Cancer Epidemiology 58 (2019) 193–198

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Trends and geographic pattern of stomach cancer mortality in Peru

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ARTICLE INFO

Keywords:
Mortality
Stomach neoplasm
Peru

ABSTRACT

Background: Stomach cancer mortality rates in South America are among the highest in the world. In Peru, stomach cancer has the highest absolute number of cancer deaths in both sexes combined. We estimated mortality rates for stomach cancer in Peru by sex and geographical region between 2008 and 2015.
Methods: We obtained death data for stomach cancer from the Peruvian Ministry of Health database. We estimated the age-standardized mortality rate (ASMR) per 100,000 persons using the direct method and the world standard population.
Results: A total of 25,020 deaths from stomach cancer were identified in the study period. At national level, stomach cancer mortality rates (per 100,000 population) for men ranged from 9.8 in 2008 to 8.8 in 2015 with a percent change of −16%, and for women from 8.8 in 2008 to 7.7 in 2015 with a percent change of −16.8%. The highlands had the highest mortality rates overall, mainly in Huancavelica and Huánuco. The rainforest had the lowest rates and the highest decline in stomach cancer ASMRs. The coast displayed intermediate rates overall.
Conclusions: Within the study period, mortality rates from stomach cancer in Peru declined by 16%. The highlands had the highest mortality rates as compared to those from the coast or rainforest region. These geographical differences in mortality could reflect a different distribution in stomach cancer risk factors as the prevalence of *H. pylori*, poor dietary habits, low socioeconomic background of the Andean population and the lack of a decentralized health system.

1. Background

Although stomach cancer incidence has decreased in the last decades [1], worldwide it remains as the third cause of cancer-related deaths, after lung and colorectal cancer [2]. Stomach cancer also remains at the fifth place among the most commonly diagnosed malignancies globally, with approximately 1.3 million incident cases [2,3] and 17.4 million Disability-Adjusted Life Years (DALY) [3].

There are large regional differences in stomach cancer rates. The highest incidence rates are in East Asia, East Europe, and South America; while the lowest ones are in North America and Western Europe [4]. According to GLOBOCAN 2018, more than two thirds of cases occurred in middle- and low-income countries, and half of the cases occurred in East Asia [2,5]. Mortality rates from stomach cancer in Central and South America are among the highest in the world, being one of the first five leading causes of cancer death in most countries [6].

In Peru, stomach cancer causes the highest absolute number of cancer deaths [2,7], and it is the third most common cancer in the country [2,7]. People of low socioeconomic status living in the highlands account for the one the highest age-standardized mortality rates (ASMR) in Peru [7,8] and Latin America [6,9].

Some differences in stomach cancer incidence and mortality can be explained by known risk factors, such as the prevalence Helicobacter pylori infection, alcohol drinking or smoking [10,11]; while others could depend on specific demographic, socioeconomic and genetical characteristics of the population [10,12]. Scanty data, however, are available from Peru. This study aims to estimate mortality rates from stomach cancer in Peru between 2008 and 2015, by sex and geographical regions.

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https://doi.org/10.1016/j.canep.2018.10.018
Received 6 September 2018; Received in revised form 23 October 2018; Accepted 28 October 2018
Available online 03 December 2018

2. Methods

2.1. Source of information

We collected mortality data from Peru Ministry of Health (MINSA) registry of deaths in the period 2008–2015. We used code C61 to identify deaths from stomach cancer, according to the International Classification of Diseases, 10th Revision [13]. The data provided by the Ministry of Health are available to anyone who requests through its online platform: https://www.minsa.gob.pe/portada/transparencia/solicitud/. These records are based on reports from health facilities located throughout the country and that are part of the leading provider of health care services (MINSA, 70%) [14]. This registry classifies deaths according to the birthplace of the patient. It does not consider the place where the patient lived or died. Although it does not include information from other sources (such as social security insurance or private insurance), it collects information about cancer in all provinces. However, the reporting system may have problems in the accuracy and comprehensiveness of the data. For this reason, the calculation was made assuming an underreporting of 40% estimated by the Peruvian Ministry of Health [7].

