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Article

Incidence, mortality, disability-adjusted life years, and trends of prostate cancer in Mexico from 2000 to 2019: Results from the Global Burden of Disease Study 2019

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Simple Summary: Worldwide, prostate cancer (PC) causes high morbidity and mortality. Thus, to develop effective strategies for prevention, diagnosis, and control of this disease is fundamental to provide updated and reliable estimations of PC burden both nationally and subnationally. Herein, we analyzed data from the Global Burden of Disease study to estimate PC incidence, mortality, and disability-adjusted life years in Mexico at the national and subnational levels from 2000 to 2019. Our results shows that PC was the top ranked cause of death among malign neoplasms in males from Mexico during 2019. Males from 70 to 79 years of age were the most affected by PC and there was an increasing trend in the burden of this cancer. There was substantial subnational heterogeneity that suggest a differential geographical patterns of change. These results provide both comprehensive and comparable estimates to assist the effort to reduce health loss due to PC in Mexico.

Abstract: In 2019, the Global Burden of Disease (GBD) estimated that prostate cancer (PC) was the 16th cause of death globally in males. In Mexico, PC epidemiology has been reported for a selected number of metrics and years, although without including the most up-to-date estimates. Herein, we describe and compare the burden and trends of PC in Mexico and its 32 states from 2000 to 2019. For this, we extracted online available data from the GBD 2019 to estimate the crude and age-

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standardized rate (ASR per 100,000 people) of incidence, mortality, and disability-adjusted life years (DALYs). In Mexico, PC caused 27.1 thousand (95% uncertainty intervals, 20.6-36.0 thousand) incident cases, 9.2 thousand (7.7-12.7 thousand) deaths, and 161.5 thousand (122.7-219.5 thousand) DALYs in males of all ages in 2019. Among states, Sinaloa had the greatest ASR of incidence and Guerrero the highest values of deaths and DALYs. The burden of PC showed an increasing trend, although the magnitude of change differed between metrics and locations. We found both an increasing national trend and subnational variation in the burden of PC. Our results confirm the need for updated and timely estimates to design effective diagnostic and treatment campaigns in locations where the burden of PC is the highest.

Keywords: Age-standardized rate; Burden of disease; Cancer epidemiology; Malign neoplasm; Sociodemographic index; Subnational heterogeneity

1. Introduction

Prostate cancer (PC) is defined as the uncontrolled growth of cells from the glandular epithelium that acquire the ability to scatter [1]. As a disease entity, PC is marked by extensive clinical and biological heterogeneity. Therefore, the clinical presentation of this malignancy may vary from relatively indolent organ-confined to highly invasive and rapidly progressive tumors [2]. Although the only well-known risk factors for PC are older age, black race, and a familiar history of the neoplasm [3], there is some evidence that excess body fat, adult attained height, high amounts of dietary fat intake, consumption of dairy products, and diets high in calcium increase the risk of developing PC [4, 5]. In addition, other factors have been associated with both a higher incidence and difference in the mortality of PC, including socioeconomic and educational disparities, access and quality of care, and differences in the type of treatment [6].

PC is a major cause of morbidity and mortality in men. This neoplasm is the most common noncutaneous malignancy [7] and the second most frequently diagnosed cancer among men worldwide [8]. According to the most recent iteration of the Global Burden of Disease study (GBD 2019), the age-standardized rate of PC was ranked as the 16th cause of death for males globally in 2019 [9]. In addition, during this same year, there were an estimated 1,410 thousand incident cases and 487 thousand deaths due to PC [10]. In low-income countries, the importance of this malady is even more dramatic. In Latin America, the burden of PC follows the global trend, as reports indicate that PC is the most diagnosed malign neoplasia and the second leading cause of cancer death [11]. Increased public awareness and the ease of prostate-specific antigen (PSA) testing have placed PC as a public health priority in low- and middle-income settings [12].

Previous reports have demonstrated international heterogeneity in the burden of PC across nations [13, 14], including countries from Latin America [15]. In the Americas, this geographical and temporal variation might be a reflection of national differences in diagnostic and treatment practices, access to healthcare, registration, and awareness [11]. Consequently, there is a need for a further detailed characterization of the local burden of PC. This information will provide a better overview of the patterns and trends of this disease, especially in countries with high incidence and mortality. This is the case in Mexico, where PC was the 4th-ranked cause of death among 29 groups of cancers in males of all ages during 2019 [10]. Even though previous studies have described the burden of PC in Mexico, these have used a narrow scope that included only a limited number of years, population coverage, localities, and epidemiological metrics, thus providing a partial or too broad geographical coverage of the burden and trends of this disease [16, 11, 17, 18]. In addition, regardless of the importance of PC, Mexico does not possess a malignant tumor follow-up registry [19]; thus, providing timely and accurate epidemiological estimates represents an opportunity to inform updated and reliable

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information for effective health system planning and appropriate resource allocation to attend to this malign neoplasm. We herein, using estimates from the GBD 2019, present a detailed and comparative epidemiological description of the burden and trends of PC in Mexico at the national and subnational levels and by age group from 2000 to 2019.

2. Methods

2.1 Overview

The present study was performed using results from the Global Burden of Disease Study 2019 (GBD 2019). The GBD published the most comprehensive and systematic assessment of health loss caused by 369 diseases and injuries and their associated risk factors in 204 countries and territories from 1990-2019 [20]. The GBD provides an updated descriptive epidemiology of an exhaustive list of diseases and injuries, integrating fatal and nonfatal outcomes for a hierarchical cause list. A detailed description of the approach and modeling steps of the GBD are provided elsewhere [9]. The GBD publications complied with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations [21].

2.2 Data input sources and case definition

For the cancer burden estimation, the GBD used several types of data sources, including vital registration systems, national cancer registry systems, and verbal autopsy data. A detailed list and information regarding data input sources used in the estimation process are available on the Global Health Data Exchange (GHDx) Data Input Sources Tool (http://ghdx.healthdata.org/gbd-2019/data-input-sources). To calculate the burden of PC in Mexico, the GBD used 166 data input sources that corresponded to Vital Registration Death Data, household surveys, censuses, and Multiple Indicator Cluster surveys from the National Institute of Statistics and Geography (INEGI) available from 1980 to 2017. For this study, PC cases for incident and mortality data were identified as codes C61-C61.9, D07.5, D29.1, D40.0, Z12.5, Z80,42, and Z85.46 according to the International Code of Diseases 10th (ICD10) and codes 185-185.9, 222.2, 236.5, V10.46, and V76.44 for ICD9 [22].

