Mortality from all causes before and during the COVID-19 pandemic in Peru: The role of sociodemographic factors and accessibility

Antonio M. Quispe (drantonioquispe@gmail.com)
Universidad Continental
Lucía Vargas
Universidad Nacional Mayor de San Marcos
Wilter C. Morales-García
Unidad de Salud Pública, Universidad Peruana Unión
Javier L. López-Gonzales
Facultad de Ingeniería y Arquitectura, Universidad Peruana Unión
Jorge Sánchez-Garcés
Facultad de Ingeniería y Arquitectura, Universidad Peruana Unión

Article

Keywords: COVID-19, SARS-CoV-2, Mortality, Sociodemographic Factors, Epidemiology, Peru

Posted Date: October 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2160215/v1

Abstract

Peru suffered the highest mortality rates worldwide during the COVID-19 pandemic. In this study, we assessed the Peruvian districts' all causes of mortality-associated sociodemographic factors before and during the COVID-19 pandemic using mixed-effects Poisson regression models. During the pre-pandemic and the first four COVID-19 waves, the Peruvian districts reported mean weekly mortality of 22.3 (standard deviation 40.4), 29.2 (38.7), 32.5 (47.2), 26.8 (38.9), and 24.4 (38.0), respectively. We observed that before the COVID-19 pandemic, the districts' weekly deaths were associated with the human development index ((HDI) adjusted incidence rate ratio (aIRR) 0.11 (95% confidence interval 0.11–0.12)), accessibility (aIRR 0.99 (0.99–0.99)), poverty (aIRR 0.99 (0.99–0.99)), and anemia (aIRR 0.99 (0.99–0.99)). However, during each of the first four COVID-19 waves, the magnitude of association between the districts' weekly deaths and HDI decreased (first, aIRR 0.61 (0.58–0.64); second, aIRR 0.54 (0.52–0.57); third, aIRR 0.20 (0.19–0.22); fourth, aIRR 0.17 (0.15–0.19)), but the association with accessibility (aIRR 0.99 (0.99–0.99)), poverty (aIRR 0.99 (0.99–0.99)), and anemia (aIRR 0.99(0.99–0.99)) remain constant. Before and during the COVID-19 pandemic, a solid association existed between all-cause mortality and the district's sociodemographics, increasing with lower HDI, accessibility, poverty, and anemia rates.

Introduction

The COVID-19 pandemic increased mortality to historic levels, with a cumulative official death toll by September 2022 of over 6.55 million deaths directly attributed to COVID-19 worldwide, according to ourworldindata.org. Among the hardest-hit countries, Peru stands alone as the country with the highest mortality due to COVID-19 for a second year straight1. Currently, Peru continues leading the tragic ranking of countries with the higher cumulative mortality, with over 6.5 deaths per million people. This mortality is so high that the second-ranked country, Bulgaria, had cumulative mortality below 5.5 COVID-19 confirmed deaths per million people. Furthermore, all other countries have cumulative mortalities below five COVID-19 confirmed deaths per million people, according to ourworldindata.org.

To prevent deaths, particularly in developing countries, further understanding the sociodemographic-associated factors of all-cause mortality is essential. This association was significant during COVID-19 because it highlights its reality as a social phenomenon[1]. Factors such as the human development index (HDI) can help decision-makers further understand the COVID-19 pandemic impact at the macro and microregional levels because all the elements used for its calculation (life expectancy, education, and gross national income per capita) are associated with COVID-19 mortality[2]. Living conditions also play a crucial role in the epidemiology of COVID-19 mortality since comorbidities and poor healthcare coverage enhance SARS-CoV-2 mortality[3]. The sociodemographic factors can help us further understand the dynamics of COVID-19 mortality and input our new knowledge into decision-making to prevent deaths based on reliable indicators[4].

To understand the mortality risk during the COVID-19 pandemic, we need to understand its complex and interrelated association with the socioeconomic factors at the macro and micro-regional levels[5]. We certainly can explore this association with more detail at the district level rather than at the country level, as usually reported. Furthermore, the variability of the death risk across COVID-19 waves may help us to understand what happens with such association when the death risk is higher (as in the first and second COVID-19 wave in Peru, due to the deathliest SARS-CoV-2 variants, including the index and the Delta virus, respectively) versus lower (as in the third and fourth waves in Peru, due to Omicron BA.1 and BA.5, respectively)[6]. Hence, in this study, we aimed to assess the districts' weekly death from all causes by the epidemiological week before and during each of the first four COVID-19 waves in Peru. We believe that the variability of the death risk across COVID-19 waves should help us understand the intricacies of the association between mortality from all causes and socioeconomic factors.

Results

Mortality before and during the COVID-19 pandemic in Peru

According to our segmented regression analysis, the first COVID-19 wave lasted 38 weeks (epidemiological weeks 10-2020 to 37-2020), the second wave 46 weeks (epidemiological weeks 38-2020 to 41-2021), the third wave 30 weeks (epidemiological weeks 42-2021 to 19-2022) and the fourth wave at least 11 weeks (epidemiological weeks 20-2022 to 30-2022) (Fig. 1). During these periods, we observed higher mean weekly mortality during the second (32.5 ± 47.2 deaths per 100,000 people), first (29.2 ± 38.7), third (26.8 ± 38.9), and fourth (24.4 ± 38.0) COVID-19 waves, all higher than before the COVID-19 pandemic (22.3 ± 40.4). Furthermore, we observed high variability of the mean weekly mortality across the districts of each region and COVID-19 wave, ranging from Ucayali in the first wave (7.3 ± 4.6 deaths per 100,000 people) to Amazonas in the second wave (56.2 ± 142.5 deaths per 100,000 people) (Table 1).

Table 1
District's weekly mortality variability before and during the COVID-19 pandemic across the regions of Peru, 2017–2022.