2.2. Setting

Peru is divided into 25 provinces located in one of the 3 geographical regions: coast, highlands, and rainforest [15,16]. The coast is an urbanised area of low-altitude bounded in the West by the Pacific Ocean [16]. It is the most populated region (56.3% of the total population) and covers 11.7% of the national territory [15]. The highlands (or Peruvian Andes) covers the 27.9% of the national territory, including 29.7% of the population [15]. The rainforest (Peruvian Amazon) covers the largest area of the country (60.3% of the Peruvian territory) and contains 14.0% of the total population [15]. Fig. 1 shows Peru map divided by regions and provinces.

2.3. Statistical and spatial analysis

We used the software R 3.4.1 [17] for the statistical analyses. We estimated age-standardized mortality rates (ASMR) per 100,000 persons using the direct method and the world standard population. As denominator, we used the population in five-year age groups, provided by the National Statistics Institute [18]. The spatial analysis was conducted with the package *spdep* of R [19,20]. We obtained the geographical and cartographic outputs with the GeoDA software [21]. Maps were presented for each year, shading each province according to its ASMR interval.

3. Results

In the period 2008–2015, stomach cancer caused 25,020 deaths in Peru (13,322 in men and 11,688 in women) with a male-to-female (M:F) ratio of 1.1. Fig. 2 shows ASMRs for stomach cancer per year, at national and regional level for both sexes. In 2008, Peru had an ASMR (per 100,000 population) for men of 9.8, and for women of 8.8. Both sexes had their highest rate in 2010 (11.0 for men, 10.2 for women) and the lowest in 2015 (8.8 for men, 7.7 for women). We refer to point

Fig. 1. Peru geographical zones by provinces. Source: National Statistics Institute [18].

