Spatial Analysis of Cerebrovascular Disease Mortality before and during the COVID-19 Pandemic in Peru, 2017-2022

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Abstract

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Cerebrovascular disease (CVD) is a significant global health concern, ranking as the second leading cause of death and disability worldwide, with 7.3 million deaths in 2021. The COVID-19 pandemic exacerbated existing healthcare challenges, particularly for non- communicable diseases like stroke. Peru, one of the hardest-hit countries in Latin America, faced severe strain on its healthcare system. This study analyzed the geographic distribution of CVD mortality in Peru before and during the COVID-19 pandemic. We employed a secondary analysis of stroke-related deaths from 2017 to 2022, sourced from the National Informatic System of Deaths (SINADEF), and population estimates from the National Registry of Identification and Civil Status (RENIEC). We estimated age- and sex-adjusted standardized mortality ratios (SMR) of stroke. The spatial analysis utilized a Poisson- Lognormal model implemented in R, using the INLA and sf packages for small area estimation. We identified areas with higher-than-expected stroke SMRs, and areas with lower

ratios than the national average. Pre-COVID years showed consistent spatial patterns with higher SMRs than the national average in northern, central, and southern departments. During the COVID-19 pandemic, these patterns mostly persisted and intensified, with continued high SMRs in the same regions. An overall increase in stroke mortality was observed during the pandemic, particularly in 2020 and 2021. The findings highlight persistent geographical disparities in stroke mortality in Peru. Limitations include potential inaccuracies in the SINADEF registry, insufficient differentiation between stroke types, and underreporting in rural areas. Despite these limitations, the study provides valuable insights for targeted healthcare interventions and resource allocation. Regions in the Northwest and South of Peru consistently showed higher stroke SMR than the national average. While the SMR increased, patterns also remained stable across the years. These findings emphasize the need for improved resource allocation and healthcare infrastructure resilience to address both immediate and long-term public health challenges. Lastly, enhanced coverage and accuracy of national registries are crucial for effective public health planning and intervention strategies.

Background

Globally, CVD stands as a significant public health concern with varying incidence and outcomes according to the WHO.[1] According to the Global Burden of Disease (GBD) study in 2019,[2] CVD is the second leading cause of death and the third leading cause of death and disability, with 12.2 million prevalent cases (95% UI 11.0–13.6) and 101 million incident cases (93.2–111), respectively. The study also attributes 6.55 million (6.00–7.02) deaths to stroke. Furthermore, in 2019, low-income countries exhibited a standardized age-related mortality rate for CVD 3.6 (3.5–3.8) times higher than that of high-income countries, according to the World Bank classification.[2]

The World Stroke Organization reported a significant decline in stroke admissions globally during the COVID-19 pandemic in 2020, with nearly 90% of surveyed members across 100 countries observing a median decrease of 50–70%.[3] The reasons behind this decline remain ambiguous but may be attributed to fewer patients seeking care, COVID-19-related mortality, or potentially a genuine decrease in stroke incidence, potentially influenced by lifestyle changes amid the pandemic.[3,4]

Latin America had the world's fourth-largest burden of CVD (6.8 million disability-adjusted life years), with an estimated prevalence of 32 per 1000 inhabitants and a higher incidence in males (261) than females (217).[5] In Peru, the age-standardized incidence ranged from 93.9 to 109.8 per 100,000 person-years between 2010 and 2018.[6,7] In low-income settings, such as certain Latin American countries, challenges related to healthcare access, affordability of medications, and socioeconomic disparities play a significant role in shaping the higher incidence of CVD.[2,5]

Understanding geographical differences in cerebrovascular mortality rates is essential for optimizing emergency medical services and the healthcare system, improving health outcomes in marginalized communities and for those with limited access to care.[2] In the US, there is substantial disparity in stroke mortality rates across counties[8] and the 90th percentile for stroke mortality was predominantly in the south. Stroke mortality has been linked to environmental exposures, housing, population density, and access to healthcare.[2,9] These findings suggest the importance of evaluating the efficacy of health interventions across local areas with varying levels of cardiovascular disease risk, to identify priority areas for the implementation and capacity-building of healthcare facilities. In Latin America, research on geographic patterns impacting stroke outcomes is limited. However, studies in Colombia and Brazil have identified factors such as traffic congestion;[10,11] with centers reporting 94.83% reduction in service area offered by stroke centers in Bogota.[11] Likewise, spatial overlap of centers in urban areas may lead to inefficient resource allocation, while living in rural areas is associated with higher mortality rates due to insufficient resources to treat stroke.[10–12]

The COVID-19 pandemic left a profound impact worldwide with over 774 million confirmed cases and over 7 million deaths globally as of January 2024.[13] Peru, in particular, faced significant challenges, ranking among the top 15 countries globally in reported COVID-19 cases and standing as the second most affected country in Latin America, after Brazil.[14] Peru is currently still being affected by the pandemic, with more than 4 million cases and more than 220,000 deaths, with a fatality rate of 4.87% as of January 31, 2024.[15] The pandemic has placed immense strain on hospital emergency services, hospitals, intensive care units, and resulted in high mortality rates.[14]

