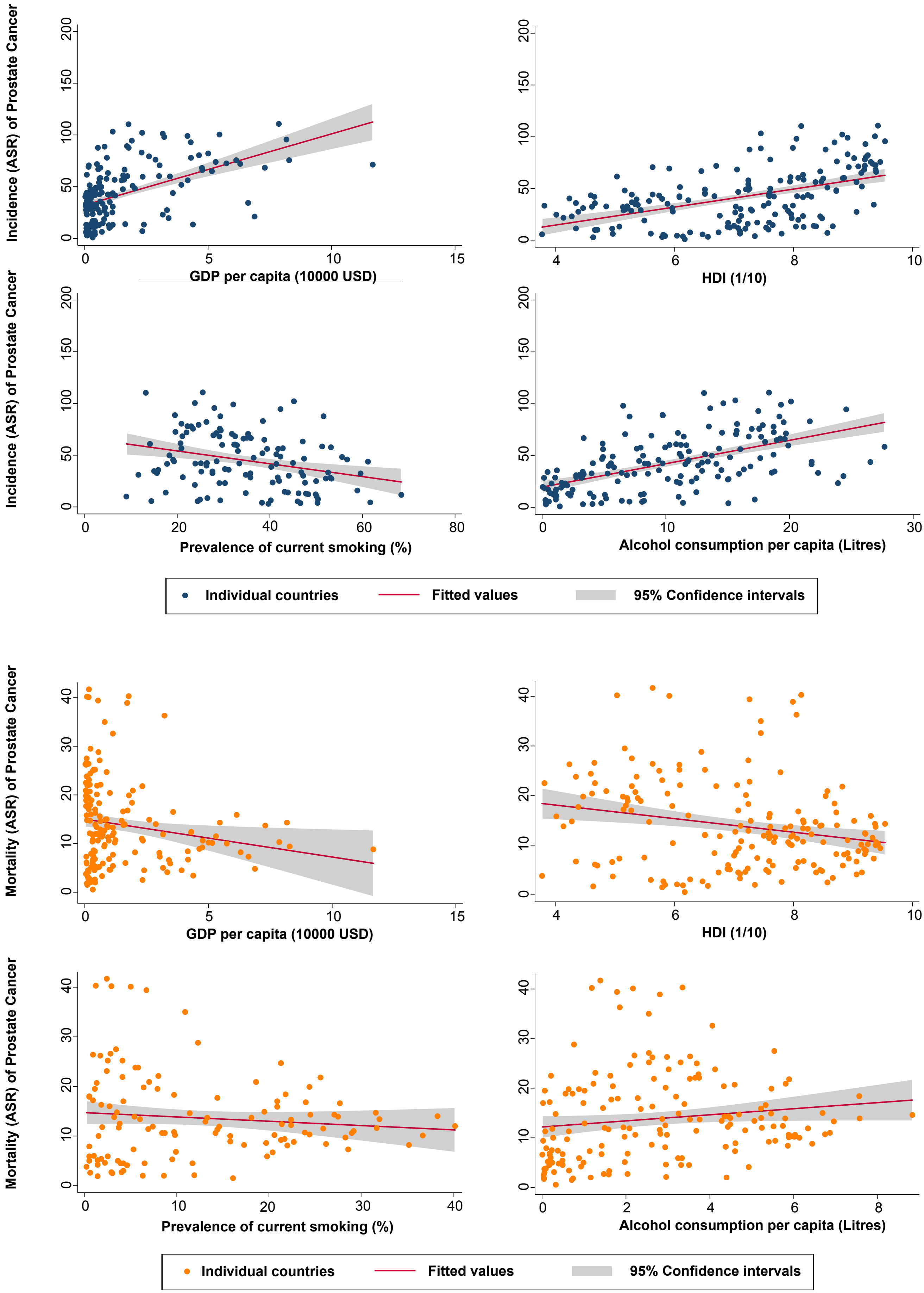
Appendix – Supplementary data.

Figure 1 - The global burden of prostate cancer in 2020, males, all ages.