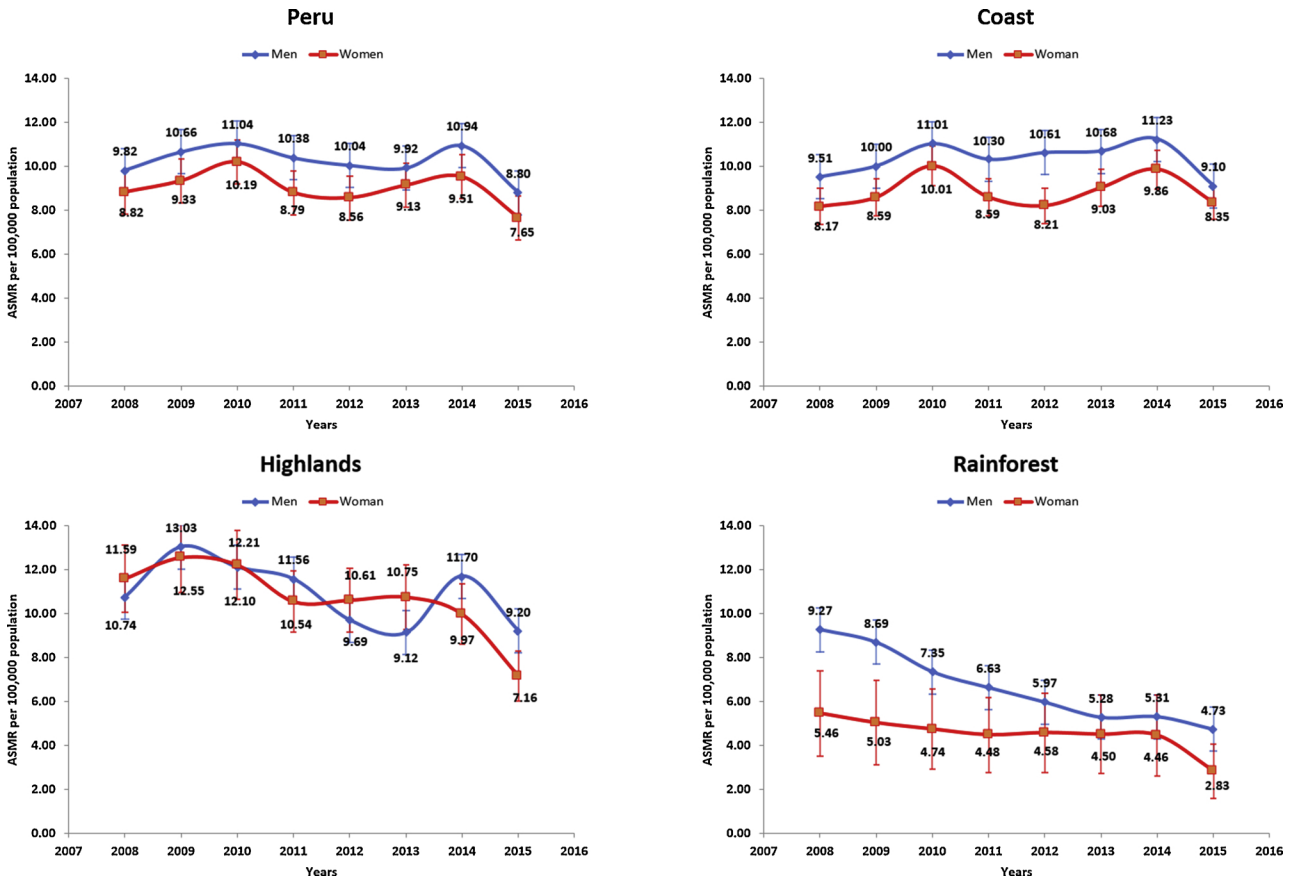

Fig. 2. National and regional age-standardized mortality rates per 100,000 population for stomach cancer per year and gender, 2008–2015.

estimates only. Regarding the coast, men had an ASMR of 9.5 in 2008, reaching their highest point in 2014 with a rate of 11.2 and then decreasing to 9.1 in 2015. Women had an ASMR of 8.2 in 2008, reaching their highest level in 2010 with 10.0 and decreasing to 8.4 in 2015. For the highlands, men had an ASMR of 10.7 in 2008, reaching the highest rate in 2009 with a value of 13.0 and declining to 9.2 in 2015. Women had an ASMR of 11.6 in 2008, the highest rate was in 2009 with a value of 12.6 and decreasing to 7.2 in 2015. The ASMRs for stomach cancer in the rainforest showed a gradual decline over the whole period for both sexes. Men had the highest ASMR in 2008 with 9.3, and the lowest in 2015 with 4.7. Women also had the highest ASMR in 2008 with 5.5, reaching their lowest point in 2015, too, with a rate of 2.8. Therefore, the highest rates were found in the highlands and the lowest in the rainforest region.

Overall, there was a favorable trend for both sexes throughout the study period. Table 1 shows the ASMRs for stomach cancer between 2008–2011 and 2012–2015 according to sex and divided by provinces, regions and national level. In men, the ASMRs decreased from 10.5 in 2008–2011 to 8.8 in 2012–2015 (16% reduction), and in women from 9.3 in 2008–2011 to 7.7 in 2012–2015 (16.8% reduction). The same pattern was observed in the three regions; the rainforest presented the greatest decrease in its ASMRs (42.9% reduction for men, 29.9% for women). On average, in the coastal region, the ASMRs decreased by 10.3% in men and by 11.4% in women. In the highlands, the ASMRs lowered by 23.2% in men and by 25.1% in women.

Fig. 3 shows the geographic distribution of ASMR for stomach cancer per year, according to provinces and sex. The provinces that had the highest ASMR (red color) for men and women were Huancavelica and Huánuco, both located in the highlands, followed by the provinces of Junin and Pasco (salmon color). The coastal provinces of Ancash, Ica, La Libertad and Lima had ASMRs between 13 and 18.9 per 100,000 for both sexes. The lowest rates for both sexes were in the rainforest region, mainly in Amazonas, Loreto and Madre de Dios.

Almost all provinces exhibited higher ASMRs for men than for women, except for Huancavelica, Moquegua, Puno and Tacna, were women had higher ASMRs. There were positive variations in some provinces. In men, strong upward trends (changes over 30%) were seen in Amazonas, Lambayeque, Madre de Dios, Moquegua and Piura. In contrast, Loreto, Tumbes and Ucayali had the most marked decrease in their ASMRs, with falls over 65%. In women, increases in ASMRs were not as high as those observed for men. The provinces with rises in rates were Ayacucho, Huancavelica, Ica, La Libertad, Lambayeque (which had the greatest rise of 53.9%), Madre de Dios, Moquegua and Piura, while the major decreases were observed in Tumbes and Ucayali, with declines of 77.1% and 66.9%, respectively.

