RESEARCH ARTICLE

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Prostate Cancer Mortality in Peru: An Update from 2003 to 2017

J Smith Torres-Roman^{1,2,3*}, Carlos Quispe-Vicuña², Miguel A Arce-Huamani^{1,2}, Carlos A Dávila-Hernandez^{2,3}, Bryan Valcarcel², José Fabián Martinez-Herrera^{2,4}

Abstract

Objective: We estimated the mortality trends for prostate cancer in Peru and its geographical areas between 2003 and 2017. Material and Methods: We obtained recorded prostate cancer deaths from the Peruvian Ministry of Health Database between 2003 and 2017. Age-adjusted mortality rates per 100,000 men-year were computed with the direct method using the world standard SEGI population. We estimated the annual percent change (APC) using the Joinpoint regression program. Results: A total of 38,617 prostate cancer deaths were reported between 2003 and 2017, with a mortality rate ranging from 18.21 to 19.94 deaths per 100,000 men-year. Since 2006, Peru has experienced a decrease of 2.2 deaths per year, whereas the mortality rate in the coastal region has declined by 2.9% per year. The highlands and rainforest regions showed stable trends throughout the entire study period. According to provinces, only Moquegua had a significant decrease (APC: -6.0, 95%CI: -11.4, -0.2, p<0.05) from 2003 to 2017. Conclusions: Although mortality rates are decreasing, there is a high mortality burden by prostate cancer in Peru and by geographical regions, being mostly concentrated in the coastal region. The rainforest provinces deserve the most attention. Our findings suggest wide health care disparities among the different regions of Peru that need greater public health attention to reduce the burden of mortality by prostate cancer.

Keywords: Prostate cancer- spatial clustering- mortality trends- Peru

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Introduction

With more than 1 million new cases (7.1% of all sites) and 360,000 deaths (3.8% of all sites) in 2020, prostate cancer is the second most common cancer diagnosis and the fifth leading cause of cancer-related death in men worldwide (Sung and Ferlay et al., 2021). In 2020, Northern Europe had the highest incidence rate (above 80 per 100,000 men), whereas the Caribbean had the highest mortality rate (above 25 per 100,000 men) (Sung and Ferlay 2021). Taking into account the current lifestyles and age structures, the number of men with prostate cancer will likely increase in the future, leading to a further increase in mortality in middle- and low-income countries.

Mortality by prostate cancer in Latin America (LA) is roughly 14 deaths per 100,000 men, being higher than that reported in North America and Europe (Hashim and Boffetta et al., 2016). Indeed, prostate cancer is the leading cause of cancer-related death in Ecuador, Chile, and Venezuela (Sung and Ferlay 2021). However, these studies are limited to a few countries and do not include countries such as Peru (Carioli and Bertuccio et al., 2020, Carioli and La Vecchia et al., 2017). Despite this, great efforts have been made to provide an overview of the mortality trends for prostate cancer in Peru. For example, one study in Peru reported mortality rates above 20 deaths per 100,000 men, being highest in the coastal region (Torres-Roman and Ruiz et al., 2019).

Since the implementation of the "Plan Esperanza" in 2012, which aimed to reduce the overall cancer mortality including mortality by prostate cancer, there has been no comprehensive analysis of mortality trends over the last years (Vidaurre and Santos et al., 2017). We, therefore, aimed to estimate the mortality trends of prostate cancer in Peru and its geographical regions between 2003 and 2017.

Materials and Methods

Design and Study Setting

This observational study is a secondary data analysis using the database from the Ministry of Health (MINSA) of Peru from 2003 to 2017, which is publicly available upon

¹Cancer Research Networking, Scientific University of the South, Lima, Peru. ²Latin American Network for Cancer Research (LAN-CANCER), Lima, Peru. ³Professional School of Human Medicine, San Juan Bautista Private University, Chincha Branch, Ica, Peru. ⁴Cancer Center, Medical Center American British Cowdray, Mexico City, Mexico. *For Correspondence: jstorresroman@gmail.com

request through the following link: http://www.minsa.gob.pe/portada/transparencia/solicitud/. This database is a population-based registry of death certification that gathers the death counts for all-cause mortality aggregated into five age groups (0-11, 12-17, 18-29, 30-59, and \geq 60). Deaths from prostate cancer were identified with the code "C61" of the International Classification of Diseases, Tenth Revision (ICD-10).