2.3 Estimation of prostate cancer burden

A detailed description of the PC incidence and mortality estimates for the GBD have been previously published in a paper focused on 29 cancer groups [22]. GBD organizes diseases and injuries in a comprehensive hierarchy of levels, which includes neoplasms as one of 22 groups of level 2 and 30 cancers among level 3 groups [10]. The modeling framework and a detailed flowchart including specific codes for the cancer burden estimation in the GBD are provided in the following web address: http://ghdx.healthdata.org/gbd-2019/code/cod-2. In brief, as described previously in a study of gastric cancer that used GBD estimates [23], the modeling steps included 1) calculating the mortality-to-incidence ratio (MIR) using data sources that included incidence and mortality for PC, 2) collecting the incidence of PC for each cancer registry, 3) estimating PC mortality by multiplying the incidence data by the corresponding MIR, 4) including PC mortality sets into the PC cause of death database using the Cause of Death Ensemble model (CODEm) and processing the data to estimate the cancer-specific mortality of PC, and 5) calculating the incidence of PC by the estimated cancer-specific mortality of PC and MIR. All estimations were made by location, year, and age group with 95% uncertainty intervals (UIs) reported. For all estimates, uncertainty was propagated through each modeling step, with UIs representing the 2.5th and 97.5th percentiles of the distribution of 1,000 random draws performed at each step [10].

2.4 Reporting standards

To estimate the PC burden in Mexico, we used data publicly available from the online GHDx query tool [24]. We collected data at the national level and for the 32 states,

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including Mexico City, for the period from 2000 to 2019. To summarize the PC burden, we used the crude and age-standardized rate (ASR) per 100,000 people for the incidence, mortality, and disability-adjusted life-years (DALYs) from 2000 to 2019 in males. The DALYs incorporate both the fatal and nonfatal burden of PC and correspond to the sum of years lived with disability (YLDs) and years of life lost (YLLs) [25]. To estimate YLDs, the disability weight (ranging from 0 "no health loss" to 1 "dead") caused by a specific sequelae disease is multiplied by the prevalence of such disease, whereas the YLLs represent the sum of years of life lost due to premature mortality multiplied by the standard life expectancy [26]. In addition, the trends of PC burden were assessed by plotting the annual estimates for the time series from 2000 to 2019 and by estimating the percentage change in crude and ASR of the incidence, mortality, and DALYs during the last decade (2010 to 2019).

2.5 Analysis of prostate cancer burden and sociodemographic index

To assess the association between the burden of PC and a metric indicating the specific position of a location within a spectrum of development, we used the sociodemographic index (SDI), which represents a composite indicator that includes fertility, education, and income [26]. The SDI is stratified into quintiles and ranges from 0 to 1, indicating the theoretical minimum and maximum level of development relative to these relevant health outcomes. For our study, we used subnational SDI estimates for Mexico during 2019 [27]. We performed a non-parametric Spearman correlation analysis to assess the linear association between the subnational SDI and the incidence, DALYs, and mortality. We considered a $p < 0.05$ as significant. All figures were constructed with Prism 9. (GraphPad, Software Inc. CA, USA).

3. Results

3.1 National and subnational estimates of prostate cancer burden in 2019

In Mexico, there were 27.1 thousand (95% UI, 20.6 to 36.0 thousand) incident cases of PC and 9.2 thousand (95% UI, 7.7 to 12.7 thousand) deaths in 2019 for men of all ages. By the same year, the age-standardized incidence and mortality rates were estimated at 52.3 (40.0 to 70.1) cases and 19.4 (14.7 to 26.7) deaths per 100,000 people, respectively. In addition, PC was estimated to cause 161.5 thousand (122.7 to 219.5 thousand) DALYs in 2019, with an age-standardized rate estimated at 319.5 (244.1 to 432.5) DALYs per 100,000 people (**Table 1**).

Table 1. Estimates of prostate cancer burden in Mexico.

Estimate	Counts (95% UI)			% change 2010 to 2019	ASR (per 100,000)
	2000	2010	2019		2019
Incidence	11,444 (8,883 to 14,016)	17,784 (14,346 to 23,397)	27,096 (20,602 to 36,016)	52.4 (24.0 to 88.0)	52.3 (40.0 to 70.1)
Deaths	4,812 (3,795 to 6,138)	6,864 (5,674 to 9,075)	9,256 (7,077 to 12,678)	34.8 (13.0 to 62.0)	19.4 (14.7 to 26.7)
DALYs	85,401 (66,271 to 105,182)	118,808 (96,913 to 157,677)	161,552 (122,755 to 219,505)	35.9 (14.0 to 64.0)	319.5 (244.1 to 432.5)

ASR = Age-standardized rate.

According to the age-standardized global ranking of the 45 groups of diseases and injuries included in level 3 of the GBD, with 15.3 (13.0 to 18.6) deaths per 100,000 people, PC was ranked as the 16th cause of death for males worldwide in 2019. In contrast, PC caused a higher burden of disease in males from Mexico because at the national level, this disease was estimated to have the 11th highest mortality rate (**Figure 1a**). Additionally, PC caused the 22nd highest age-standardized rate of DALYs in Mexico in 2019, whereas at the global level, this disease occupied the 37th position, with an estimated 244.1 (211.8 to 297.7)

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DALYs per 100,000 people. In addition, among the 27 cancer groups included in the GBD, PC had the top-ranked age-standardized death rate per 100,000 people due to neoplasms in Mexico during 2019, whereas at the global level, PC was ranked 4th only behind lung, colorectal and stomach cancer (**Figure 1b**).