The COVID-19 pandemic significantly disrupted the delivery of prevention and treatment services for non-communicable diseases (NCDs) in the Americas, according to a report by the

Pan American Health Organization/World Health Organization (PAHO/WHO).[16] A survey, involving 158 countries globally and 28 Member States of PAHO, revealed that 64% of these countries experienced partial interruptions in health services, and two had complete shutdowns. In contrast, 25% managed to keep services operational. This interruption affected the care of chronic diseases such as cancer, cardiovascular diseases, and diabetes, with many people no longer receiving planned treatments. Moreover, healthcare personnel and resources have been reassigned to address COVID-19 demands, exacerbating the challenge of ensuring continuous care of NCDs.[16,17]

In this context, this study analyzed the spatial distribution of cerebrovascular disease mortality in Peru before and during the COVID-19 pandemic between the years 2017 to 2022, using death records from the National Informatic System of Deaths (SINADEF in Spanish).

Data Description

This study was conducted using individual-level death records from the SINADEF.[18] In 2019, SINADEF coverage accounted for 62.15% of all deaths in Peru based on death estimations from the National Statistics and Informatics Institute (INEI in Spanish).[19] This open-access database accounts for individuals who died of any cause. We used deaths reported from January 2017 to December 2022. This database can be found at:

https://www.minsa.gob.pe/reunis/data/defunciones_registradas.asp.

The National Registry of Identification and Civil Status (RENIEC) has district-level population estimates disaggregated by sex and age for the years 2017 to 2022, including people living in Peru and abroad. We used data published in the RENIEC website (https://portales.reniec.gob.pe/web/estadistica/baseDatos).[20]

Geographic boundaries for Peru are available at the INEI website in a shapefile format for the first, second, and third administrative levels.[21] Peru is divided into departments (N=25, 24 departments and 1 constitutional province), provinces (N=196), and districts (N=1874). Ubigeo is a coding system that represents the three administrative levels in Peru. Geographical zones in Peru can be divided in coastal, highlands and jungle regions (see Figure 1). They can be accessed at https://proyectos.inei.gob.pe/microdatos/, selecting “Mapa de Pobreza”.

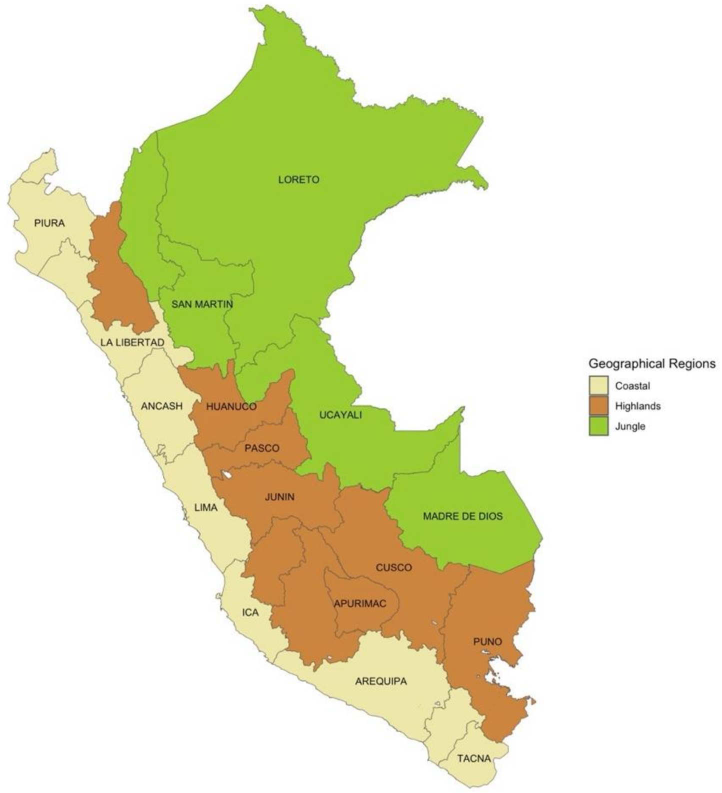

Figure 1. Geographical regions of Peru by department.

Methods

This study is an observational retrospective study. The mortality rate numerator included all deceased individuals, who were registered in the SINADEF, and who died between January 2017 and December 2022 with stroke as the primary cause of death. Stroke deaths were initially identified with ICD-10 codes G45, G46, or I60–69. We excluded individuals with violent deaths and those whose primary cause of death was unclear, incomplete, or discordant. Extensive data cleaning was performed as stroke deaths had been registered under different labels. Mortality data was tabulated according to ICD-10, death year, age, sex, and ubigeo code, indicating department, province, and district. We calculated expected deaths by multiplying each administrative level's age- and sex-specific population by the age- and sex-specific overall mortality rate of the population (ie, for Peru as a whole), and then summing across age and sex:

$$E_i = \Sigma_{age,sex}\left(Population_{age,sex,i} \cdot Peru\ Mortality\ Rate_{age,sex,i}\right)$$

These specific mortality rates were calculated considering data across the 6 years, and by each separate year. All-year calculation was used to understand the increase in mortality across years, while the each-year calculation was used to explore differences in spatial patterns by year. Standardized Mortality Ratios (SMR) were calculated using the following formula:

$$SMR_i = \frac{Y_i}{E_i}$$

where Y_i and E_i represent the observed and expected death count, respectively, in area i.