	Pre pandemic (Mean ± SD)	**1st Wave (Mean ± SD)**	**2nd Wave (Mean ± SD)**	**3rd Wave (Mean ± SD)**	**4th Wave (Mean ± SD)**
Total deaths (n)	319,976	168,995	214,225	87,460	27,458
Weekly mortality	22.3 ± 40.4	29.2 ± 38.7	32.5 ± 47.2	26.8 ± 38.9	24.4 ± 38.0
By Region					
Amazonas	52.8 ± 154.1	47.7 ± 81.4	56.2 ± 142.5	44.5 ± 96.7	54.4 ± 159.3
Ancash	39.7 ± 50.5	48.1 ± 62.8	53.9 ± 68.4	47.1 ± 61.2	42.1 ± 45.7
Apurimac	37.7 ± 86.6	39.5 ± 61.2	50.0 ± 87.3	41.8 ± 65.2	38.2 ± 45.5
Arequipa	24.9 ± 36.9	38.8 ± 46.1	42.2 ± 46.1	32.9 ± 42.3	31.2 ± 40.5
Ayacucho	39.8 ± 61.8	46.6 ± 67.0	49.6 ± 64.5	44.2 ± 53.8	38.0 ± 51.9
Cajamarca	17.4 ± 19.4	21.2 ± 21.8	23.3 ± 24.3	21.7 ± 23.9	20.7 ± 25.1
Callao	8.7 ± 6.1	20.1 ± 13.0	17.6 ± 11.4	10.9 ± 6.7	9.5 ± 6.3
Cusco	20.2 ± 16.1	21.6 ± 16.9	25.2 ± 20.3	21.7 ± 17.4	22.3 ± 17.6
Huancavelica	39.8 ± 39.6	45.2 ± 40.5	50.9 ± 49.7	46.0 ± 48.1	42.2 ± 39.1
Huánuco	18.2 ± 15.0	21.1 ± 17.4	22.8 ± 19.5	20.2 ± 16.5	17.4 ± 13.7
Ica	14.2 ± 14.0	23.4 ± 18.0	25.3 ± 22.8	16.2 ± 17.2	14.7 ± 12.3
Junín	25.5 ± 27.9	31.1 ± 29.1	37.7 ± 35.0	30.2 ± 33.3	26.5 ± 27.5
La Libertad	13.8 ± 13.3	20.2 ± 18.1	19.7 ± 16.4	16.1 ± 13.5	13.5 ± 11.6
Lambayeque	11.7 ± 11.9	21.3 ± 18.4	15.0 ± 16.5	9.5 ± 10.1	9.0 ± 10.1
Lima	16.0 ± 32.5	31.1 ± 42.3	34.9 ± 47.6	24.6 ± 42.5	23.1 ± 38.8
Loreto	8.4 ± 9.9	13.6 ± 13.0	11.2 ± 7.7	10.5 ± 6.6	10.4 ± 15.3
Madre de Dios	16.3 ± 14.3	21.1 ± 16.1	20.4 ± 14.3	18.8 ± 11.7	19.0 ± 16.1
Moquegua	28.6 ± 36.5	41.4 ± 49.0	38.6 ± 46.0	40.5 ± 49.9	29.3 ± 36.1
Pasco	16.9 ± 14.6	20.4 ± 18.6	24.7 ± 24.1	17.9 ± 14.6	19.4 ± 19.7
Piura	11.3 ± 10.4	19.4 ± 17.1	18.8 ± 15.5	15.3 ± 13.8	12.7 ± 11.1
Puno	20.9 ± 17.1	25.2 ± 20.1	29.2 ± 24.2	26.6 ± 21.1	21.9 ± 16.3
San	14.6 ± 13.9	18.6 ± 17.3	20.0 ± 20.8	16.7 ± 14.3	16.6 ± 13.8
Tacna	25.3 ± 39.4	33.7 ± 41.0	36.2 ± 51.4	34.9 ± 47.6	22.8 ± 33.7
Tumbes	13.1 ± 8.7	20.3 ± 13.8	20.5 ± 13.8	15.5 ± 9.3	13.6 ± 9.5
Ucayali	7.3 ± 4.6	11.4 ± 10.6	10.7 ± 6.8	9.0 ± 5.3	7.6 ± 5.1
Legend: Mortality is expressed in weekly death counts per 100 000 people.					

Sociodemographic variability of the Peruvian districts

We observed significant variability in each of the sociodemographics explored in our study, including elevation, the number of communities, accessibility, HDI, vulnerability, and the prevalence of undernourished children, anemia, poverty, and extreme poverty (Table 2 and Fig. 2). The districts in Peru range from regions with a mean elevation of 56 ± 36 meters above the sea level (m.a.s.l) in Callao to 3723 ± 681 m.a.s.l. Regarding the number of communities, we observed a wide range from Callao (1 ± 0 communities) to Pasco (94 ± 92 communities). Regarding accessibility to Metropolitan Lima, we also observed a wide range from Callao (1 ± 0 communities and 120 ± 59 min) to Tumbes (8706 ± 84 min). We observed that among the 25 regions of Peru only seven had mean districts HDI over 0.5, including Callao (0.68 ± 0.06), Moquegua (0.59 ± 0.11), Ica (0.58 ± 0.07), Madre de Dios (0.58 ± 0.08), Arequipa (0.54 ± 0.12), Lima (0.54 ± 0.18), and Tumbes (0.53 ± 0.06). Like with the HDI, the Peruvian districts exhibited a large variability across regions in terms of the VFII, with some regions having mean district VFII within the moderate range (0.60–0.79), including Cajamarca (0.65 ± 0.11), Huancavelica (0.64 ± 0.11), Puno (0.63 ± 0.11), Huánuco (0.63 ± 0.13), and Apurimac (0.60 ± 0.12). In terms of undernourished children, we observed only seven regions with districts with a mean prevalence over 10%, including Piura (13.3% ± 13.2), La Libertad (13.1% ± 17.0%), Ancash (12.1% ± 21.4%), Huancavelica (11.4% ± 26.6%), Lambayeque (11.2% ± 12.9%), Huánuco (10.3% ± 20.3%) and Lima (10.3% ± 11.2%). Likewise, the anemic prevalence in children varies largely across districts with eight regions having a prevalence of anemia in children over 40% including Junín (54.1% ± 31.0%), Pasco (44.3% ± 19.4%), Madre de Dios (44.3% ± 17.1%), Ucayali (43.6% ± 14.4%), Ancash (42.6% ± 28.2%), La Libertad (42.5% ± 23.7%), and Cusco (40.1% ± 23.8%). In terms of poverty the regions with a mean poverty prevalence by district over 40% were Cajamarca (58.8% ± 12.6%), Ayacucho (45.1% ± 13.1%), Loreto (44.3% ± 10.3%), Puno (44.3% ± 9.6%), Apurimac (42.2% ± 9.5%), La Libertad (41.6% ± 16.8%), and Pasco (40.5% ± 13.5%). Finally, in terms of extreme poverty the regions with a mean extreme poverty prevalence by district over 20% were Cajamarca (36.7% ± 14.7%), Ayacucho (27.8% ± 12.8%), La Libertad (24.8% ± 20.9%), Pasco (21.7% ± 12.5%), Apurimac (21.3% ± 11.2%), and Huánuco (20.6% ± 10.2%).