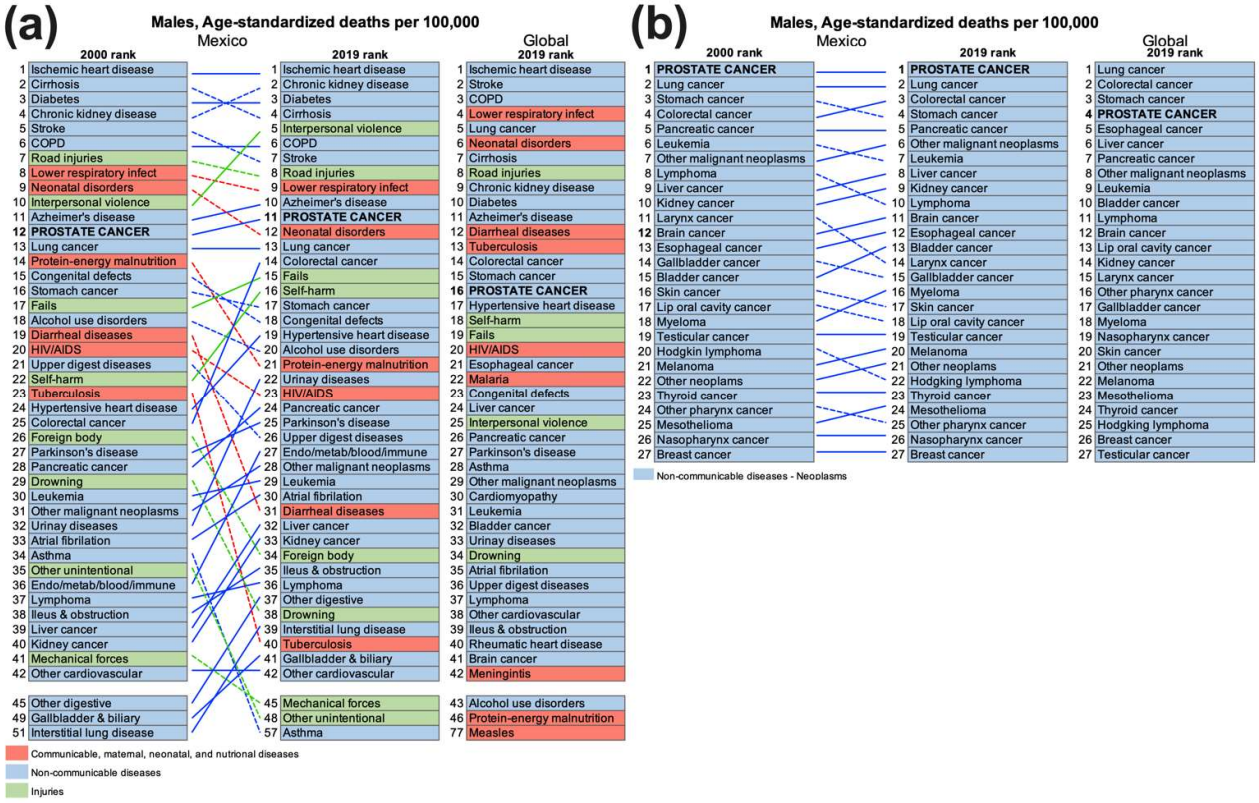

Figure 1. Change in the ranking of (a) the 45 diseases and injuries included in the GBD hierarchy level 3; and (b) the 27 groups of neoplasms included in the GBD for Mexico from 2000 to 2019 and global ranking during 2019.

At the subnational level, the highest number of incident cases in 2019 occurred in the state of Mexico (2.8 thousand, 2.1 to 4.2) and Mexico City (2.5 thousand, 1.8 to 3.5), whereas with 165 (118 to 250) new cases of PC, the state of Campeche had the lowest incidence of this neoplasm (**Supplementary Table 1**). The age-standardized incidence rate showed a different pattern because with 85.2 (56.7 to 118.1) and 74.9 (49.7 to 104.0) new cases per 100,000 people, Sinaloa and Baja California Sur had the highest estimations, and Puebla (36.1, 26.0 to 54.9) and Oaxaca (33.8, 24.7 to 53.9) had the lowest (**Figure 2a**). Likewise, the number of deaths for all ages due to PC showed great subnational heterogeneity, as the highest estimates in 2019 were found in Mexico (908, 680 to 1,368) and Mexico City (809, 586 to 1,120), whereas Campeche (58, 43 to 90) and Baja California Sur (52, 34 to 73) had the lowest mortality due to this cancer (**Supplementary Table 2**). The age-standardized mortality rate ranged from 29.8 (23.7 to 46.9) to 14.2 (10.2 to 24.2) deaths per 100,000 people in Guerrero and Tlaxcala, respectively (**Figure 2b**). Finally, the estimation of DALYs ranged from 14.4 thousand (10.3 to 19.7 thousand) in Mexico to 1.0 thousand (0.67 to 1.4 thousand) in Campeche (**Supplementary Table 3**), and the age-standardized rate was the highest in Guerrero, where PC caused 487.4 (391.4 to 718.2) DALYs per 100,000 people (**Figure 2c**).