Peru is a country in South America with 31 million inhabitants. It has three geographical regions (the coast, highlands, and rainforest), divided into 25 administrative provinces (Ruiz and Torres-Roman et al., 2019). The coastal region covers 11.7% of the national territory and has the largest number of inhabitants in Peru (57%). The highlands covers 28% of the national territory with around 30% of the total population, whereas the rainforest region is the largest of the country, accounting for 60% of the national territory but only contains 14% of the Peruvian population.

In Peru, there is an approximately 46% of underreporting of deaths with fluctuations across the years and geographical areas (Torres-Roman and Gomez-Rubio et al., 2020, Ministerio de Salud, 2013) ranging between 19% (province of Ica) and 78% (province of Loreto). Therefore, the degree of underreported deaths in each province and year was corrected using the underreporting coefficient as in a previous study (Torres-Roman and Gomez-Rubio 2020).

 $R = 100 - (OD/ED) \times 100$

R = Underreporting rate.

OD = number of deaths observed for each province.

ED = number of deaths estimated for each province.

Statistical and Spatial Analysis

The age-standardized mortality rates (ASMRs) were estimated per 100,000 men-year using the direct method and the world standard SEGI population . As a denominator, we used the population counts provided by the National Institute of Statistics and Informatics (Instituto Nacional de Estadistica e Informatica, 2020) . Mortality trends were analyzed using the Joinpoint regression Program Version 4.7.0 (National Cancer Institute 2020). We fitted joinpoints for Peru and its geographical regions. We analyzed the Annual Percentage Change (APC) (Howlader and Noone et al., 2016) based on the trend of each segment, estimating whether these values were statistically significant at a level of significance of 0.05. The provinces with zero deaths in any given year did not allow this analysis and we considered it as not applicable (NA). The significance levels utilized herein are based on the Monte Carlo permutation method and the calculation of the annual percentage change of the ratio, utilizing the logarithm of the ratio.

Results

We identified 38,617 deaths from prostate cancer in Peruvian men between 2003 and 2017. Table 1 shows the ASMRs in Peru, including regions, and provinces. Mortality rates (per 100,000 men-year) in the overall population decreased from 19.94 in 2003-2007 to 18.21

in 2013-2017 (8% reduction). According to the different regions, the rainforest showed the largest percentage decline (22% reduction) from 17.41 in 2003-2007 to 13.58 in 2013-2017 and mortality in the coast region decreased from 21.77 in 2003-2007 to 19.23 in 2013-2017 (12% reduction). In contrast, the highlands region slightly increased from 15.97 in 2003-2007 to 17.25 in 2013-2017. In the latest period of observation (2013-2017) the coast (19.23) had the highest mortality rate, followed by the highlands (17.25) and the rainforest (13.58). When comparing the provinces, we found an approximate five-fold variation in mortality rates in the 2013-2017 period, ranging from 5.49 in Ucayali to 25.8 in Huanuco. Similarly, compared to the 2003-2008 period, the percentage of mortality rates increased in 10 provinces, ranging from 6% to 52%, while 15 provinces showed a percentage reduction of mortality rates from 1% to 68%.

Table 2 and Figure 1 show the temporal analysis of mortality trends. The overall population showed a significant upward mortality trend (APC= 13.3, 95% confidence interval [CI]: 1.4, 26.6) from 2003 to 2006,

Table 1. Age-Standardized (World Population) Mortality Rates per 100,000 men-year for prostate cancer in Peruvian provinces between 2003-2007, 2008-2012, and 2013-2017, and the corresponding percentage change.