Table 2
Sociodemographic variability of the Peruvian districts, 2017–2022

Region	Elevation (m.a.s.l)	Communities (No)	Accessibility (min)	HDI	VFII	Undernourishment (%)	Anemia (%)	Poverty (%)	Extreme poverty (%)
Amazonas	1874 ± 781	38 ± 35	5557 ± 470	0.37 ± 0.09	0.56 ± 0.12	7.9 ± 16.1	17.6 ± 19.9	39.9 ± 11.8	19.2 ± 13.8
Ancash	2740 ± 916	45 ± 35	2591 ± 608	0.37 ± 0.11	0.55 ± 0.14	12.1 ± 21.4	42.6 ± 28.2	36.9 ± 13.7	11.2 ± 8.3
Apurimac	3230 ± 344	51 ± 36	3920 ± 429	0.32 ± 0.08	0.60 ± 0.12	8.8 ± 21.0	31.1 ± 23.5	42.2 ± 9.5	21.3 ± 11.2
Arequipa	2149 ± 1331	43 ± 79	5435 ± 719	0.54 ± 0.12	0.35 ± 0.16	9.5 ± 10.0	31.1 ± 28.5	20.3 ± 12.2	9.3 ± 12.4
Ayacucho	3003 ± 663	63 ± 62	3198 ± 522	0.35 ± 0.09	0.58 ± 0.13	8.4 ± 18.7	35.1 ± 22.0	45.1 ± 13.1	27.8 ± 12.8
Cajamarca	2126 ± 703	50 ± 33	5400 ± 628	0.32 ± 0.09	0.65 ± 0.11	9.6 ± 23.6	23.9 ± 17.9	58.8 ± 12.6	36.7 ± 14.7
Callao	56 ± 36	1 ± 0	120 ± 59	0.68 ± 0.06	0.16 ± 0.04	1.0 ± 7.1	18.1 ± 10.0	13.5 ± 10.1	0.7 ± 0.8
Cusco	3070 ± 983	77 ± 62	5116 ± 514	0.36 ± 0.13	0.57 ± 0.16	8.5 ± 16.8	40.1 ± 23.8	35.6 ± 13.1	9.9 ± 7.4
Huancavelica	3282 ± 446	68 ± 62	2158 ± 303	0.33 ± 0.10	0.64 ± 0.11	11.4 ± 26.6	38.8 ± 27.8	39.8 ± 12.8	17.1 ± 8.7
Huánuco	2499 ± 1165	73 ± 58	2189 ± 453	0.35 ± 0.09	0.63 ± 0.13	10.3 ± 20.3	28.3 ± 21.7	36.7 ± 12.4	20.6 ± 10.2
Ica	573 ± 859	29 ± 23	2206 ± 585	0.58 ± 0.07	0.26 ± 0.11	3.8 ± 7.7	27.4 ± 21.1	4.9 ± 4.9	1.0 ± 5.7
Junín	3065 ± 1006	36 ± 47	1591 ± 328	0.45 ± 0.10	0.45 ± 0.15	8.7 ± 18.4	54.1 ± 31.0	26.4 ± 9.7	6.9 ± 6.1
La Libertad	1851 ± 1380	42 ± 29	4173 ± 477	0.38 ± 0.17	0.49 ± 0.21	13.1 ± 17.0	42.5 ± 23.7	41.6 ± 16.8	24.8 ± 20.9
Lambayeque	232 ± 640	40 ± 39	5765 ± 245	0.49 ± 0.10	0.32 ± 0.15	11.2 ± 12.9	34.9 ± 18.8	20.4 ± 11.3	4.4 ± 12.7
Lima	1728 ± 1470	33 ± 37	726 ± 427	0.54 ± 0.18	0.35 ± 0.17	10.3 ± 11.2	32.0 ± 27.5	18.0 ± 9.7	5.1 ± 6.1
Loreto	129 ± 29	47 ± 29	7620 ± 1828	0.34 ± 0.10	0.59 ± 0.12	9.3 ± 26.4	31.7 ± 15.0	44.3 ± 10.3	16.1 ± 7.5

Legend: m.a.s.l., meters above the sea level; HDI, human development index; VFII, vulnerability to food insecurity index.