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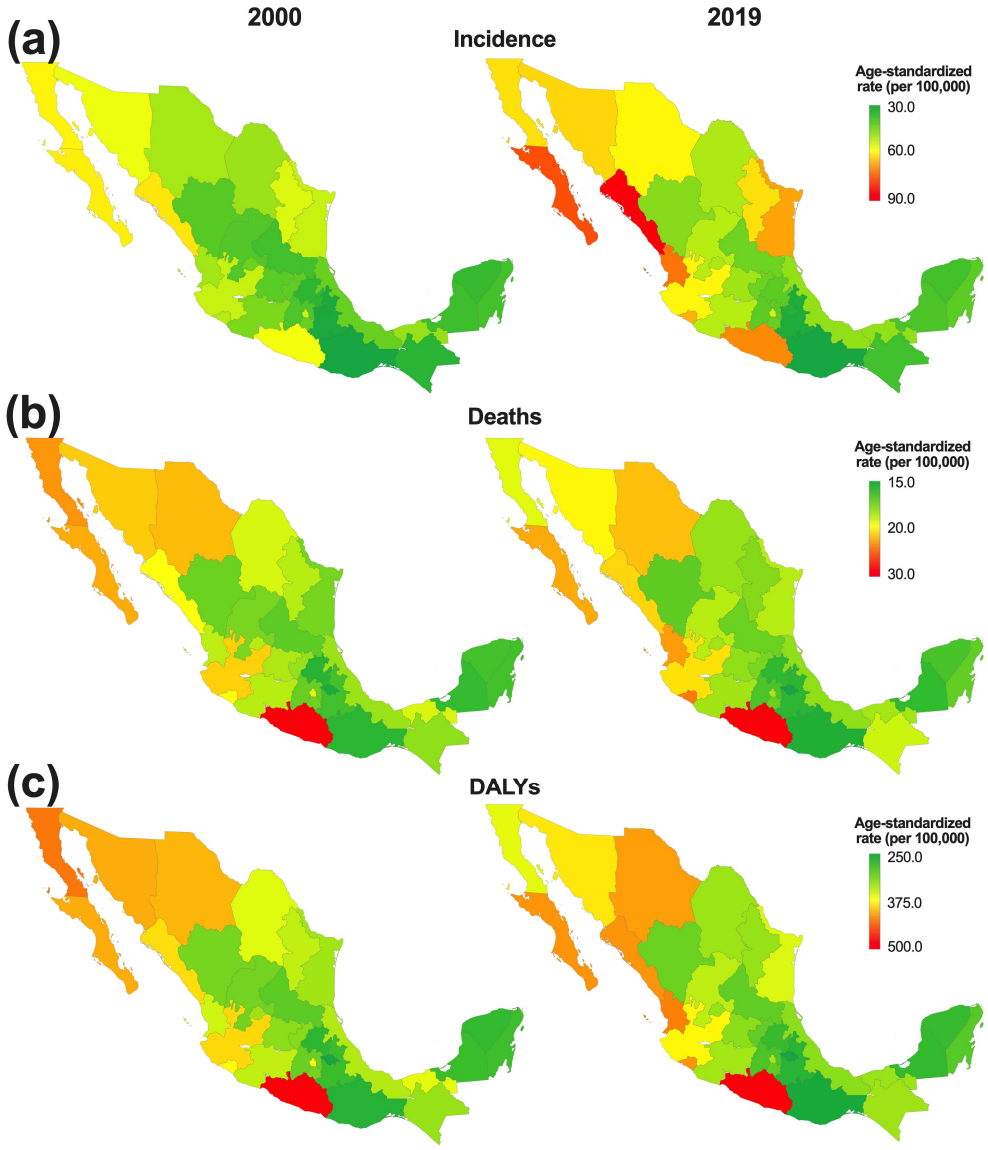

Figure 2. Change in the subnational age-standardized (a) incidence; (b) deaths; and (c) DALYs per 100,000 people due to prostate cancer in Mexico from 2000 to 2019.

3.2 National burden of prostate cancer by age group

To assess the specific pattern of PC burden according to the age groups, only estimates from 40 to >95 years were included (**Table 2**). In Mexico, with an estimated 5.2 thousand (3.9 to 7.2 thousand) new incident cases in 2019, the age group of 70 to 74 years showed the peak of PC incidence, whereas this neoplasm caused the highest burden of disease in the age group of 75 to 79 years as the number of DALYs (29.8, 23.4 to 40.6 thousand) and the death counts (1.8, 1.4 to 2.5 thousand) peaked in this group (**Figure 3a**). However, the count rates per 100,000 showed a contrasting pattern of the burden of PC because the higher estimates of incident cases (564.2, 431.9 to 821.5) and DALYs (5,111, 3,969.9 to 7,279) peaked in the age group of 85 to 89 years. In contrast, with an estimated 817.9 (569.6 to 1,172) deaths per 100,000 people, the group aged >95 years was the most affected by PC (**Figure 3a**).

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Table 2. Estimates of prostate cancer burden by age group in Mexico in 2019 and change from 2010 to 2019.

Age group	Rate (95% UI) per 100,000					
	Incidence	% change 2010-2019	Deaths	% change 2010-2019	DALYs	% change 2010-2019
40-44	2.4 (1.7 to 3.3)	19.2 (-9.1 to 58.3)	0.3 (0.2 to 0.4)	2.4 (-19.7 to 33.0)	16.1 (10.8 to 21.6)	3.7 (-17.8 to 34.0)
45-49	8.9 (6.2 to 12.4)	15.7 (-12.5 to 51.1)	1.1 (0.8 to 1.6)	-0.9 (-24.1 to 28.2)	51.6 (36.3 to 73.6)	0.6 (-21.4 to 28.0)
50-54	29.9 (20.6 to 41.5)	12.7 (-15.0 to 46.9)	3.5 (2.3 to 4.8)	-3.6 (-26.2 to 25.7)	147.3 (100.4 to 197.3)	-1.9 (-23.1 to 25.2)
55-59	82.6 (57.1 to 112.1)	17.5 (-11.0 to 53.7)	9.9 (6.7 to 13.8)	0.5 (-22.3 to 31.0)	372.1 (261.4 to 509.2)	2.6 (-19.0 to 31.5)
60-64	192.1 (139.5 to 261.2)	16.4 (-10.2 to 50.6)	28.1 (19.9 to 38.1)	0.2 (-21.4 to 28.1)	898.9 (655.4 to 1,193.5)	2.0 (-18.1 to 27.5)
65-69	325.0 (237.3 to 434.4)	14.9 (-9.2 to 45.7)	58.6 (41.3 to 80.0)	-0.9 (-20.8 to 24.9)	1,569.5 (1,141.9 to 2,122.1)	0.9 (-17.3 to 24.3)
70-74	440.4 (331.5 to 611.0)	9.8 (-11.5 to 35.8)	114.1 (84.5 to 155.6)	-4.1 (-22.4 to 19.6)	2,451.3 (1836.2 to 3,282.7)	-2.6 (-19.6 to 19.0)
75-79	529.6 (410.1 to 721.0)	8.4 (-11.5 to 31.9)	221.0 (169.7 to 303.4)	-3.4 (-20.2 to 17.1)	3,663.7 (2,871.9 to 4,986.0)	-2.4 (-18.3 to 16.7)
80-84	531.3 (410.1 to 716.8)	5.2 (-12.2 to 25.9)	353.2 (262.1 to 477.1)	-3.0 (-19.1 to 15.6)	4,405.9 (3,261.4 to 5,974.9)	-2.1 (-17.0 to 15.6)
85-89	564.0 (431.9 to 821.5)	2.8 (-10.4 to 18.4)	550.2 (426.0 to 787.2)	-1.9 (-15.0 to 12.5)	5,111.2 (3,969.9 to 7,279.6)	-1.5 (-14.1 to 12.4)
90-94	523.4 (382.8 to 714.9)	12.3 (-5.9 to 38.4)	680.4 (488.3 to 932.4)	8.8 (-9.2 to 36.0)	4,804.5 (3,453.7 to 6,577.8)	8.8 (-9.0 to 35.6)
>95	535.8 (382.7 to 763.7)	26.5 (11.3 to 45.4)	818.0 (569.6 to 1172.2)	22.9 (7.2 to 40.9)	4,310.5 (3,018.6 to 6,177.1)	27.3 (11.4 to 45.7)

The age groups of 60 to 79 years accounted for 69.0% of the new incident cases and 63.6% of the DALYs that were estimated in 2019 for males from 40 to >90 years. In contrast, the highest percentage of deaths due to PC in Mexico occurred in the age group of 70 to 89 years (68.6%) (**Figure 3b**). Finally, the number of annual deaths estimated from 2000 to 2019 per age group showed both a consistent increase in the number of deaths estimated each year and a steady contribution for almost each age group included in the analysis (**Figure 3c**).