4. Discussion

This study identified and quantified a decrease in the ASMRs for stomach cancer in both sexes (men: −16.0%, women: −16.8%) from 2008 to 2011 to 2012–2015, in Peru. Stomach cancer mortality in several Latin American countries will continue to decline [22] and these decreasing trends are thought to be attributable to the decrease in incidence rates, as the reductions reported in other countries of the region (Argentina, Brazil, Chile and Costa Rica) [6], in addition to the control of *H. pylori* infection and enhancements in conservation of foods and other dietary factors [5,6]. Moreover, this study has similar rates to those reported by *Sierra et al.* who compares stomach cancer burden across Central and South America [6]. For Peru, the ASMRs (2001–2005) were 12.4 per 100,000 population for men and 10.5 for women [6]. Our estimates in 2008–2015 for both sexes were

Table 1
Provincial, regional and national age-standardized mortality rates per 100,000 population for stomach cancer in men and women in 2008–2011 and 2012–2015, and the corresponding percentage change in rates.

	Men			Women		
	2008–2011	2012–2015	% change (2008–2015)	2008–2011	2012–2015	% change (2008–2015)
Peru	10.47	8.80	−16.0	9.28	7.72	−16.8
Coast	10.21	9.15	−10.3	8.84	7.83	−11.4
Highlands	11.86	9.11	−23.2	11.72	8.78	−25.1
Rainforest	7.99	4.56	−42.9	4.93	3.46	−29.9
Amazonas	5.01	7.42	48.1	3.70	3.60	−2.7
Ancash	9.31	9.01	−3.3	9.86	8.71	−11.7
Apurimac	7.24	7.83	8.2	6.91	6.73	−2.5
Arequipa	6.87	5.16	−24.9	6.10	4.76	−22.0
Ayacucho	12.99	9.52	−26.7	10.90	12.79	17.4
Cajamarca	11.01	8.69	−21.0	10.66	5.00	−53.1
Callao	12.46	10.05	−19.4	8.15	7.64	−6.2
Cusco	4.88	3.55	−27.3	4.43	3.34	−24.6
Huancavelica	23.05	19.16	−16.9	25.50	25.94	1.7
Huanuco	26.54	18.48	−30.4	24.86	17.55	−29.4
Ica	12.42	10.79	−13.1	7.81	9.18	17.5
Junin	17.26	13.26	−23.2	17.16	12.42	−27.6
La Libertad	11.22	12.80	14.1	11.03	11.44	3.7
Lambayeque	7.85	11.05	40.8	6.11	9.41	53.9
Lima	11.52	9.31	−19.2	9.87	7.76	−21.4
Loreto	4.84	1.59	−67.2	2.08	1.14	−45.0
Madre de Dios	6.64	8.69	30.9	3.64	3.88	6.7
Moquegua	3.69	4.90	32.7	4.09	5.17	26.4
Pasco	14.92	11.81	−20.9	13.67	11.15	−18.4
Piura	5.19	6.99	34.8	5.45	6.43	18.1
Puno	3.09	3.17	2.5	5.05	3.76	−25.5
San Martin	9.81	5.96	−39.3	6.51	6.25	−3.9
Tacna	5.32	3.18	−40.2	7.22	3.21	−55.6
Tumbes	9.36	3.58	−61.8	8.67	1.99	−77.1
Ucayali	14.10	4.44	−68.5	9.29	3.08	−66.9

lower than the previous ones, confirming the trend towards the decrease in cancer mortality in the region [23].

The highest rates for stomach cancer were observed in the highlands provinces of Huancavelica and Huánuco, both with an elevated proportion (around 40%) of population living in poverty [7,8,24]. Likewise, the General Directorate of Epidemiology from Peru [7] and *Piñeros* et al. [8] indicated that most deaths came from the highlands, where a high incidence of poverty exists [18]. This scenario may explain the lower rates of the coast, a more developed region, compared to the highlands ones, but it does not fully address why the rainforest, which has a poverty index as high as in the highlands, has the lowest mortality rates over the 8-year study period. Therefore, additional risk factors must influence these outcomes in the highlands for both men and women. The differences observed may partially reflect deficient reporting systems as elsewhere in the country; however, mortality rates have remained consistently low all along. In Lima (Peru), *Chirinos et al.* conducted a case-control study of stomach cancer [25]. Patients with stomach cancer usually came from the Andean zone (highlands), had a low socioeconomic background, low consumption of fruits and vegetables and used firewood, charcoal, or kerosene to cook, which may be related to nitrosamines exposure [10,25]. Additionally, people from the highlands tended to preserve food by salting and drying it in the sun (dry potatoes -*charqui*-, dried fish) [25] and this may increase the risk for stomach cancer. A meta-analysis reported that tobacco, alcohol drinking, high consumption of red or processed meat and excessive consumption of salt were associated with a moderate increase in gastric cancer risk in Latin America [10]. In contrast, high levels of education and fruit and vegetable consumption were associated with a moderately reduced risk [10].