Descriptive analysis calculated summary statistics such as mean, standard errors, median, interquartile range, etc. to summarize mortality. Our geographic unit of analysis included departments, provinces, and districts. To address the spatial aspect of the data, we employed disease mapping techniques and smoothing using Poisson-Lognormal spatial models, and spatial and non-spatial random effects.

We added spatial (ICAR) random effects to the model and parameterized in terms of variance and proportion that is spatial. The model where β_0 is the intercept; and b_i, the random effects in area *i* is:

- *Stage 1*: Likelihood and linear model:

$$Y_i|SMR_i \sim \text{Poisson}(E_i \cdot SMR_i)$$
$$\log(SMR_i) = \beta_0 + b_i$$

- *Stage 2*: b_i is an area-specific random effect that captures variation in the (log) relative risk of disease in area i. This random effect is given by the sum of two components, e_i (unstructured spatially) and S_i (structured spatially). The prior distribution for e_i is $e_i|\sigma_e^2 \sim_{iid} \text{N}(0, \sigma_e^2)$ and the prior distribution for S_i is intrinsic conditional autoregressive (ICAR). INLA's bym2 model was used for this random effect, and the parameterization is in terms of the total variance σ_b^2 and the proportion of that variation that is structurally spatially ϕ.

$$b_i = e_i + S_i$$

- *Stage 3:* Penalized complexity priors were used for the marginal variance σ_b^2 (u = 0.5/0.31, alpha = 0.01) and mixing parameter ϕ of b_i (u = 0.5, alpha = 0.5). An improper normal prior was used for the intercept ($\beta_0 \sim N(0, \infty)$). The overall hyperprior on the hyperparameters β_0, σ_b^2, ϕ, assuming independent priors, is given by:

$$p\left(\beta_0, \sigma_b^2, \phi\right) = p(\beta_0)\, p\left(\sigma_b^2\right) p(\phi)$$

We obtained smoothed SMRs and its Uncertainty Intervals (UI) at 95%. These approaches helped provide an understanding of geographic disparities in stroke mortality from 2017 to 2022. Analysis was conducted using the package INLA and sf in R version 4.3.3. Additionally, a chronic disease comparator (i.e. prostate cancer) was used to asses temporal changes. Ethical approval was obtained for the study though the data does not contain any personal identifiers.

Results

Our study investigated the spatial distribution of stroke mortality across different administrative levels in Peru: departments, provinces, and district levels. There were 17,155 and 26,671 stroke-related deaths, between the years 2017-2019 and 2020-2022, respectively. The stroke-related Standardized Mortality Ratio (SMR) varied considerably across different administrative units. The temporal-spatial analysis of SMR before and during the COVID-19 pandemic are illustrated in Figure 2 and Figure 3. At the department level, SMR's 25^{th} and 75^{th} quartiles ranged from 0.88 to 1.28. San Martin, a northern jungle department, consistently exhibited the highest SMR across the years 2018 to 2022, ranging up to 1.90, 95% UI [1.71-2.12] in 2020, indicating a two-fold higher mortality compared to the national average.