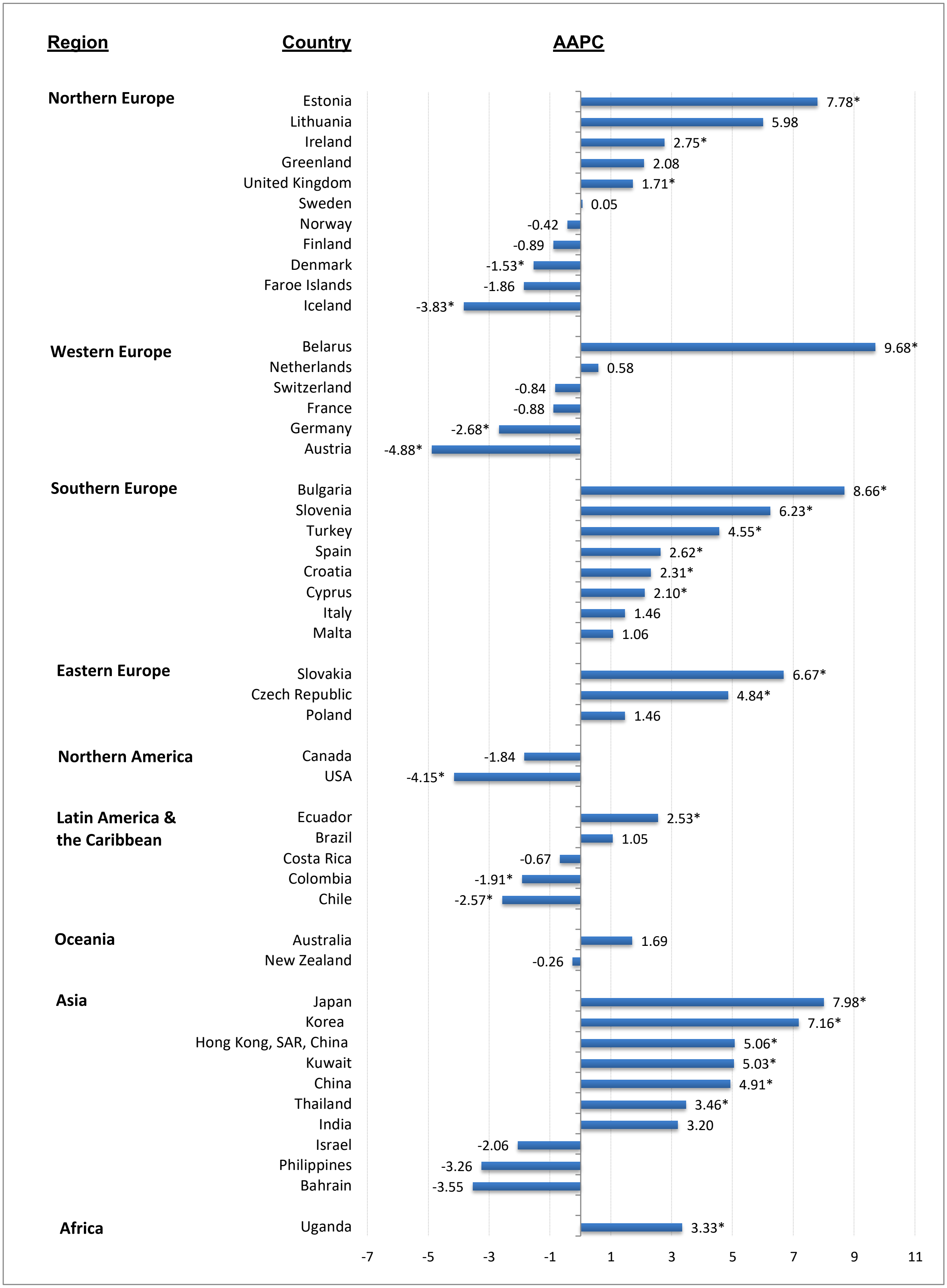
ASR, age standardized rate; Data source: GLOBOCAN 2020 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization

Figure 2 - Correlations with GDP, HDI, smoking, and alcohol drinking.