Region	Elevation (m.a.s.l)	Communities (No)	Accessibility (min)	HDI	VFII	Undernourishment (%)	Anemia (%)	Poverty (%)	Extreme poverty (%)
Madre de Dios	296 ± 106	28 ± 16	6822 ± 726	0.58 ± 0.08	0.38 ± 0.09	9.4 ± 11.2	44.3 ± 17.1	6.8 ± 4.4	0.2 ± 0.2
Moquegua	2216 ± 1221	65 ± 71	6827 ± 332	0.59 ± 0.11	0.39 ± 0.17	5.8 ± 8.4	24.2 ± 17.4	16.3 ± 10.1	4.3 ± 5.0
Pasco	2933 ± 1377	94 ± 92	1775 ± 404	0.44 ± 0.10	0.49 ± 0.13	5.7 ± 16.3	44.3 ± 19.4	40.5 ± 13.5	21.7 ± 12.5
Piura	546 ± 783	44 ± 59	7491 ± 431	0.42 ± 0.13	0.44 ± 0.19	13.3 ± 13.2	23.7 ± 16.2	34.3 ± 14.2	13.3 ± 12.4
Puno	3723 ± 681	85 ± 77	7151 ± 531	0.33 ± 0.10	0.63 ± 0.11	6.4 ± 13.4	39.8 ± 17.7	44.3 ± 9.6	17.5 ± 7.7
San	465 ± 280	33 ± 23	4639 ± 584	0.42 ± 0.09	0.50 ± 0.14	6.0 ± 11.9	28.2 ± 17.4	26.8 ± 10.1	9.3 ± 7.1
Tacna	1990 ± 1331	31 ± 31	7816 ± 273	0.48 ± 0.14	0.41 ± 0.15	8.7 ± 4.0	23.7 ± 30.8	19.8 ± 8.6	8.1 ± 8.7
Tumbes	36 ± 36	15 ± 9	8706 ± 84	0.53 ± 0.06	0.27 ± 0.09	3.2 ± 9.4	27.7 ± 12.3	11.5 ± 3.2	0.4 ± 0.3
Ucayali	197 ± 44	55 ± 28	3953 ± 708	0.41 ± 0.10	0.46 ± 0.13	9.5 ± 18.7	43.6 ± 14.4	16.6 ± 10.3	1.8 ± 2.0

Legend: m.a.s.l., meters above the sea level; HDI, human development index; VFII, vulnerability to food insecurity index.

Correlation of district sociodemographic data in Peru

We observed in our correlation analysis a high correlation between HDI and VFII (Pearson *r* =-0.916; p-value < 0.001). Likewise, we observed a moderate correlation between HDI and undernourishment (Pearson *r* =-0.655; p-value < 0.001), undernourishment and VFII (Pearson *r* =-0.637; p-value < 0.001), elevation and HDI (Pearson *r* =-0.564; p-value < 0.001), and between elevation and vulnerability (Pearson *r* =-0.524; p-value < 0.001) (Table 3).

Table 3
Correlation of district sociodemographic data in Peru, 2017–2022

		Elevation	Commu-nities	Accessi-bility	HDI	VFII	Undernou-rishment	Anemia
Communities	Person's *r*	0.332	1.000					
	p-value	0.000						
Access	Person's *r*	-0.004	0.118	1.000				
	p-value	0.223	0.000					
HDI	Person's *r*	-0.524	-0.361	-0.238	1.000			
	p-value	0.000	0.000	0.000				
Vulnerability	Person's *r*	0.564	0.378	0.165	-0.916	1.000		
	p-value	0.000	0.000	0.000	0.000			
Undernou-rishment	Person's *r*	0.439	0.305	-0.003	-0.655	0.637	1.000	
	p-value	0.000	0.000	0.314	0.000	0.000		
Anemia	Person's *r*	0.392	0.160	-0.046	-0.171	0.156	0.267	1.000
	p-value	0.000	0.000	0.000	0.000	0.000	0.000	
Poverty	Person's *r*	0.020	0.341	0.141	-0.241	0.260	0.331	-0.006
	p-value	0.000	0.000	0.000	0.000	0.000	0.000	0.070

Legend: HDI, human development index; VFII, vulnerability to food insecurity index.

Regression analysis of weekly deaths from all causes by district

First, we fit a series of raw two-level Poisson mixed effects regression models adjusting the weekly deaths from all causes in each district by population as an offset variable and epidemiological weeks (Table 4). Here we observed that the strongest association was between the death counts and HDI and accessibility, regardless of the period of interest. Consequently, to prevent collinearity, we move forward in our variable selection, excluding elevation, vulnerability, and undernourishment due to their high correlation with HDI. In our regression analysis, we observed that before the COVID-19 pandemic, the districts' weekly mortality was associated with the human development index ([HDI], adjusted incidence rate ratio = 0.11, 95% confidence interval = 0.11–0.12), accessibility (0.99; 0.99–0.99), poverty (0.99; 0.99–0.99), and anemia (0.99; 0.99–0.99). However, consistently during each of the first four COVID-19 waves, the magnitude of association between the district weekly mortality and HDI decreased and varied significantly across waves (first, 0.61: 0.58–0.64; second, 0.54: 0.52–0.57; third, 0.20: 0.19–0.22; fourth, 0.17: 0.15–0.19), but the association with accessibility (0.99: 0.99–0.99), poverty (0.99: 0.99–0.99), and anemia (0.99; 0.99–0.99) remained constant.

Table 4
Sociodemographic factors associated with mortality from all causes before and during the COVID-19 pandemic in Peru

	Pre pandemic IRR (95% CI)	**1st Wave IRR (95% CI)**	**2nd Wave IRR (95% CI)**	**3rd Wave IRR (95% CI)**	**4th Wave IRR (95% CI)**
Raw IRR					
HDI	1.29*** (1.24–1.34)	0.90*** (0.85–0.99)	0.82*** (0.78–0.85)	0.33*** (0.31–0.35)	0.28*** (0.25–0.32)
Accessibility	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)
Poverty	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)
Anemia	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	1.00 (0.99–1.00)
Undernourishment	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	1.00*** (1.00–1.01)	1.00*** (1.00–1.01)
Vulnerability	0.99 (0.98–1.03)	1.02 (0.99–1.06)	1.07*** (1.04–1.10)	1.82*** (1.75–1.90)	1.85*** (1.72–2.00)
Extreme poverty	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)	1.02*** (1.02–1.02)	1.02*** (1.02–1.02)
Altitude	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)	1.00*** (1.00–1.00)
Adjusted IRR*					
HDI	0.11*** (0.11–0.12)	0.61*** (0.58–0.64)	0.54*** (0.52–0.57)	0.20*** (0.19–0.22)	0.17*** (0.15–0.19)
Accessibility	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)
Poverty	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)
Anemia	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)	0.99*** (0.99–0.99)
Undernourishment	-	-	-	-	-
Vulnerability	-	-	-	-	-
Extreme poverty	-	-	-	-	-
Altitude	-	-	-	-	-
Legend: IRR, Incidence rate ratio; 95% CI, 95% confidence interval; *, mixed effects Poisson regression models with the log of the population of each district as a structural predictor (offset) adjusting for the epidemiological week.					