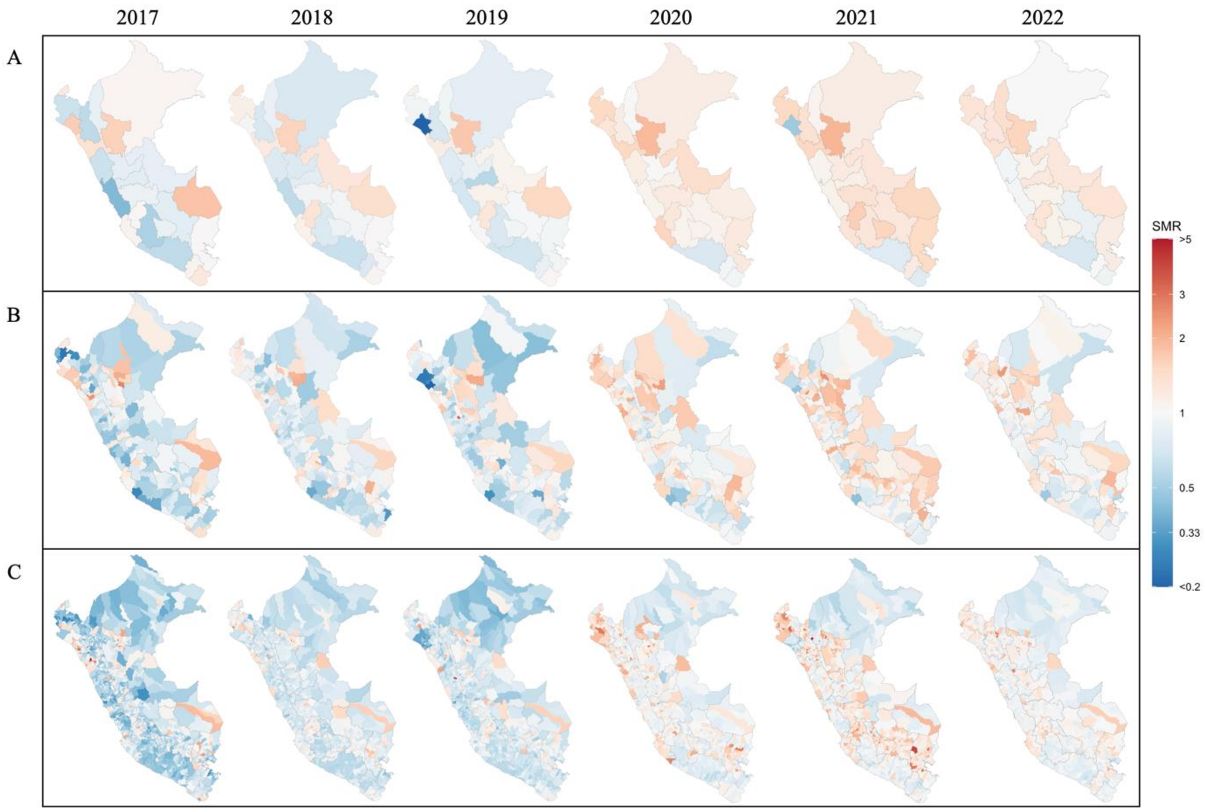

Figure 2. Age- and sex-adjusted stroke-related Standardized Mortality Ratio (SMR) by (A) department, (B) province, and (C) district, 2017-2022. SMR calculated using all-year estimates. *Lognormal Spatial Smoothing Model.*

At the province level, SMR's quartiles ranged from 0.76 to 1.20, while at the district level, SMR quartiles ranged from 0.70 to 1.05. Asuncion province in the highlands of Ancash department displayed the highest SMR with a value of 3.46, 95% UI [2.03-5.88] in the year 2019. Provinces such as Lamas in the jungle department of San Martin (2.15, 95% UI [1.59-2.90]), Otuzco in the highlands of La Libertad department (2.43, 95% UI [1.88-3.15]), Picota (2.70, 95% UI [1.82-4.00]), and San Martin (2.11, 95% UI [1.70-2.62]), both at San Martin department, were also among the ones with the highest SMR during 2017-2019. The provinces with the higher SMR since 2020 were Marañon (2.19, 95% UI [1.44-3.36]), between the highlands and jungle of Huanuco department, Rioja (2.51, 95% UI [1.98-3.19]), again in San Martin, San Marcos (2.14, 95% UI [1.55-2.96]), San Martin (2.31, 95% UI [1.89-2.82]) and San Pablo (2.51, 95% UI [1.69-3.74]), both in the highlands of Cajamarca department, and

Utcubamba (2.39, 95% UI [1.89-3.02]) in the jungle department of Amazonas.

All these provinces are located in the North of Peru, with the exception of Marañon, located in Central Peru. While the spatial distribution of stroke mortality appeared stable from 2017 to 2019, there was a clear increase of SMRs in most regions in 2020 and 2021, with a slight decrease in 2022 (see figure 2).

Similarly, the districts that exhibited higher mortality were mostly located in the north of Peru, particularly areas in the highlands and jungle. Stroke mortality in Northern districts as Llapa (4.19, 95% UI [2.42-7.26]) in Cajamarca, and Lonya Grande (6.08, 95% UI [3.75-9.86]), and Southern districts as Nuñoa (3.94, 95% UI [2.25-6.89]) in the highlands of Puno, was higher in 2021.