3.3 National and subnational trends of prostate cancer burden from 2000 to 2019

In Mexico, the burden of PC showed a consistent increasing trend in the number of incident cases, DALYs, and deaths over the studied period for males of all ages (**Figure 4a**). However, the magnitude of change differed between these metrics during the last decade from 2010 to 2019 (**Table 1**). The incidence of PC for all ages increased from 11.4 thousand (8.9 to 14.0 thousand) in 2000 to 17.8 thousand (14.3 to 23.4 thousand) cases in 2010, with a further increase of 52.4% (24.0 to 88.0) in the incident cases from 2010 to 2019. From 2000 to 2010, the number of deaths increased from 4.8 thousand (3.8 to 6.1 thousand) to 6.9 thousand (5.7 to 9.1 thousand) and reached a final increase of 34.8% (13.0 to 62.0) from 2010 to 2019, whereas the number of DALYs increased 35.9% (14.0 to 64.0) during the same period.

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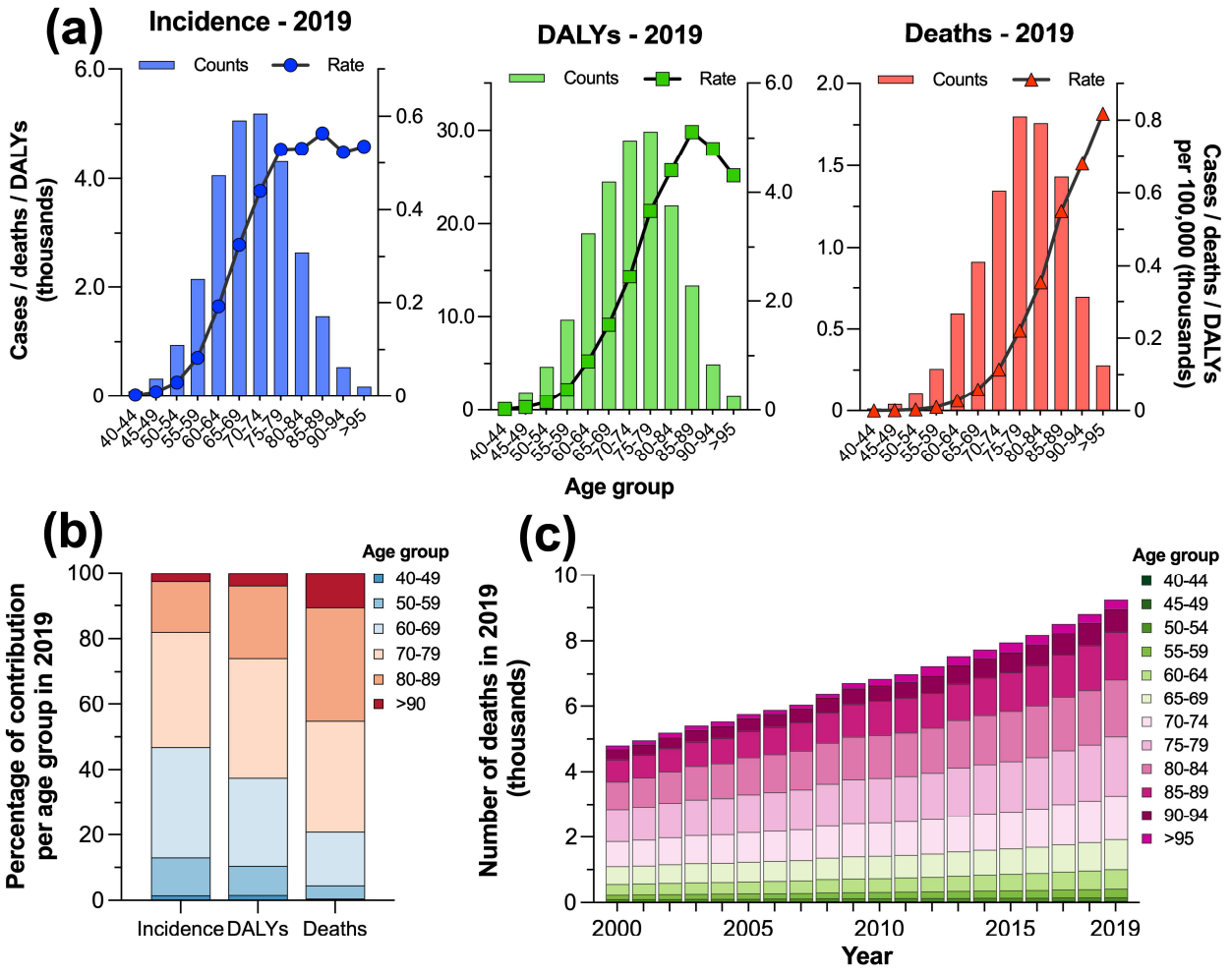

Figure 3. (a) Prostate cancer burden by age group and rate per 100,000 people in Mexico in 2019; (b) relative contribution per age group to the counts of incident cases, deaths and DALYs; and (c) contribution per age group to the annual number of deaths due to prostate cancer in Mexico from 2000 to 2019.

At the national level, the trends of the age-standardized rates showed a contrasting pattern (**Figure 4b**). The incident cases of PC per 100,000 people increased from 43.8 (34.2 to 53.7) at the beginning of the period to 47.1 (38.1 to 60.0) by 2010, with a further increase of 11.2% (-9.5 to 36.4) from 2010 to 2019. In contrast, both the age-standardized DALYs and deaths per 100,000 people caused by this neoplasm showed a trend toward slightly reduced values from 2000 to 2010 as the DALYs rate increased from 334.1 (261.9 to 416.) to 320.7 (263.1 to 425.7) and the death rate from 20.5 (15.9 to 26.0) to 19.5 (16.2 to 25.8). However, no further reduction was observed from 2010 to 2019 in the age-standardized rate of DALYs (-0.41, 16.4 to 19.6) and deaths (-0.88, -16.6 to 18.7) per 100,000 people.