Discussion

Our results showed that before and during the COVID-19 pandemic, a solid association existed between all-cause mortality and the district's sociodemographics, increasing with lower HDI, accessibility, poverty, and anemia rates. However, during the COVID-19 waves, the magnitude of the association between the district's weekly deaths from all-cause and HDI decreased, while its association with accessibility, poverty, and anemia rates remained constant. During the COVID-19 pandemic, the district's weekly mortality reached its highest levels during the first and second COVID-19 waves and the lowest during the third and fourth waves. However, the association between the district's weekly deaths and HDI was the weakest during the first and second waves and the strongest during the third and fourth waves, regardless of the accessibility, poverty, and anemia rates.

Mortality is strongly associated with human development for several reasons. Those with higher HDI have timely access to diagnostics and treatment, better healthcare, and faster disease recovery than those with lower HDI[7,8]. During the COVID-19 pandemic, researchers have estimated that around 47% of the incidence of COVID-19 was associated with HDI[9]. Furthermore, in some Latin-American countries, it has been estimated that at least 20–40% of the case fatality rate depends on the HDI[10]. Across countries, countries with high HDI prevented more COVID-19 deaths, confirmed that the most significant fraction of their cases and deaths were due to COVID-19, and even had higher recovery rates[11,12]. However, contrary to expected, within Peru and during the deathliest COVID-19 waves, those districts with higher HDI had higher death counts. We can explain such inverse association for several reasons. First, Peru is a very centralized country, with the capital Lima concentrating most of the resources necessary to prevent COVID-19 deaths, such as oxygen, hospital beds, certified physicians, and sufficient specialist to attend to COVID-19 patients in hospital facilities. Second, the COVID-19 epidemic started in the wealthiest districts of Lima and expanded to the poorest districts of Lima and the country.

From a social perspective, the inequalities and inequities that increased mortality before the COVID-19 pandemic were mitigated during the first days of the COVID-19 pandemic[13]. At that time, the world faced a deathly disease without knowing much about its pathogenicity or epidemiology, and more importantly, without any effective treatment to prevent COVID-19 deaths[14]. In such a scenario, those with the economic resources to travel overseas were the first to be exposed to imported cases, which explains why the first cases and deaths were reported within the wealthiest districts in Peru[15]. Peru's Government acted promptly, imposing a national lockdown just ten days after its first case was registered but still suffered from one of the highest excess deaths worldwide[16]. On March 11, 2020, the Peruvian president declared a general quarantine with social distancing interventions, including school and university closures, and on March 16, 2020, Peru declared a national emergency. Three months later, the wealthiest districts of Lima, which coincidently were the districts with the largest elder population, reported the highest mortality rates in the country with an estimated reproduction number of ~ 2.3 (95% CI: 2.0-2.5)[17]. On the contrary, during the first COVID-19 wave, those districts located at a higher elevation in Peru had the lowest COVID-19 incidence and mortality[18], and also the latest to peak compared to those districts with lower elevation[6]. Regardless, the inequalities and inequities that drive mortality quickly catch up with cities such as Iquitos becoming the city with the highest seroprevalence of anti-SARS-CoV-2 antibodies worldwide and one of the deathlier histories of the COVID-19 pandemic in Peru[19]. Despite authorities' efforts, Iquitos hospitals became overwhelmed, and medical oxygen shortages contributed mainly to the tragic humanitarian crisis that led a peak with over 100 deaths per day in a small city of 400,000 people.

Regarding the spatial distribution of COVID-19 mortality, overall, it was higher among the urban than in the rural areas, and within the cities, it highlighted the long-standing health inequalities[20]. Furthermore, neighborhoods with higher social vulnerability within the cities had lower testing and mortality rates[21]. Since the beginning of the COVID-19 pandemic in Wuhan, medical facilities' accessibility and spatial inequality have played a crucial role in the mortality variability within and across districts[22]. In our study, we observed an inverse association between the mortality from all cases with accessibility to Lima, poverty, and anemia. Such inverse associations remain invariable before and during the COVID-19 pandemic when adjusted for HDI and epidemiological week, which certainly reflects the fact that Peru is a very centralized country with substantial inequalities in access to health facilities across its districts.

Our study has several limitations. First, this study relied mainly upon the quality of the open data available and disaggregated at the district level, which is prone to information and selection bias. However, some of the strengths of our study, including a high study power and rigorous data analysis, allowed us to increase the study's internal validity. Second, some COVID-19 waves were shorter than others so we may lose some accuracy in our estimations. However, it might not be enough to invalidate the comparisons across waves due to our high study power. And third, the external validity of our study is limited to Peru and other highly centralized countries, which is a characteristic of most developing countries but not of developed countries.

In conclusion, a solid association exists between the district's weekly deaths from all-cause and the district sociodemographics data. Before the COVID-19 pandemic, the district's weekly deaths increased with lower HDI, accessibility, poverty, and anemia rates. However, during the COVID-19 waves, the magnitude of association between the district's weekly deaths from all-cause and the district's HDI decreased, keeping constant its association with the district's accessibility, poverty, and anemia rates. The COVID-19 pandemic is not over, so it is critical to address the lessons from the previous COVID-19 waves to save as many lives as possible in the next waves. The results from our study certainly can help policymakers plan and prepare to face the inequalities in medical facilities and provide the necessary healthcare resources more effectively.

Methods

Ethical considerations

Our study only used open data curated by the Peruvian Government, which publishes this data without identifiers and keeps it updated with an open license (CC BY 4.0). Therefore, following good research practices, our study was exempted from revision by the Institutional Review Board from the Universidad Peruana La Union.

Study design and population

We conducted a cross-sectional study to characterize and compare the mortality from all causes across the districts of Peru before and during the first, second, third, and fourth waves of the COVID-19 pandemic. Peru's territory encompassed 25 regions ("departamentos"), 196 provinces ("provincias"), and 1869 districts ("distritos"). This study assesses the association between the districts' weekly mortality and sociodemographics.

Study outcome and data sources.