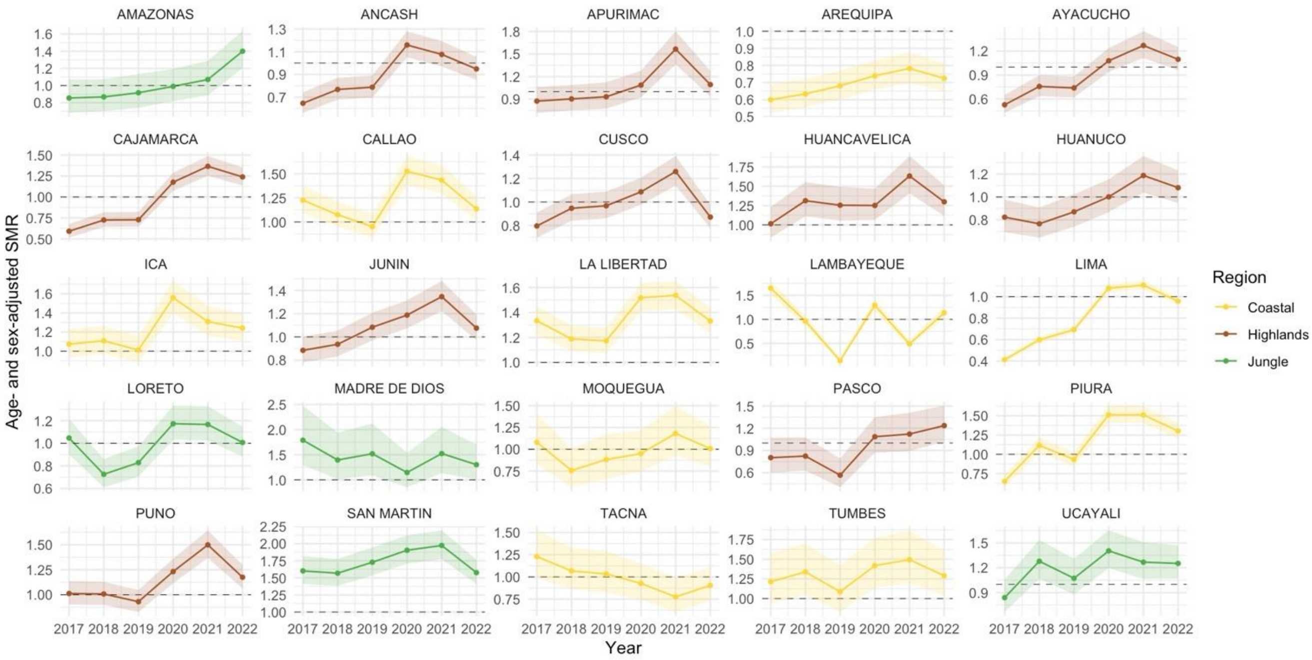

Figure 3. Age- and sex-adjusted stroke-related Standardized Mortality Ratio (SMR) by departments, geographical region and year, 2017-2022. SMR calculated using all-year estimates. *Lognormal Spatial Smoothing Model*.

Our analysis of spatial patterns by each year is shown in Figure 4. While there is very little variation across years, we observe that stroke-related affected areas continued being the most affected ones during the pandemic years. Pre-COVID years showed consistent spatial patterns with high SMRs in the Northwest, the Southeast, and Northcentral regions, including areas in the coast, highlands and jungle of Peru. At the department level, while we observed lower SMR than the national average in Loreto (most Northern department), Huanuco (highlands department), among others, smaller geographic units revealed provinces and districts with higher SMR than the national average for each year. Notably, these regions of Peru exhibited higher SMR values at each administrative level. The analysis shows a heterogeneous distribution of stroke mortality within departments.