Geographical	2003-207	2008-2012	2013-2017	%
areas				change
Peru	19.94	20.15	18.31	-8
Coast	21.77	22.38	19.23	-12
Highlands	15.97	16.27	17.25	8
Rainforest	17.41	12.98	13.58	-22
Amazonas	14.1	16.4	17.42	24
Ancash	15.05	21.04	18.15	21
Apurimac	15.31	11.13	23.26	52
Arequipa	21.62	21.57	18.51	-14
Ayacucho	16.39	17.23	18.42	12
Cajamarca	22.07	21.4	16.69	-24
Callao	20.08	22.08	21.27	6
Cusco	12.76	9.93	12.61	-1
Huancavelica	16.58	16.99	20.3	22
Huanuco	22.39	26.3	25.79	15
Ica	20.8	21.51	20.26	-3
Junin	15.84	16.41	20.15	27
La Libertad	24.52	22.3	20.39	-17
Lambayeque	25.39	22.92	22.56	-11
Lima	21.35	22.36	18.57	-13
Loreto	20.68	10.2	16.2	-22
Madre de Dios	7.42	12.74	10.69	44
Moquegua	25.8	16.15	13.67	-47
Pasco	19.16	19.49	18.09	-6
Piura	25.34	26.03	22.04	-13
Puno	9.38	12.42	11.61	24
San Martin	17.27	14.04	13.81	-20
Tacna	19.14	18.08	11.9	-38
Tumbes	21.43	24.01	12.56	-41
Ucayali	16.94	13.46	5.49	-68

Table 2. Joinpoint Analysis for Prostate Cancer in Peru and Its Regions between 2003 and 2017.

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Geographical regions		Trend 1		-	Trend 2	
	Period	APC	95%CI	Period	APC	95%CI
Peru	2003-2006	13.3*	1.4, 26.6	2006-2017	-2.2*	-3.7, -0.8
Coast	2003-2006	15.0*	2.2, 29.5	2006-2017	-2.9*	-4.5, -1.4
Highlands	2003-2017	1.4	-0.2, 3.0			
Rainforest	2003-2017	-1.6	-4.8, 1.7			

APC, Annual percent change

followed by a percentage decrease of 2.2 (95% CI: -3.7, -0.8) after the year 2006. The coast region experienced a similar trend with an annual increase of 15% (95% CI: 2.2, 29.5) between 2003 and 2006, followed by a decrease after 2006 (APC=-2.9, 95% CI: -4.5, -1.4). In contrast, the highlands (APC=1.4, 95% CI: -0.2, 3.0) and the rainforest (APC =-1.6, 95% CI: -4.8, 1.7) regions had stable trends during the entire study period with some fluctuations. Among the provinces, only Moquegua experienced an annual 6% decrease in mortality rates (95% CI: -11.4, -0.2) from 2003 to 2017. Most of the provinces had a downward trend, although none of these results were statistically significant (Table 3 and Figure 2).

Discussion

This study analyzed the mortality trends for prostate cancer in Peru and its geographical areas over a period of 15 years. We identified variable trends within the regions of Peru. The coast was the only region with decreasing trends after 2006, following an initial upward trend from

2003 to 2006, while the highlands and the rainforest regions had stable trends for the whole period. Similarly, analysis of the provinces found only one province (Moquegua) presenting a significant reduction in mortality trends, suggesting wide geographical disparities between the administrative regions of Peru.

We identified roughly 20 deaths per 100,000 men in Peru, similar to other LA countries such as Cuba and Venezuela, but higher compared to Argentina, Brazil, Chile, and Colombia, which are below 15 per 100,000 men (Carioli and Bertuccio, 2020; Reis et al., 2020). This demonstrates heterogeneity in prostate cancer mortality rates in LA countries. However, although Peru is among the countries with the highest prostate cancer mortality rates in LA, a significant decrease has been reported in recent years. In 2007, Peru approved the "Concerted Health Plan" to reduce mortality by prostate cancer, promote prevention, screening, early diagnosis, and implement protocols to improve primary care delivery. Moreover, a nationwide public health program called 'Plan Esperanza' was implemented in 2012 in Peru to increase