We used the district's death counts per epidemiological week as the study outcome for our regression analysis and the district's mortality per epidemiological week for our descriptive analysis. We calculated the weekly mortality by multiplying the accumulated death counts per epidemiological week by 100,000 and dividing the product by the estimated annual population.

Using the Peruvian Open Data National Repository, we obtained the death counts, population estimates, and the districts' sociodemographic and geographical boundaries. Specifically, we got the death counts from all causes from the National System of Deaths (SINADEF), the annual estimated population from the National Registry of Identification and Civil Status (RENIEC), and the Peruvian administrative boundaries from the ArcGIS public repository. We obtained the district sociodemographic data from the National Center for Strategic Planning (CEPLAN), including HDI, vulnerability to food insecurity index (VFII, which is a combined measure of the annual average income per capita, the degree of urbanization, non-poverty population, population with access to water, and gross domestic product of food from the agricultural, livestock and fishing sectors), and the prevalence of anemia, undernourished children, and percentages of the population living in poverty or extreme poverty. Finally, we obtained the district's accessibility to the capital of Peru, Lima, using the data and code from the Malaria Atlas Project.

Statistical Analysis

We delimited the beginning and end of each COVID-19 wave in Peru by using the segmented regression method described by Muggeo VM[23], which we first reported in a previous manuscript[6]. Then, we performed a descriptive analysis to characterize the district's weekly mortality across the regions of Peru. Then, we describe the districts' sociodemographic variability across the regions of Peru by summarizing each of our variables of interest and elaborating district maps using the QGIS program. Next, we assessed Pearson's correlation of the district's demographics to prevent collinearity in our regression analysis. After this verification, we evaluated the association between the district's weekly death counts and sociodemographics before and during the first four COVID-19 waves in Peru. For this purpose, we fit a series of mixed effects Poisson regression models adjusting for the epidemiological week and using the log of the population of each district as a structural predictor (offset). In each model, we assessed the potential sociodemographic-associated factors to the district's weekly death counts: accessibility, HDI, VFII, poverty, poverty, extreme poverty, anemia, undernourishment, elevation, and the number of communities in each district. Finally, we use forward selection to determine the variables selected for the multivariate model using the Akaike Information Criteria (AIC). We use STATA^{tm} MP version 14.0 (StataCorp LP, College Station, Texas) for the statistical analysis and a 95% confidence interval for each of our estimates.

Declarations

Acknowledgments

We thank Dan Rosenfeld (London School of Economics) for his English revision and his feedback on the writing of the manuscript. Additionally, we would like to thank the Peruvian Ministry of Health and CEPLAN for their diligent work in curating the open data sources, which were vital for our study.

Author Contributions

AMQ and JSG were responsible for the study's conceptualization, design, funding acquisition, investigation, methodology, software, and validation. AMQ and LV were accountable for the data analysis and visualization, and AMQ for the project administration, supervision, and resources. JSG, WCMG, and JLLG were accountable for the data management. In addition, all the authors contributed to the writing – original draft, writing– review & editing, and agreed to be accountable for the work.

Data availability statement

The data used in our study is open data curated by the Peruvian government and freely available at the Peruvian Open Data National Repository. Such datasets are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication). Specifically, the data used in our study can be downloaded from the following:

- SINADEF all causes death counts: https://www.datosabiertos.gob.pe/dataset/informaci%C3%B3n-de-fallecidos-del-sistema-inform%C3%A1tico-nacional-de-defunciones-sinadef-ministerio.
- RENIEC annual estimated population: https://www.datosabiertos.gob.pe/dataset/poblaci%C3%B3n-peru
- ArcGIS Peruvian administrative boundaries: https://www.arcgis.com/home/item.html?id=3c38316056264065867996b799cbc7c
- CEPLAN sociodemographic data by Peruvian district: https://www.ceplan.gob.pe/informacion-sobre-zonas-y-departamentos-del-peru/
- Malaria Atlas Project accessibility data and code: https://malariaatlas.org/research-project/accessibility-to-healthcare/

Conflict of interests

The authors declare no conflict of interest.

References

1. Winston, L., McCann, M. & Onofrei, G. Exploring Socioeconomic Status as a Global Determinant of COVID-19 Prevalence, Using Exploratory Data Analytic and Supervised Machine Learning Techniques: Algorithm Development and Validation Study. JMIR Form Res **6**, e35114, doi:10.2196/35114 (2022).
2. Thazhathedath Hariharan, H. *et al.* Global COVID-19 Transmission and Mortality-Influence of Human Development, Climate, and Climate Variability on Early Phase of the Pandemic. *Geohealth* **5**, e2020GH000378, doi:10.1029/2020GH000378 (2021).
3. Campbell, T., Galvani, A. P., Friedman, G. & Fitzpatrick, M. C. Exacerbation of COVID-19 mortality by the fragmented United States healthcare system: A retrospective observational study. Lancet Reg Health Am **12**, 100264, doi:10.1016/j.lana.2022.100264 (2022).
4. Barbosa, I. R. *et al.* Incidence of and mortality from COVID-19 in the older Brazilian population and its relationship with contextual indicators: an ecological study. Revista Brasileira de Geriatria e Gerontologia **23**, doi:10.1590/1981-22562020023.200171 (2020).
5. Drefahl, S. *et al.* A population-based cohort study of socio-demographic risk factors for COVID-19 deaths in Sweden. Nat Commun **11**, 5097, doi:10.1038/s41467-020-18926-3 (2020).
6. Toyama, M., Vargas, L., Ticliahuanca, S. & Quispe, A. M. Regional clustering and waves patterns due to COVID-19 by the index virus and the lambda/gamma, and delta/omicron SARS-CoV-2 variants in Peru. Gates Open Research **6**, doi:10.12688/gatesopenres.13644.1 (2022).