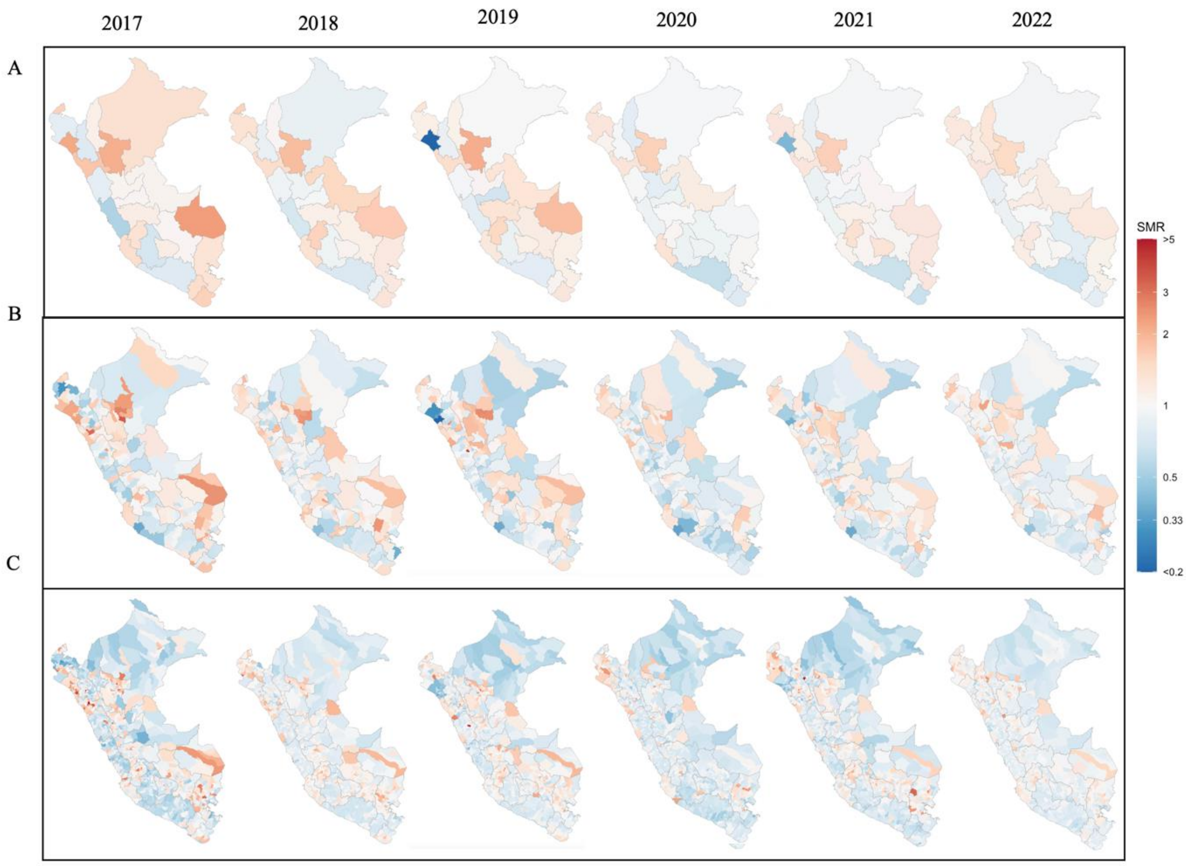

Figure 4. Age- and sex-adjusted stroke-related Standardized Mortality Ratio (SMR) by (A) department, (B) province, (C) district, and year, 2017-2022. SMR calculated using each-year estimates. *Lognormal Spatial Smoothing Model.*

Likewise, before applying spatial smoothing techniques, we observed notable disparities in stroke mortality. Crude mortality rates increased considerably during the COVID-19 pandemic when compared to a different chronic disease (i.e. prostate cancer) (see figure 5), with an overall increase within departments, provinces, and districts (see Appendix 1-4). Specifically, certain areas within Loreto exhibited among the highest crude stroke mortality values in the country, highlighting the importance of examining subregional patterns of disease burden. While larger geographic units can exhibit higher or lower mortality, this analysis demonstrates the importance of focusing on smaller units (provinces and districts) as these can potentially exhibit a higher mortality that expected.

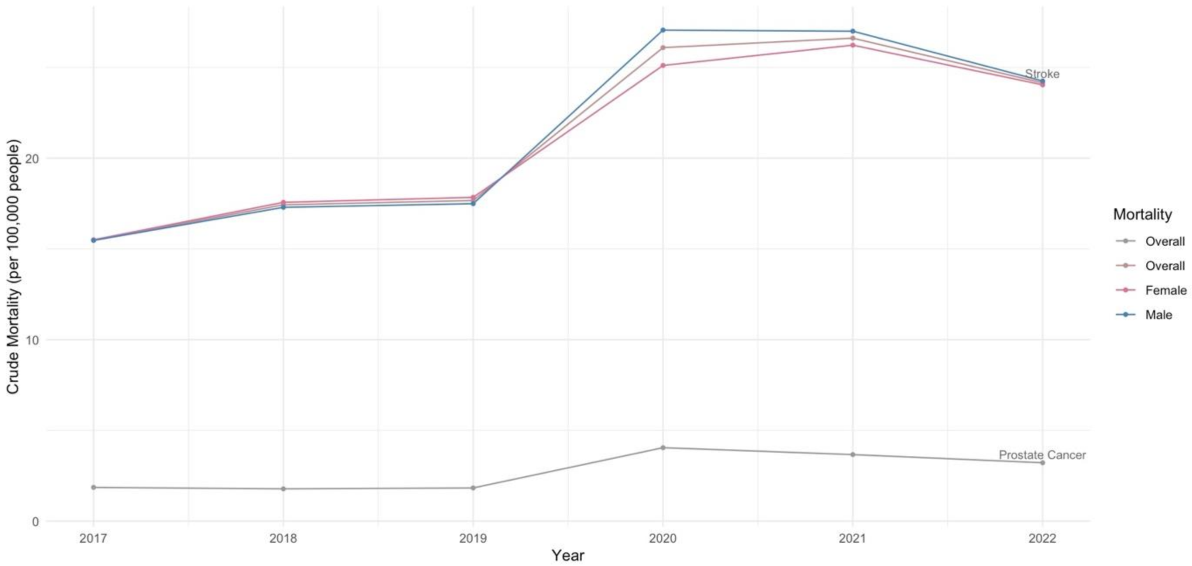

Figure 5. Crude stroke-related mortality per 100,000 people in Peru by sex and year, 2017-2022. Prostate cancer patterns added only to compare stroke with another chronic disease.

Discussion: conclusion and limitations

This study contributes to the understanding of the geographic distribution of patients with cerebrovascular disease in Peru. We identified potential regional disparities in the distribution of stroke deaths, particularly in the North and South of Peru, mostly in the highlands and jungle.

Peru has an uneven population distribution. While 55.6% of the population resides in the coast, only 29.6% and 14.5% resides in the highlands and jungle, respectively.[21] According to INEI estimates in 2020, 29.7% of the population is concentrated in Lima, the capital of Peru. However, we observed that outside this urban area, mostly districts along the highlands and nearby coast and jungle of Peru had a higher risk of death than the national average.