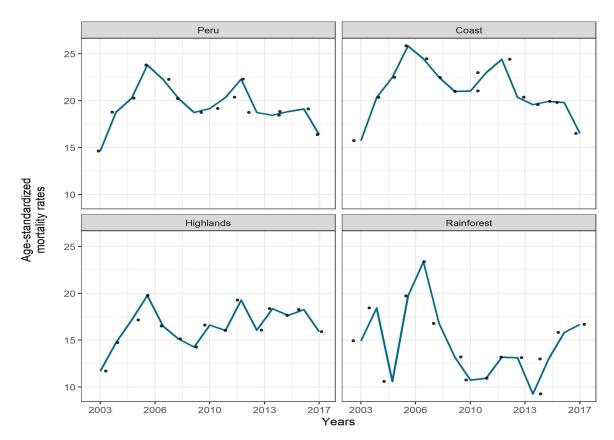


Figure 1. Age-Standardized Mortality Trends Per 100,000 men-year for Prostate Cancer in Peru and Its Major Regions between 2003 and 2017.

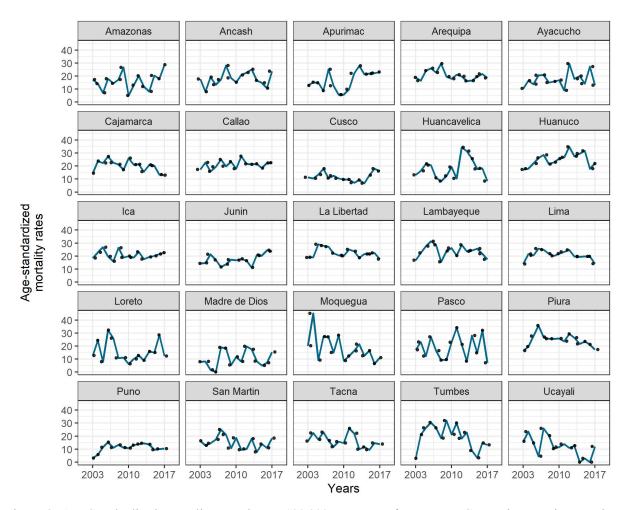


Figure 2. Age-Standardized Mortality Trends Per 100,000 Men-Year for Prostate Cancer in Peruvian Provinces between 2003 and 2017.

Table 3. Joinpoint Analysis for Prostate Cancer in Peruvian Provinces between 2003 and 2017.

Provinces	APC	95CI%
Amazonas	2.3	-3.9, 8.8
Ancash	1.5	-2.8, 6.1
Apurimac	5.1	-1.4, 12.0
Arequipa	-1.1	-3.3, 1.1
Ayacucho	1.8	-2.4, 6.1
Cajamarca	-2.3	-5.0, 0.5
Callao	1	-0.9, 2.9
Cusco	0.1	-3.8, 3.9
Huancavelica	1.1	-4.6, 7.2
Huanuco	1.8	-0.9, 4.6
Ica	-0.2	-2.1, 1.8
Junin	2.7	-0.1, 5.6
La Libertad	-1.0	-3.0, 1.0
Lambayeque	-0.3	-3.0, 2.5
Lima	-0.7	-3.1, 1.7
Loreto	-0.7	-6.9, 6.1
Madre de Dios	NA	
Moquegua	-6.0*	-11.4, -0.2
Pasco	-0.8	-7.4, 6.3
Piura	-0.7	-3.3, 2.0

Table 3. Continued

APC	95CI%
4.1	-0.9, 9.4
-2.2	-6.3, 2.0
-3.2	-6.7, 0.3
-2.6	-11.9, 7.8
NA	
	4.1 -2.2 -3.2 -2.6

APC, Annual percent change

cancer screening services and decrease the out-of-pocket expenditure of people diagnosed with cancer (Vidaurre and Santos, 2017). In 2013, the creation of the National Plan for Comprehensive Cancer Care and Improving Access to Oncology Services improved the access to health services for patients with cancer by expanding the capacity of the country to finance access to early diagnosis. This program was launched between 2013 and 2015, benefiting more than 16 million people with primary prevention and more than 2.5 million people with secondary prevention through cancer screening of cervical, breast, gastric, colon, and prostate cancer (Vidaurre and Santos, 2017). Our analysis has only captured the mortality rates after five years of the implementation of these programs. Therefore, our current findings likely reflect the early process of these programs, and mortality rates will likely reduce more

rapidly in the future.