At the subnational level, the temporal change in the burden of PC showed both a heterogeneous spatial pattern evidenced in the maps depicted in **Figure 2** and contrasting trends according to the time series presented in **Figure 4b**.

Regarding the age-standardized incidence per 100,000 people, all the states except Guerrero, Tabasco, and Campeche followed the national trend and thus showed an increase in the incident cases of PC during the period of 2010 to 2019. The estimated increases ranged from 4.4% (-20.3 to 37.6) in Oaxaca to 26.8% (-5.5 to 73.2) in Baja California

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Sur. In addition, four states, including Colima, Chihuahua, Sinaloa, and Baja California Sur, had estimated increases higher than 20% during the period, whereas 16 states had changes lower than the national estimate of 11.2% (**Figure 4c**).

In contrast to the national pattern, the age-standardized rate of DALYs per 100,000 people increased from 2010 to 2019 in 16 states, among which Baja California Sur, Chihuahua, Colima, Guanajuato, and Sinaloa had an increase that ranged from 4.6 to 10.9%. In contrast, eight states showed a reduction in the rate of DALYs caused by PC, which fluctuated between -12.7% (-26.2 to 7.15) in Guerrero and -3.1% (-22.3 to 18.3) in Aguascalientes. Finally, for the change in the age-standardized death counts per 100,000, 11 states followed the national trend that consisted of a reduction in the rate of mortality caused by PC, with the highest reductions estimated in Guerrero (-15.8, -28.8 to 3.4), Sonora (-5.8, -26.2 to 16.6), and Tabasco (-5.7, -26.1 to 17.8). In contrast, Quintana Roo, Zacatecas, Sinaloa, Veracruz, San Luis Potosi, Guanajuato, Chihuahua, Baja California Sur, and Colima showed increases ranging from 2.0 to 10.9%, thus contrasting with the national trend (**Figure 4c**).

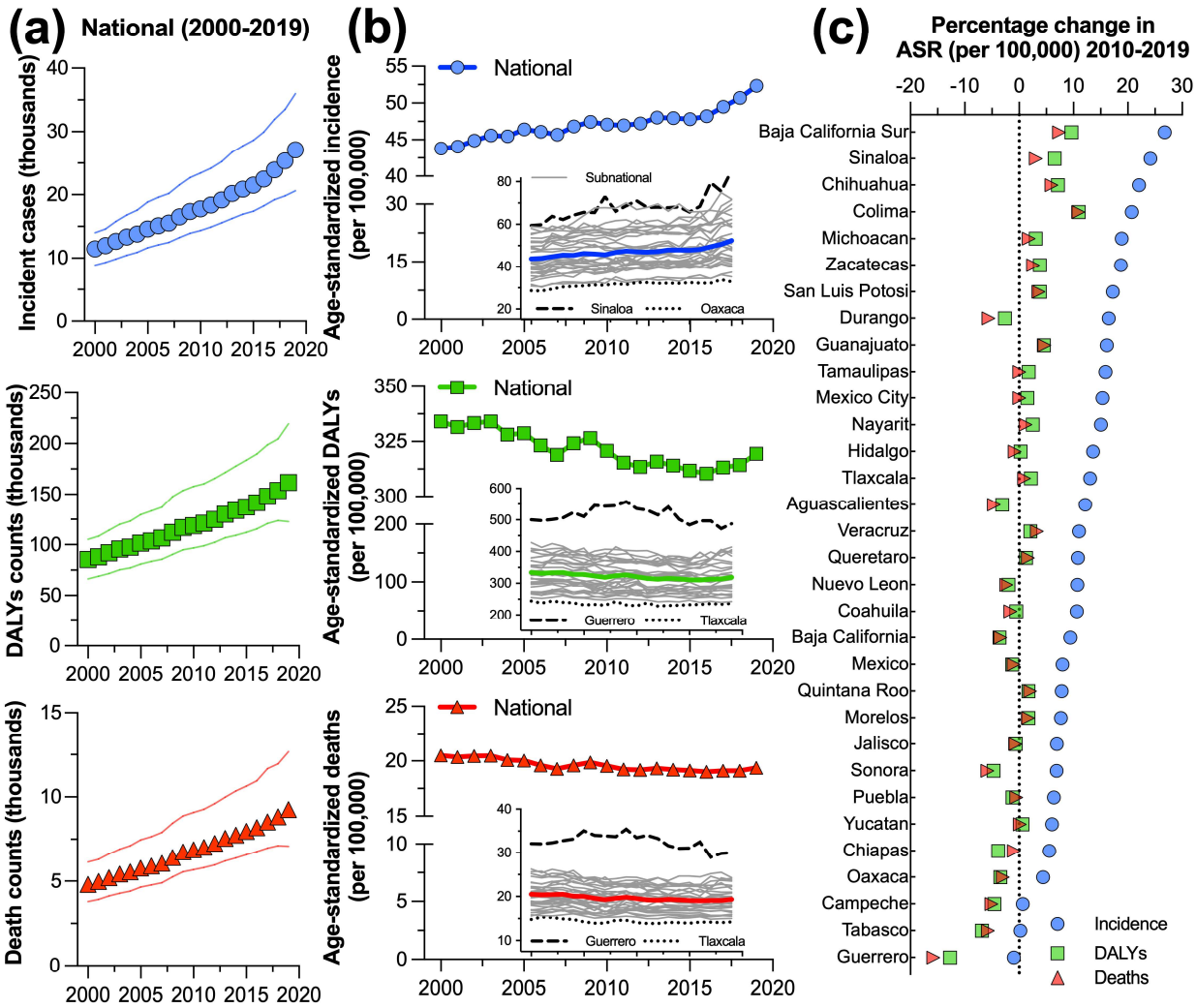

Figure 4. National trends of (a) prostate cancer incidence, DALYs, and death counts; (b) age-standardized rates per 100,000 people in Mexico from 2000 to 2019; and (c) percentage of change in the burden of prostate cancer from 2010 to 2019 at the subnational level. In b, the insert shows the subnational trends, including the names of the states with the highest and lowest rates for 2019.