Before the COVID-19 pandemic, while urban areas had been affected due to an inefficient use of resources, traffic congestion, among other spatial factors, rural districts were affected by the lack of access to health services.[11,12] This became more evident in Peru during the pandemic given the spatial patterns of more affected areas, as it did in most countries worldwide.[12,22] It is also important to mention that while stroke was largely affected by inadequate access to care, other disease-mediated factors could potentially be involved in the observed patterns given the difference when comparing with a different chronic disease (i.e. prostate cancer, figure 5).

Our study had some limitations. The study relied on death records from SINADEF. These records contained inaccuracies, or misclassifications, which could affect the reliability and validity of the findings. According to a study from the Institute for Health Metrics and Evaluation, since 2000, over 45% of deaths in Peru have been assigned a garbage ICD10 code in the latest year, impacting the quality of cause-of-death data.[23] In one Peruvian region, 17.2% of deaths were attributed to a poorly defined cause, and 9.2% of deaths had ICD-10 coding misclassification.[24] However, since the implementation of SINADEF in 2017, the quality of death registries has improved by 45%.[25]

In addition, although uncertainty intervals were the narrowest across departments, these became larger as we look at more detailed administrative level. As expected, the widest uncertainty was observed in district-level estimates. This highlights the importance of considering uncertainty in spatial analyses in smaller geographic units. Still, district-level estimates provided a general overview of focus areas to shift our resources.

Lastly, non-spatial and spatial random effects suggest that in most departments there could be random variability in death risk across different areas of Peru. However, this changes when we focus on provinces and districts, suggesting possible clusters in some areas with higher-than-expected death risk, while other areas had lower-than-expected risk.

We encourage future studies consider variables such as rural/urban area. Lastly, while underreporting of deaths in 2019 was found to be 37%; to date, underreporting of about 25% is assumed.[19] This means we could potentially underestimate the mortality rate, limiting our understanding of the stroke excess burden.

Despite these limitations, the study has provided valuable insights into cerebrovascular disease mortality patterns and the impact of COVID-19, contributing to the local and global epidemiological knowledge of cerebrovascular disease, providing a valuable baseline for future research and public health initiatives dedicated to mitigating the impact of stroke on the Peruvian population. We expect our study to facilitate recommendations for more effective allocation of medical resources and help identify specific prevention and rehabilitation strategies to improve access to stroke care services.

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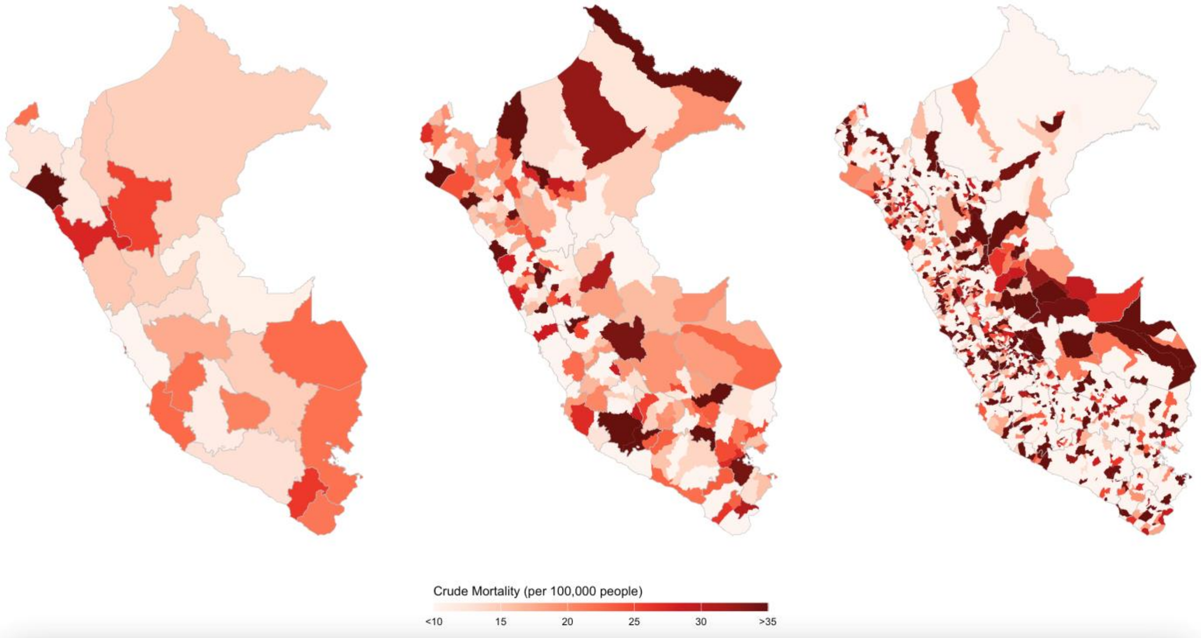
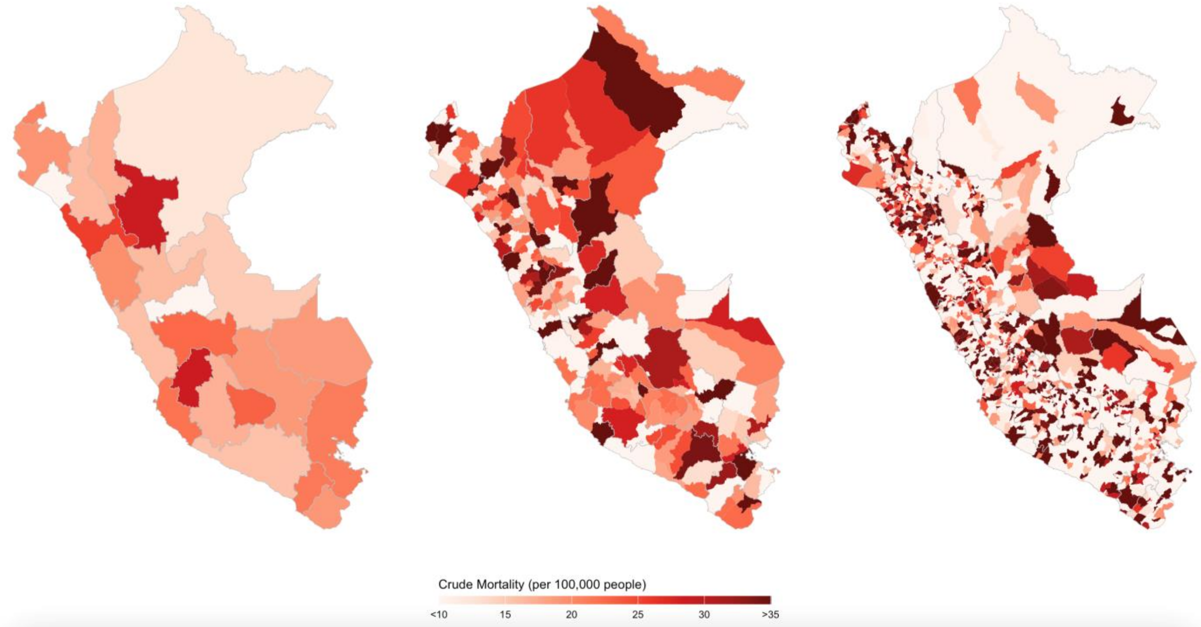
Appendices