The best recognized risk factor for stomach cancer is *H. pylori* infection. Poor sanitation and contaminated water has long been recognized as the major responsible for early and recurrent *H. pylori* infection [6] and, as a consequence, for the development of stomach cancer [10]. Provinces from the highlands have limited access to health services, lower availability of drinking water and a poorer drainage system, which could promote the spread of these bacteria [7,26]. Even though *H. pylori* prevalence has declined in Peru, it still remains high among individuals of low socioeconomic status [6]. Recently, definitive evidence of contaminated water [27] and pharmacological resistance of *H. pylori* to standard antibiotics was reported in Lima [28]. Although, there are no similar studies made on rural areas, we believe that the pattern could be replicated.

People living in the highlands may also have a genetic predisposition to develop stomach cancer but no formal correlation has been identified yet [9,12,29]. Altitude by itself seems to cluster host, bacterial, dietary and environmental factors related to the risk of stomach cancer [9]. However, the differences in stomach cancer mortality patterns presented in different provinces of the three geographical regions are not fully understood. The interprovincial migration of the Peruvian population, as well as the change in lifestyle habits (diet and sanitation) during the last decades, could be an explanation.

Mortality rates might also be explained by the scarcity of preventive health policies, such as the absence of national guidelines for early detection and timely treatment of this neoplasm [30]. In Peru, we can provide the standard of care according to international guidelines [31,32], including endoscopic resections for early stomach cancers [33]; gastrectomy and lymphadenectomy [34]; as well as perioperative chemoterapy and adjunvant treatment [35]. However, the most specialized cancer institutions are centralized on the coast and are not easily accessible to everyone. The Instituto Nacional de Enfermedades Neoplásicas (INEN) is the principal center in cancer prevention and control in Peru [30] and it is located in Lima. Two other important centers that aid in the decentralization of cancer care are located in the northern (La Libertad) and southern coast (Arequipa) [30]. Even