7. Alimohamadi, Y., Khodamoradi, F., Khoramdad, M., Shahbaz, M. & Esmaeilzadeh, F. Human development index, maternal mortality rate and under 5 years mortality rate in West and South Asian countries, 1980–2010: an ecological study. East Mediterr Health J **25**, 189–196, doi:10.26719/emhj.18.029 (2019).
8. Lee, K. S., Park, S. C., Khoshnood, B., Hsieh, H. L. & Mittendorf, R. Human development index as a predictor of infant and maternal mortality rates. J Pediatr **131**, 430–433, doi:10.1016/s0022-3476(97)80070-4 (1997).
9. Khazaei, Z. *et al.* COVID-19 Pandemic in the World and its Relation to Human Development Index: A Global Study. Archives of Clinical Infectious Diseases **15**, doi:10.5812/archcid.103093 (2020).
10. Palamim, C. V. C., Boschiero, M. N., Valencise, F. E. & Marson, F. A. L. Human Development Index Is Associated with COVID-19 Case Fatality Rate in Brazil: An Ecological Study. Int J Environ Res Public Health **19**, doi:10.3390/ijerph19095306 (2022).
11. Heo, M. H., Kwon, Y. D., Cheon, J., Kim, K. B. & Noh, J. W. Association between the Human Development Index and Confirmed COVID-19 Cases by Country. Healthcare (Basel) **10**, doi:10.3390/healthcare10081417 (2022).
12. Mirahmadizadeh, A. *et al.* Correlation between human development index and its components with COVID-19 indices: a global level ecologic study. BMC Public Health **22**, 1549, doi:10.1186/s12889-022-13698-5 (2022).
13. Lossio, J. [Covid-19 in Peru: state and social responses]. Hist Cienc Saude Manguinhos **28**, 581–585, doi:10.1590/S0104-59702021005000001 (2021).
14. Andrus, J. K. *et al.* Perspectives on Battling COVID-19 in Countries of Latin America and the Caribbean. Am J Trop Med Hyg **103**, 593–596, doi:10.4269/ajtmh.20-0571 (2020).
15. Mendoza-Saldana, J. D. & Viton-Rubio, J. E. Sociodemographic aspects of the older population in front of COVID-19 pandemic in a developing country: the case of Peru. Gac Sanit **35**, 598–599, doi:10.1016/j.gaceta.2020.09.004 (2021).
16. Taylor, L. Covid-19: Why Peru suffers from one of the highest excess death rates in the world. BMJ **372**, n611, doi:10.1136/bmj.n611 (2021).
17. Munayco, C. V. *et al.* Early transmission dynamics of COVID-19 in a southern hemisphere setting: Lima-Peru: February 29(th)-March 30(th), 2020. Infect Dis Model **5**, 338–345, doi:10.1016/j.idm.2020.05.001 (2020).
18. Accinelli, R. A. & Leon-Abarca, J. A. At High Altitude COVID-19 Is Less Frequent: The Experience of Peru. Arch Bronconeumol (Engl Ed) **56**, 760–761, doi:10.1016/j.arbres.2020.06.015 (2020).
19. Alvarez-Antonio, C. *et al.* Seroprevalence of anti-SARS-CoV-2 antibodies in Iquitos, Peru in July and August, 2020: a population-based study. Lancet Glob Health **9**, e925-e931, doi:10.1016/S2214-109X(21)00173-X (2021).
20. Ogedegbe, G. *et al.* Assessment of Racial/Ethnic Disparities in Hospitalization and Mortality in Patients With COVID-19 in New York City. JAMA Netw Open **3**, e2026881, doi:10.1001/jamanetworkopen.2020.26881 (2020).
21. Bilal, U., Tabb, L. P., Barber, S. & Diez Roux, A. V. Spatial Inequities in COVID-19 Testing, Positivity, Confirmed Cases, and Mortality in 3 U.S. Cities: An Ecological Study. Ann Intern Med **174**, 936–944, doi:10.7326/M20-3936 (2021).
22. Zhou, Z. *et al.* Mapping the Accessibility of Medical Facilities of Wuhan during the COVID-19 Pandemic. ISPRS International Journal of Geo-Information **10**, doi:10.3390/ijgi10050318 (2021).
23. Muggeo, V. M. Estimating regression models with unknown break-points. Stat Med **22**, 3055–3071, doi:10.1002/sim.1545 (2003).