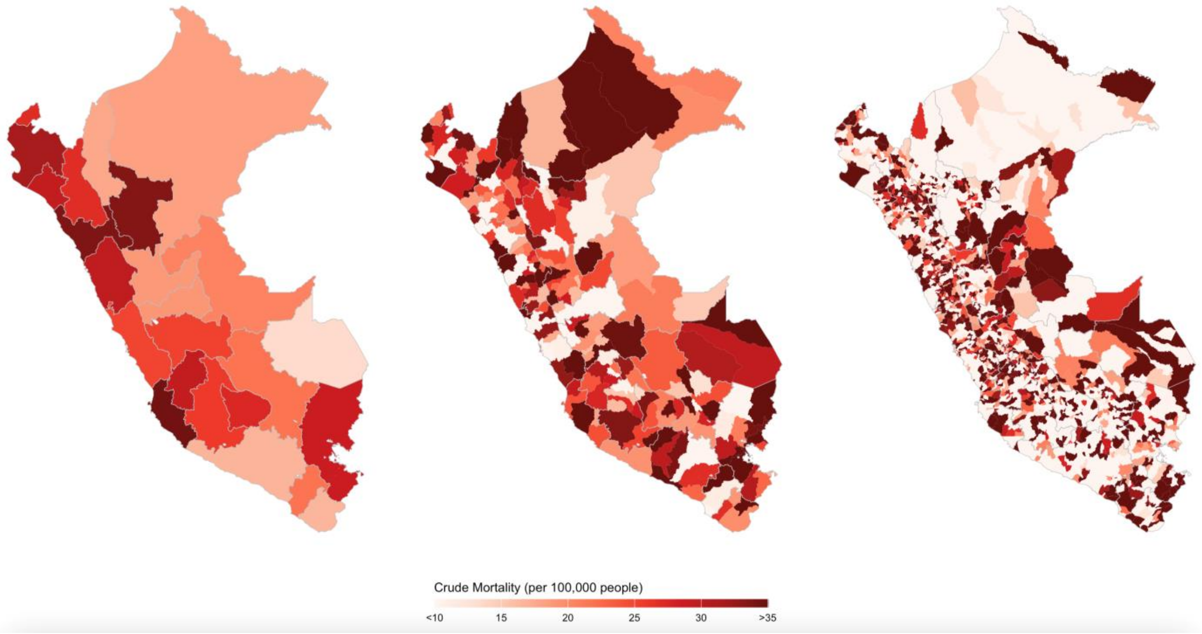
Appendix 1. Crude and unsmoothed stroke-related mortality per department, province, and district, 2017.



Appendix 2. Crude and unsmoothed stroke-related mortality per department, province, and district, 2019.



Appendix 3. Crude and unsmoothed stroke-related mortality per department, province, and district, 2020.



Appendix 4. Crude and unsmoothed stroke-related mortality per department, province, and district, 2022.