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## MORTALITY FROM CARDIOVASCULAR DISEASE IN THE FIVE MESOREGIONS OF THE STATE OF PERNAMBUCO BEFORE AND DURING THE COVID-19 PANDEMIC

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### ABSTRACT

**Background:** COVID-19, was described as excess cardiovascular death, however, hospitalizations for acute cardiovascular events decreased. **Objective:** To evaluate cardiovascular excess deaths before and during the pandemic of COVID-19 in the five mesoregions of Pernambuco. **Methods:** We used public data from the Civil Registry, to assess cardiovascular deaths in the five mesoregions of Pernambuco, stratified into specific cardiovascular deaths (OCE): acute coronary syndrome and stroke and non-specific cardiovascular deaths (OCI), between 2020 and 2021, as a reference the year 2019, as well as hospital and home deaths. **Results:** There were 927,000 cases with 21,636 deaths from COVID-19 in the mesoregions of Pernambuco. OCE decreased in Zona da Mata, Agreste, and the Metropolitan Region and increased in Sertão in São Francisco, however, there was an increase in OCI in the mesoregions, thus, for hospital OCE of 70%. In the mesoregions; the Sertão in São Francisco deaths, in which 40% were in the home and 44.3% in the hospital. A significant correlation was observed in Zona da Mata between 2019 and 2020, inversely proportional, increase in the Human Development Index (HDI) of the municipality, expecting a lower increase in cardiovascular death rate. A ratio of doctors per inhabitants in the region proved favorable to a lower death rate, due to the collapse of the health system in less developed cities (low HDI). **Conclusion:** The OCE decreased in most regions, except in the Sertão, occurring an increase. Thus, it increased in household OCI as a result of diagnostic errors. OCE increased in regions with health collapse

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## INTRODUCTION

The COVID-19 pandemic was decreed by the World Health Organization (WHO) in March 2020. Since the first notified case, in February, the pandemic evolved fast and, in June, approximately 1.136.470 cases were notified in the country, with around 51.271 deaths (WHO, 2022). Besides the confirmed deaths by COVID-19, previous reports also emphasized an increase in the total number of deaths during the pandemic when compared to the same period from past years: the mortality excess. In the period of March to May 2020, the excess in deaths in Italy was 49%, and even reached 277% in New York City (Wu, 2022). These excess deaths found during this period could have been caused by COVID-19, identified or not or other causes, being an objective metric comparable to analyse the true impact of the pandemic in the local mortality (Leon, 2020). Concomitantly, there was a reduction in hospitalization associated

with acute coronary syndromes (ACS), in high income countries (HIC). In the north of Italy, a significant reduction in ACS hospitalization was reported during the pandemic. Also was observed a 58% increase in cardiac arrest outside of the hospital, strongly associated with the cumulative incidence of COVID-19 (De Filippo et al. 2020; Baldi, 2020). In the US, an estimated reduction of 38% was reported in the activations of cardiac catheterization laboratories caused by myocardial infarction with ST segment elevation, similarly to the 40% reduction seen in Spain. This behavior could be associated with medical care evasion caused by social distancing, fear of getting COVID-19 and wrong diagnosis. Besides this, in regions where resources became scarce during the pandemic, the excess deaths could have occurred due to a collapse in healthcare, reaffirming the social disparities in the number of the deaths (Rodríguez-Leor, 2020). Brazil, with the average income population, ranks second in COVID-19 number of deaths. Nonetheless, death's distribution is heterogeneous and sub estimated due to the low rate of diagnostic tests done.<sup>1</sup> This Study goal was to analyse the excess cardiovascular

mortality during the COVID-19 pandemic in Pernambuco's five mesoregions during the pandemic years (2020, 2021) comparing it to 2019 (Painel, 2022).

## METHODS

A retrospective observational study was made using the public data bank from Civil registry (Portal da transparência) (Painel, 2022) from *Associação dos Registradores de Pessoas Naturais* (ARPEN-Brasil) for mortality data. The ARPEN represents the country's official civil registry class, and does civils' life certifications for Brazilian citizens, including death certificate. We used records from Pernambuco's five mesoregion: região Metropolitana, Zona da Mata, Agreste, Sertão e Sertão do São Francisco, from cardiovascular specific deaths (CSD) as: Stroke, Cardiac Arrest and unspecific cardiovascular deaths. The studied period was from 2020 and 2021, in which occurred the COVID-19 pandemic, and was compared to the expected deaths in 2019, non-pandemic year. The data was not collected and compared to the o sistema de informação sobre mortalidade (SIM), which is the official mortality registry because, in this system, the data only becomes available the year after making it impossible to collect 2021's data. To calculate mortality rate, a population projection made by IBGE was used. This rate was represented for each 100.000 inhabitant. The data related to medical assistance: number of doctors, nurses and hospital beds was collected through the Datasus hospital information system, as well as, the HDI from each city, using 2020 as year of reference. To calculate the mortality variation's rate 2019 was used as reference, and it was represented as a percentage originated from a ratio that used the difference between the rates found in 2020/2021 divided by the mortality rate in 2019, multiplying this ratio by 100. The data analysis consisted in a description of the characteristics of each macro region and the state of Pernambuco, presenting the rate of each type of cardiovascular death for each reference year. A correction study was made using the assistance and HDI data, stratifying the cities and the mesoregions of Pernambuco, estimating the Pearson correlation coefficient. The statistical significance used to analyze correlation was 5% ( $p < 0,05$ ) and the software used was the Stata version 14.0.