Figures

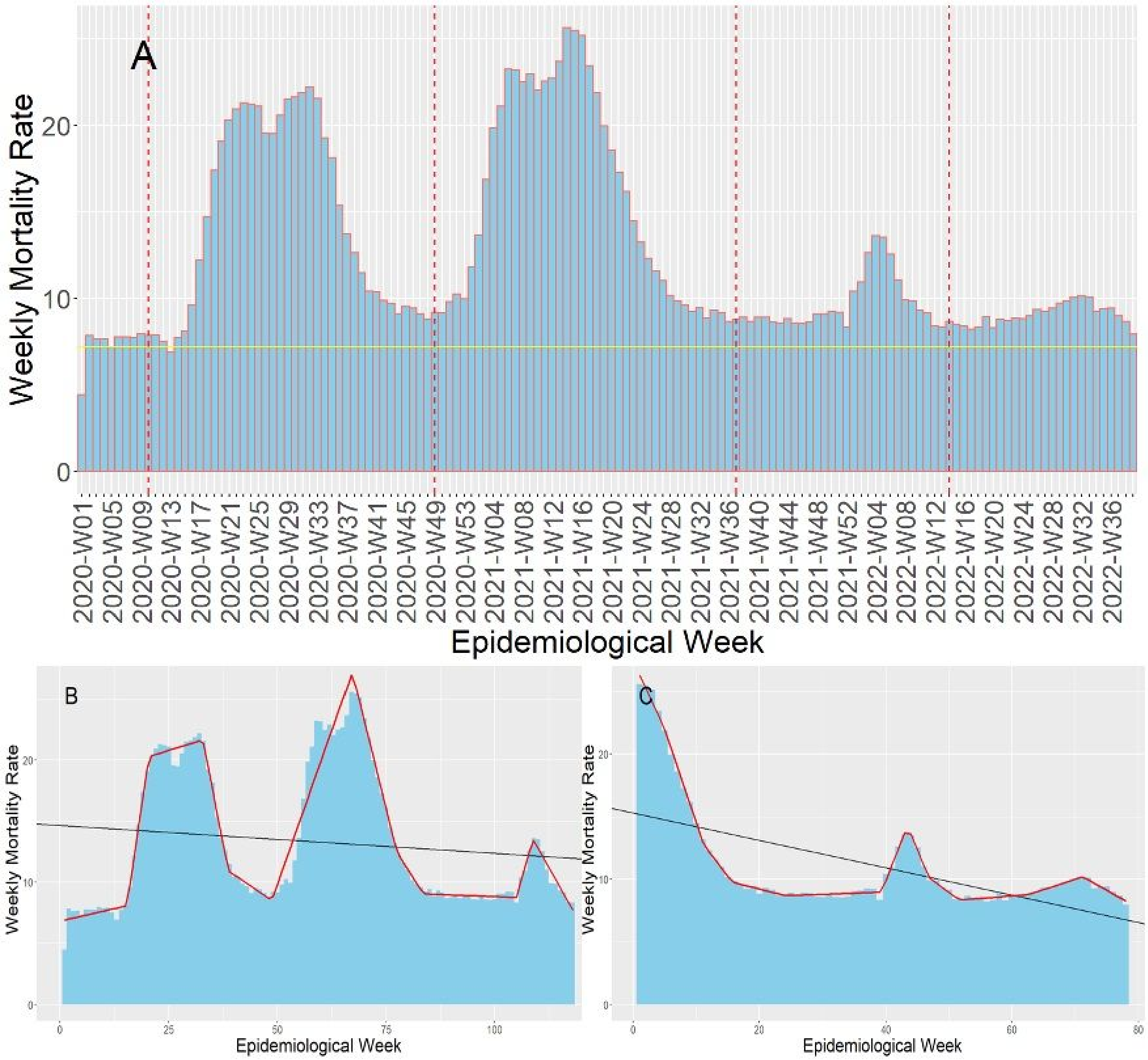

Figure 1

Segmented regression to assess the beginning and end of each of the first four COVID-19 waves in Peru

Legend: The figure shows the weekly mortality rate from all causes during Peru's first four COVID-19 waves (Fig. 1A). It also indicates the segmented regression analysis results, which we use to determine the duration of the first and second COVID-19 waves (Fig. 1B) and the beginning and end of the third and fourth COVId-19 waves (Fig. 1C) in Peru.

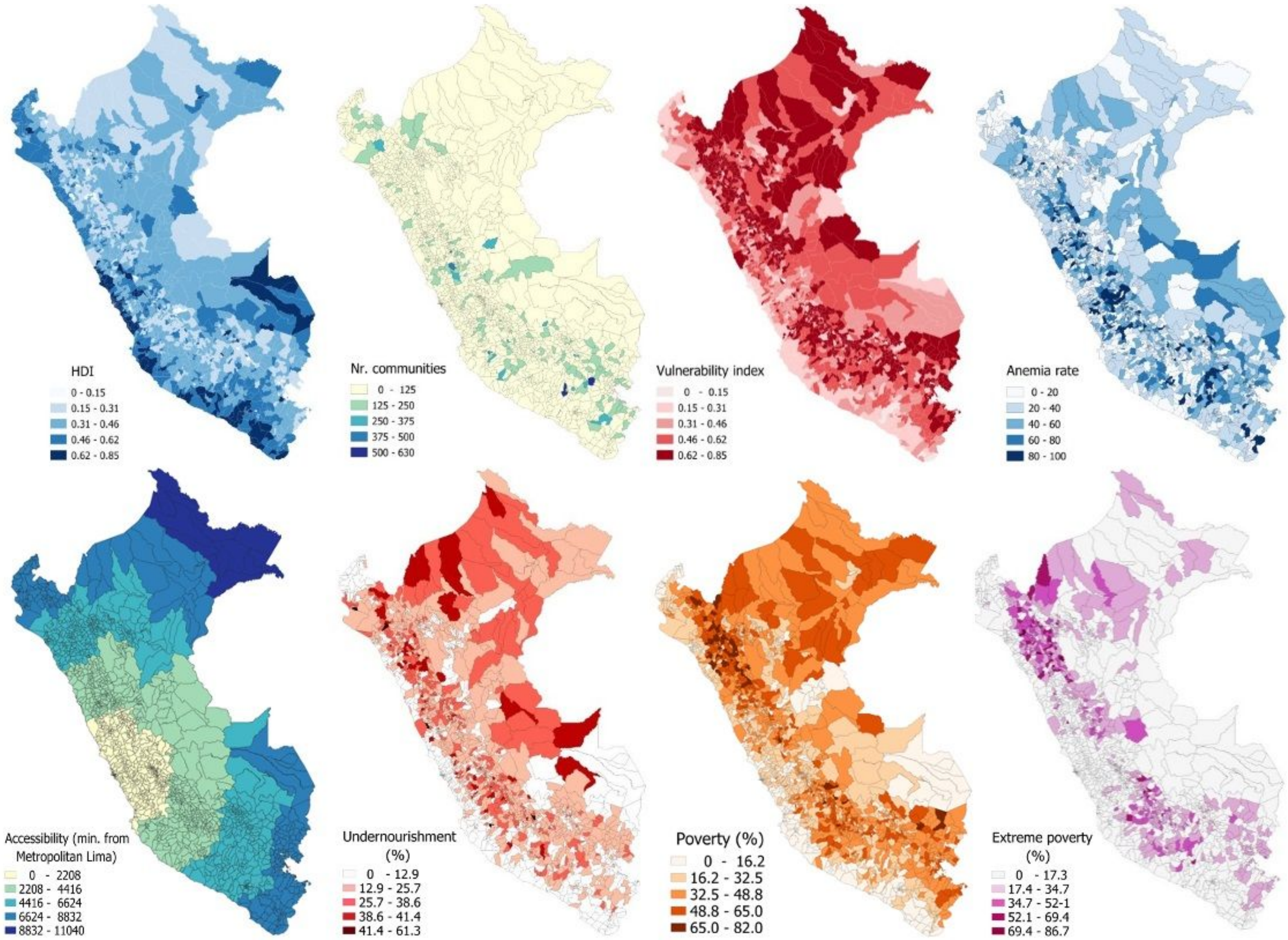

Figure 2

Variability of the district's sociodemographic in Peru

Legend: HDI, human development index