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3.4 Association of the sociodemographic index with the burden of prostate cancer at the subnational level in 2019

According to **Figure 5**, only the age-standardized incidence per 100,000 people in 2019 showed a moderate association with SDI (r=0.49, p =0.002) among the localities from Mexico, thus suggesting that in those localities with higher values of SDI, there was a higher rate of incident cases of PC. In contrast, neither the estimated age-standardized rate of DALYs nor the rate of deaths per 100,000 people of each locality from Mexico were associated with the SDI.

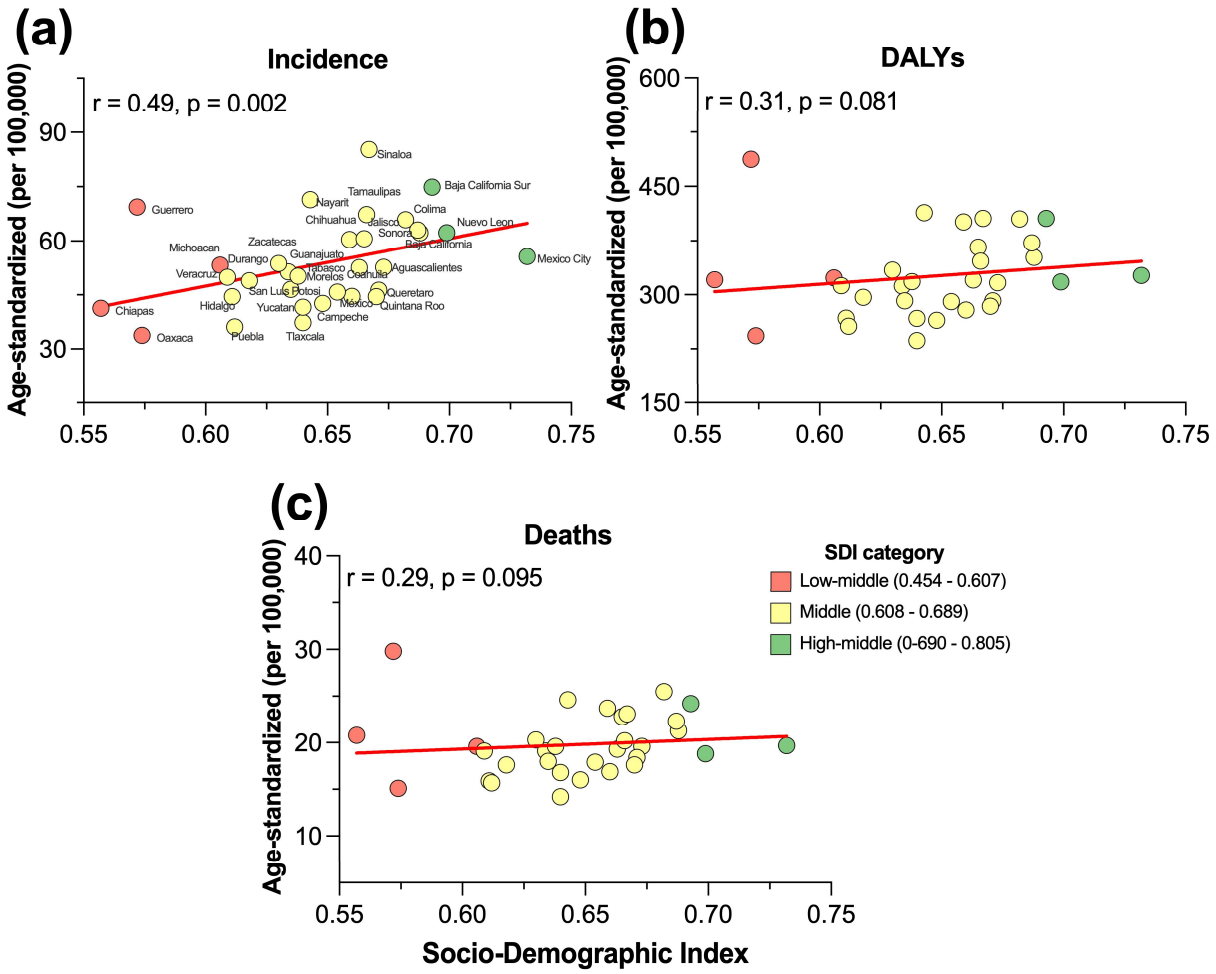

Figure 5. Association of the sociodemographic index (SDI) and age-standardized (a) incidence; (b) DALYs; and (c) death counts per 100,000 people at the subnational level in Mexico in 2019.

4. Discussion

Authors should discuss the results and how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted. Our study showed that PC caused the 11th highest mortality rate in males from Mexico during 2019, whereas this same disease was ranked as the 16th cause of death worldwide. In addition, at the national level, PC was the top ranked cause of death among 27 groups of cancers in males, while at the global level, this neoplasm was ranked 4th. Consequently, our results not only revealed that PC caused a higher burden of disease in males from Mexico when compared to the global reference but also confirmed that in some countries from Latin America, PC is among the main causes of death due to

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malign neoplasms [15]. It is worth mentioning that even though PC is linked to a high mortality in males from Mexico, the national mortality counts and death rate for this neoplasm are among the lowest in comparison to Argentina, Chile, Cuba, Brazil, Uruguay, and Venezuela, which are some of the countries with the highest mortality rates from the Americas [28, 24]. It is possible that the high mortality rates due to PC that we observed in our country and those reported in countries from Central and South America [11] might be partially associated with a delayed diagnosis because the patients affected by this malign neoplasm are frequently diagnosed at advanced stages of the disease [29]. In other types of cancers, some improvements in the management of these diseases have reduced their mortality trends [28]; however, this may not be the case for PC in Mexico because the mortality due to this malign neoplasm has increased over time.