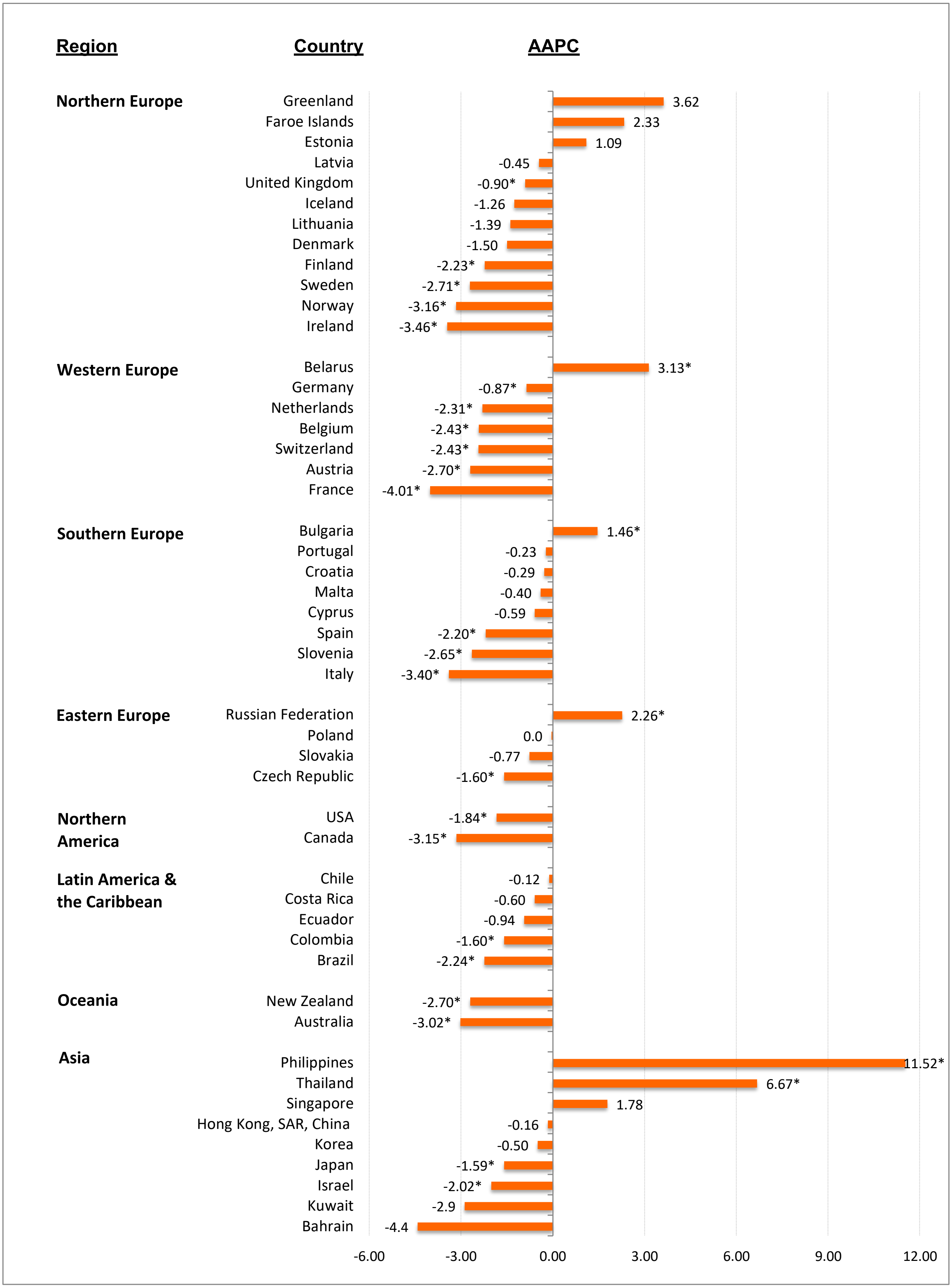
ASR, age-standardized rate; GDP, gross domestics product; HDI, human development index.

Figure 3 - The AAPC of the incidence of prostate cancer in males aged 0-85+ years.