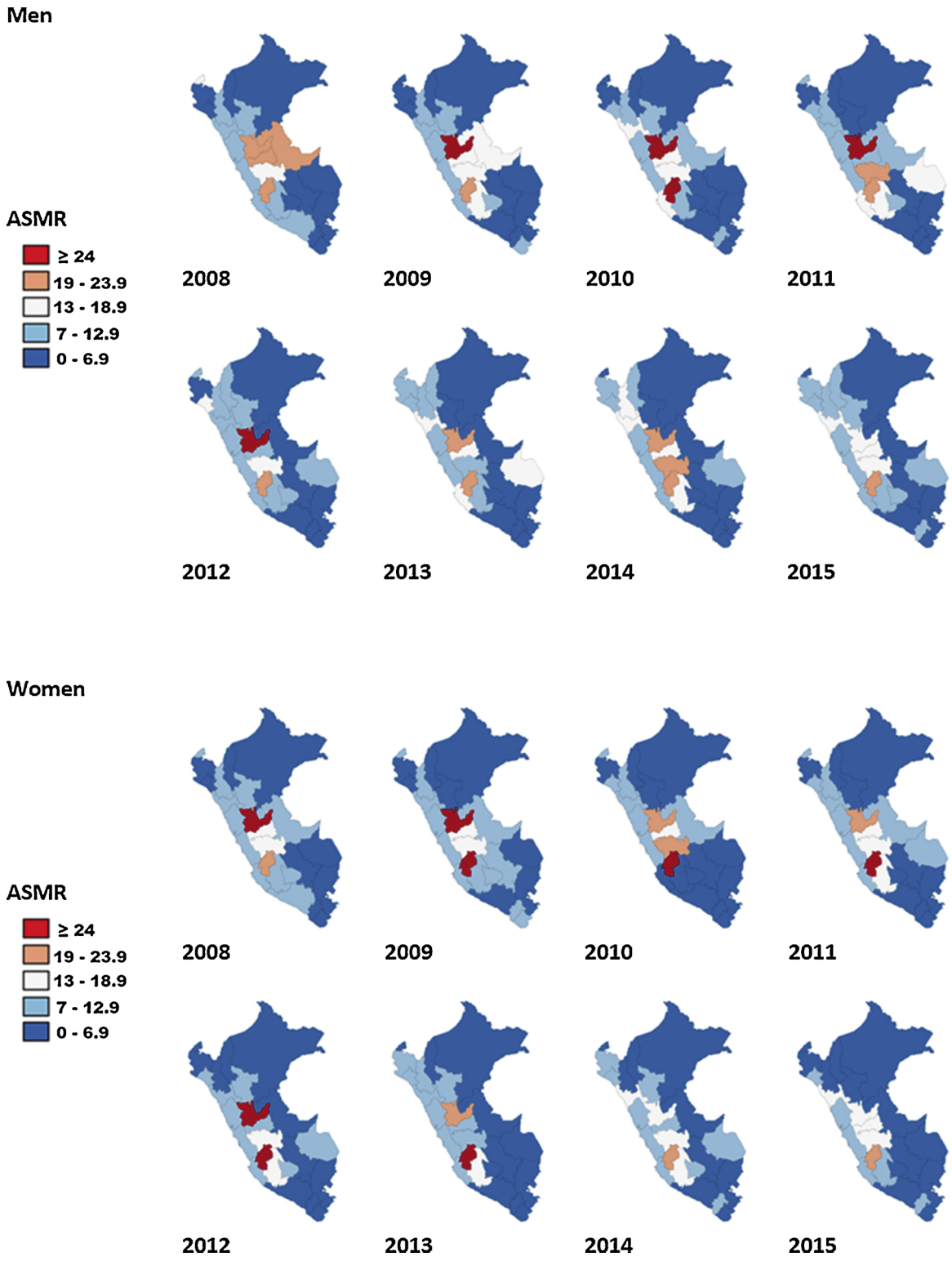

Fig. 3. Provincial age-standardized mortality rates per 100,000 population for stomach cancer per year and gender, 2008–2015.

though referrals can be made from the highlands or rainforest to more specialized institutions in the coast, there are barriers regarding access to services (travelling distance), patients' first contact with the healthcare system, and treatment coordination [36,37] that hinder the flow of patients to specialized care. This fragmented Peruvian health system [14] leads to the diagnosis of stomach cancer at advanced stages [26,34] and to a negative impact on mortality with a survival rate of 30 months, and the majority of deaths occurring in the poorest areas of the country [26].

In order to address this issues, the Comprehensive Health Insurance (SIS) started to cover the expenses from oncological care in Peru in 2008 [26,30] and this was later strengthened in 2012 with the creation of the "*Plan Esperanza*" in order to improve cancer care and access to oncological services [26,30]. An achievement of this program was that

from 2012 to 2015, 33% of stomach cancers in Peru were diagnosed at stage I or II [30]. Thus, it is plausible to expect further declines in mortality from stomach cancer in the near future.

This study has some limitations to be considered when interpreting our results. The most important is the deficit of a high quality national cancer registry and valid death certification data. We performed a secondary analysis from the Peruvian Ministry of Health database, a registry vulnerable to reporting bias, especially in the regions with poor health and communication systems. However, we corrected for under-reporting informed by the MINSA [7]. We believe therefore that the data provided in this study show, with satisfactory validity, the Peruvian epidemiological profile for stomach cancer mortality over the recent years. These findings should serve to make awareness on the importance of preventive services improvement, thereby reducing mortality through new health policies, including *H. pylori* eradication, surveillance of subjects with premalignant lesions and the promotion of healthy diet and lifestyles, in addition to reducing disparities in the access to healthcare in the three geographical regions.

Overall, our findings indicated that mortality rates due to stomach cancer have experienced a moderate decline in an 8-year period in Peru. The ASMR was the highest in 2010, and the lowest in 2015, with the highlands region concentrating the largest number of deaths in the country. This geographical and temporal pattern could reflect a different distribution in stomach cancer risk factors as the prevalence of *H. pylori*, poor dietary habits, in addition to the low socioeconomic background of the Andean population and the lack of a well-articulated and decentralized health system. These social, nutritional and host-related factors need further assessment.

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