The national pattern of PC by age showed that the death and DALYs counts peaked in the age group of 75-79 years, whereas the incident cases were the highest in the 70-74 age group during 2019. Additionally, our results showed that one-third of the incident cases during 2019 occurred in the age group of 70 to 79 years (35.2% of total incident cases), while the age group of 80-89 years accounted for 34.5% of the total deaths for the same year. Overall, our series of results concurs with the global pattern that shows a strong association between older age and an increased risk for developing PC [30-32]. Even though our analysis by age was limited to include only age groups between 40 and >95 years, we found that young males under 65 years of age were also affected by PC, although in a reduced magnitude compared with older groups >70 years. In addition, our time series of mortality due to PC revealed that from 2000 to 2019, there was a consistent increase in the number of deaths for all age groups included in the analysis. These results agree with the global trend of the burden of PC [33], according to which the proportion of patients <65 years affected by this malign neoplasm has increased over the years, possibly indicating novel alterations in the etiology and pathogenesis of the disease.

Our results showed that at the national level, the crude incidence, mortality, and DALYs counts for men of all ages increased during the assessed period, although with a variable magnitude of change. These trends toward increased incidence and mortality of PC that we report for Mexico are similar to previous results found in other countries from the Americas [34-36]. This higher incidence of PC registered over the years might be associated with both the increased use of PSA testing and changes in the exposure to potential risk factors for the disease, such as dietary fat and obesity [14, 37]. Although the increase in the incidence of PC has also been related to the development of better diagnostic techniques to detect different stages of this disease [38, 13], the lack of a malignant tumor follow-up registry and population-based cancer registries in Mexico and other countries from the Americas avoids the opportunity to collect relevant clinical information that allows a better understanding of the epidemiology of PC [19, 11].

With respect to the age-standardized rates, we found a contrasting pattern because the incidence increased, whereas the rate of death and DALYs decreased during the same period. Likewise, the subnational estimates followed a similar trend for the age-standardized rates, which were also characterized by a heterogeneous geographical pattern of change. These series of results are consistent with a previous study in which the authors assessed the burden of PC at the global level in 195 countries and regions and found not only similar trends in the age-standardized rates of incidence and mortality across all geographic regions but also broad geographical variability [33].

Previous studies have suggested that regional differences in the incidence and mortality of PC may be associated to disparities in the exposure to risk factors for this malign neoplasm, the detection rate of the disease, as well as the quality and access to oncology care [13, 39, 18]. Therefore, some of these factors might partially help explain the subnational disparity that we found in our study. Moreover, location-specific differences in the medical condition and the exercise and dietary habits might also influence the incidence and mortality of PC among males of different ages; thus, it is necessary to further study their contribution in population-based investigations. In addition, race/ethnicity also

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plays a relevant role as a risk factor; for instance, white (>50 years) and black men (>40 years) have an increased risk for PC development [40, 41]. In Mexico, the impact of race as a risk factor is as interesting as it is complex due to the genomic diversity of the country: in the north, the most frequent genetic component is European, whereas in the south, the Amerindian genetic component is predominant [42]. However, more studies are needed to assess the specific effect of race/ethnicity in males from Mexico.

A recent study by Baadeet al. [43] reviewed the geographic disparities linked to a differential outcome for PC in several countries across the globe. The authors found a contrasting pattern of the disease between urban and rural areas because in the former, PSA testing was common, survival was higher, and access to healthcare facilities was greater in comparison to the latter, where mortality due to PC was higher mostly because of a diagnosis of the disease at advanced stages. Therefore, sociodemographic determinants are relevant for the burden of PC, and Mexico is characterized by disparate socioeconomic determinants that have been linked to the burden of other types of cancer [16] as well as some infectious diseases [44]. Although a previous study found an association between the SDI and the burden of PC in 195 countries and territories [33], we only found a weak association of the SDI with the age-standardized rate of incidence. Nonetheless, our results showed that Chiapas and Guerrero, which are states characterized by the lowest values of SDI in Mexico, had a higher rate of mortality, which may be associated with low educational level, lack of access to healthcare facilities, and a high proportion of indigenous population for whom communication is difficult. In conjunction, all these factors make the diagnosis and treatment of PC difficult. Further studies that assess the specific contribution of the socioeconomic determinants among the states of Mexico are needed to expand our knowledge on the association between these factors and the incidence and mortality of PC.

5. Limitations

This study is not devoid of limitations. Although we used reliable and accurate data from the most recent iteration of the GBD, the input data sources used by the GBD to calculate the estimates of PC in Mexico varied both in completeness and quality among the 32 states; consequently, this heterogeneity may increase the risk of bias of the estimates. In addition, the lack of data input sources for some years and locations used during the modeling process may contribute to a potential lack of representativeness of the GBD estimates for some estates. Finally, the GBD only includes tobacco consumption as a potential risk factor for PC; thus, the absence of other potential risk factors, such as local levels of PSA screening, management of diagnosis and treatment, as well as other clinical features of the disease preclude us to carry on further analysis of their association with the incidence and mortality of this malign neoplasm.

6. Conclusions

To the best of our knowledge, this study represents the most updated and comprehensive report in Mexico that describes the burden and trends of PC at the national and subnational levels from 2000-2019. Our results demonstrated that PC caused a significant burden of disease, as this malign neoplasm was among the main causes of death in men during 2019. In addition, the trends described in our study for the incidence and mortality due to PC are similar to those reported for countries from the Americas. In addition, we also found subnational variation in the burden of PC. Our results confirm the need for updated and timely estimates of PC because understanding the epidemiological trends and disparities in PC at the subnational level may guide efficient healthcare planning as well as adequate resource allocation aimed at increasing disease screening, treatment, and survivor care.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Supplementary Table 1: Estimates of prostate cancer incidence at the

national and subnational levels in Mexico; Supplementary Table 2: Estimates of prostate cancer mortality at the national and subnational levels in Mexico; Supplementary Table 3: Estimates of prostate cancer DALYS at the national and subnational levels in Mexico.

Author Contributions: We used the Credit taxonomy to define co-authorship according to the following categories: conceptualization, SABO and DD; methodology, SABO, MAFG, EAM, ELL; software, DZV, FJT, and FGV; formal analysis, SABO, DMBC, and DD; investigation, VJPC, CAR, and DD; data curation, SABO, EAM, ELL, and FJT; writing—original draft preparation, JACG, JMM, MAFG, and JMMO; writing—review and editing, VJPC, CAR, and DD; visualization, DZV, FJT, and FGV; supervision, JACG, and JMM; project administration, MAFG, JMMO, and DD. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The datasets analyzed in the current study are available at the GHDx website (http://ghdx.healthdata.org/gbd-2019/data-input-sources). Besides, all the estimations used to perform the analyses and construct the figures are available from the corresponding author upon reasonable request.

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Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

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