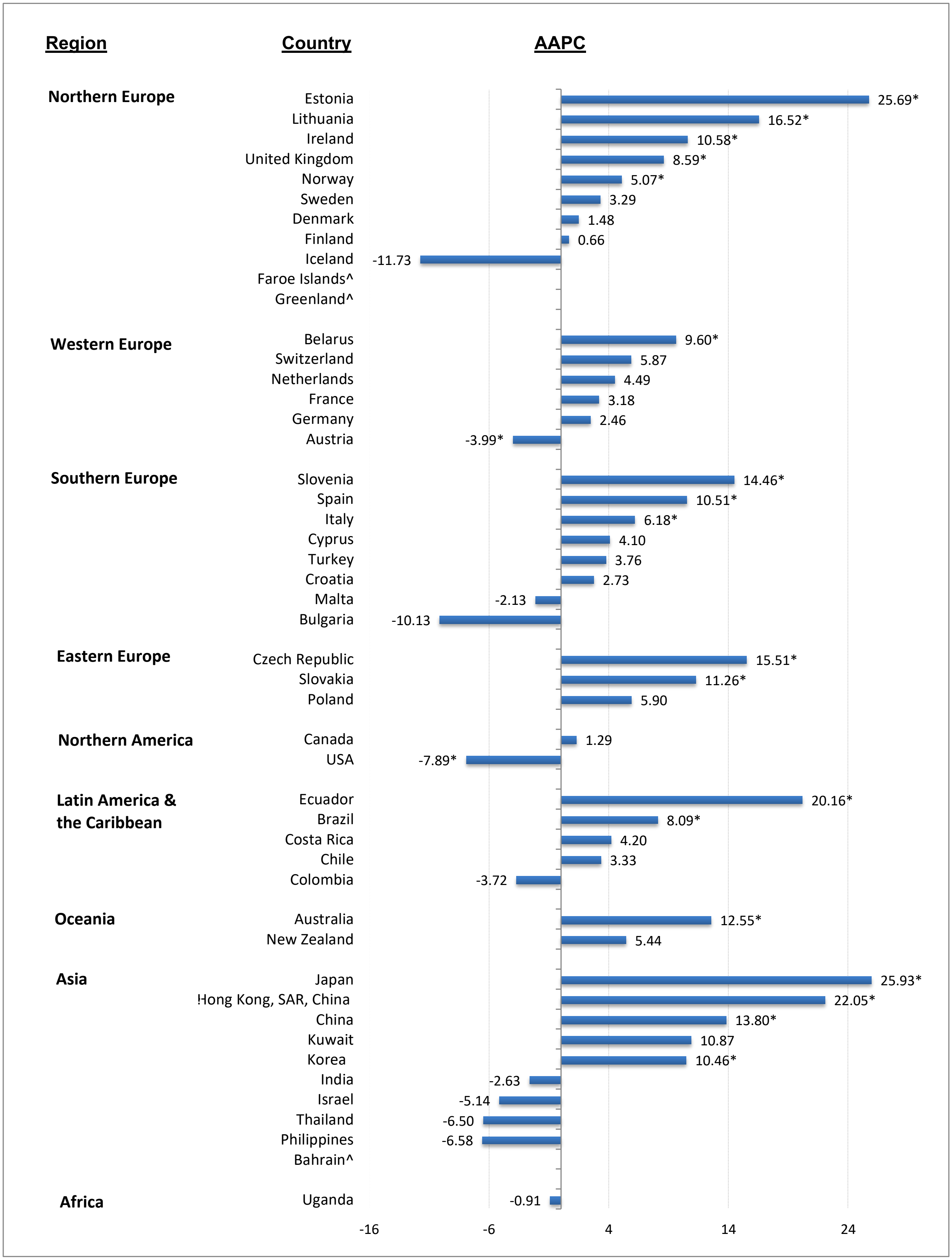
AAPC, average annual percent change; SAR, special administration region; *, statistically significant in the joinpoint regression.

Figure 4 - The AAPC of the mortality of prostate cancer in males aged 0-85+ years.



AAPC, average annual percent change; SAR, special administration region; *, statistically significant in the joinpoint regression.

Figure 5 - The AAPC of the mortality of prostate cancer in males aged < 50 years.



AAPC, average annual percent change; SAR, special administration region; *, statistically significant in the joinpoint regression; ^, AAPC was not available due to zero values encountered.