We found differences in mortality by region. For instance, the coast was the only region that experienced a decline in mortality after 2006, while the other regions showed stable trends. However, higher mortality rates were concentrated in the coast region. This outcome could be related to better information systems in the coastal region, since these areas are more developed and have a higher concentration of oncology workforce and centralized treatment in the urban coastal cities, allowing early diagnosis of cancer. In addition, disparities in mortality among the regions may be due to ethnic and racial differences (Fletcher and Marchese et al., 2020). The coastal region concentrates a greater population of black race, which, according to other studies, is a population with typically higher mortality rates from prostate cancer (Fletcher and Marchese, 2020; Zeng et al., 2015). Underreporting of deaths in Peru could also explain the difference in mortality among regions. Before the implementation of the National System of Information on Deaths (SINADEF) in 2017, the mortality registry coverage was 54.2% (Vargas-Herrera et al., 2018), most likely associated with rural areas located in the highlands and rainforest. However, we corrected for the underreporting in these locations to provide more valid estimates on mortality by prostate cancer.

Some provinces such as Moquegua (13.2%), Lima (13.1%), Ancash (13.6%), Huancavelica and Puno (13.0%) showed increases in mortality by prostate cancer. A possible factor to explain the increase in the mortality rate of prostate cancer on the coast could be obesity (Instituto Nacional de Estadistica e Informatica 2017), which has been associated with an increased risk of prostate cancer mortality. Indeed, in 2017 it was reported that the coast was home to people with a higher body mass index compared to the highlands and jungle (Discacciati and Orsini et al., 2011; Kim et al., 2019), and in recent years there has been a notable increase in obesity in our country.

Despite the implementation of the 'Plan Esperanza' and the efforts to provide community-wide diagnosis and treatment, Peru still has centralized treatment in the metropolitan areas where most of the oncology workforce resides. The Ministry of Health of Peru reported that more than 70% of oncologists work only in Lima and Callao, two of the largest metropolitan cities in Peru. Therefore, individuals living in rural communities far away from these cities experience difficulties to reach a health care facility and probably abandon the treatment for prostate cancer, posing a challenge to further reduce the mortality rates in these settings. This situation could explain the statistically significant downward trends in the coast, while in the highlands and the rainforest, that have most of the rural communities, trends in mortality remained stable. Moreover, most of the trends related to cancer development according to the geographical setting were described by Piñeros et al. (Piñeros et al., 2017) and most of the information acquired came from the coast region. Therefore, the coast region has better access to improvements in many areas, and registration of cases from prostate cancer patients in the coast region should Limitations

be more reliable.

This study has limitations to address. First, the mortality registry for the 2003-2017 period had underreporting of data. However, we corrected deaths for different underreporting coefficients to provide more reliable results. Moreover, incidence data is not captured by any national registry. Therefore, we could not compare the relation between the incidence of and mortality by prostate cancer. However, this study reports the national, regional, and provincial mortality trends for prostate cancer over a 15-year period. Our results provide a current perspective of the trends in mortality by prostate cancer in the country.

In conclusion, mortality rates from prostate cancer in Peru vary according to the geographical region. Our results suggest that the coast is the only region that has benefited from the national health care programs implemented in the early 2010s. Therefore, policymakers and public health practitioners should mobilize resources to the highlands and rainforest to provide prompt case identification and treatment accessibility to decrease the mortality from prostate cancer in these regions.

Author Contribution Statement

J. Smith Torres-Roman, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft, Writing - review & editing; Carlos Quispe-Vicuña, Writing - original draft, Writing - review & editing; Miguel A. Arce-Huamani, Writing - original draft, Writing - review & editing; Carlos A. Dávila-Hernandez, Writing - original draft, Writing - review & editing; Bryan Valcarcel, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft, Writing - review & editing; Jose F. Martinez-Herrera, Supervision, Investigation, Writing - original draft, Writing - review & editing.

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Not applicable

Declarations

Ethics approval and consent to participate: Ethical approval and participant consent were not necessary as this study involved the use of a previously published secondary database.

Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. You can also request the raw data through the following form:

https://www.minsa.gob.pe/portada/transparencia/ solicitud/, placing your personal data and the information to be requested.

Conflict of Interests

All the authors declare that they have no competing

interests.

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