## RESULTS

Figure 1 synthesizes the deaths rate found in Pernambuco and the states' five mesoregions, highlighting the Agreste, with the highest rates of CSD and CUD in the three years studied. Table 1 presents the demographic data, health resources and the total number of cardiovascular or other causes deaths in the five mesoregions of Pernambuco. Cities from the regions Metropolitana, Sertão and Sertão de São Francisco are the most developed when compared to others cities, as is shown by their HDI. It is noticeable, when looking at the HDI, that the mesoregions of Metropolitana and Sertão do São Francisco are the ones with the best index, as well as, the best conditions in healthcare in relation to number of doctors, nurses and hospital beds, per 100 thousand inhabitants. When compared to the number of deaths expected in 2020, there was an excess in total deaths in all cities, with greater effect on those with lower HDI. When the excess mortality by non-COVID deaths was evaluated, was found that it was relevant in all five mesoregions, but in smaller proportions in Sertão do São Francisco. Because of the change in contribution by each cause of death between 2019 and 2020, we evaluated cardiovascular deaths tendencies. When considering specific there was a reduction in CSD, to the CUD, there was a substantial increase to all five mesoregions from Pernambuco. Table 2 shows these changes, revealing that the increase in CUD happened in parallel with ACS, showing percentual variation in deaths in each mesoregion, caused by CSD (ACS plus Stroke) and CUD causes. Stratifying the mortality rate by the deaths caused by cardiovascular disease, the Stroke and cardiac arrest had a higher mortality rate in Pernambuco between 2019 and 2020 (67,3 and 68 per 100 thousand versus 35,9 per 100 thousand in unspecific causes) nonetheless the CUD causes increased between 2020 and 2021, during COVID period, in Pernambuco and in all its' mesoregions (Table 2). Using 2019 as a reference year, figure 2 presents the variation in mortality rate by cardiovascular disease in 2020 and 2021, period in which Pernambuco's increase was 5,8% in 2020 and 7,8% in 2021; similarities were found in the mesoregions, specially in Sertão and Sertão de São Francisco, because the increase seen was from 10,2% to 16,5% and 17,7% e 19,5%, respectively in between 2020 and 2021

**Table 1. Demographic profile, deaths and mortality from cardiovascular disease and other non-COVID-19 causes, in the five mesoregions of the state of Pernambuco**

Quality	Pernambuco	RM	Zona da Mata	Agreste	Sertão	Sertão de São Francisco
Demographic data						
2020's population	9.616.621	3.997.057	1.352.235	2.282.502	1.033.015	625.113
HDI	0,705	0,678	0,599	0,575	0,597	0,611
Health resources						
Doctors	154	241	75	82	84	151
Nurses	86	124	41	59	59	84
Hospital beds	224	292	165	160	215	172
Mortality						
Cardiovascular disease						
2019						
Deaths	15.919	5.885	2.430	5.000	2.156	448
Mortality <sup>a</sup>	171,4	147,2	179,7	219,1	208,7	71,7
2020						
Deaths	16.850	6.005	2.264	5.324	2.375	522
Mortality <sup>a</sup>	181,4	150,2	194	233,3	229,9	83,5
2021						
Deaths	17.160	6.290	2.597	5.199	2.538	536
Mortality <sup>a</sup>	184,7	157,3	192,1	227,8	245,7	85,7
Others cause, Not COVID-19						
2019						
Deaths	63.881	24.233	9.395	19.824	8.368	2.061
Mortality <sup>a</sup>	687,6	606,3	694,8	868,5	810,1	329,7
2020						
Deaths	75.655	29.906	10.985	22.915	9.491	2.358
Mortality <sup>a</sup>	814,4	748,2	812,4	1.003,90	918,8	377,2
2021						
Deaths	78.947	32.325	11.313	22.839	10.208	2.262
Mortality <sup>a</sup>	849,8	808,7	836,6	1.000,60	988,2	361,2

<sup>a</sup> For each 100 thousands inhabitants

using 2019 as reference. It is noticeable that the variation in the mortality rate by due to causes other than COVID-19 were more expressive when compared to cardiovascular causes, in which an increase of 18.4% in 2020 and 23.6% in 2021 was observed in Pernambuco's rate. Regarding the mesoregions, shown in Figure 3, metropolitana stands out with an increase greater than that of Pernambuco (23.4% in 2020 and 33.4% in 2021), and the Sertão do São Francisco with a lower impact caused by the pandemic in its' mortality rate by other causes with a variation of 14.4% in 2020 and 9.6% in 2021, below that found in other mesoregions.

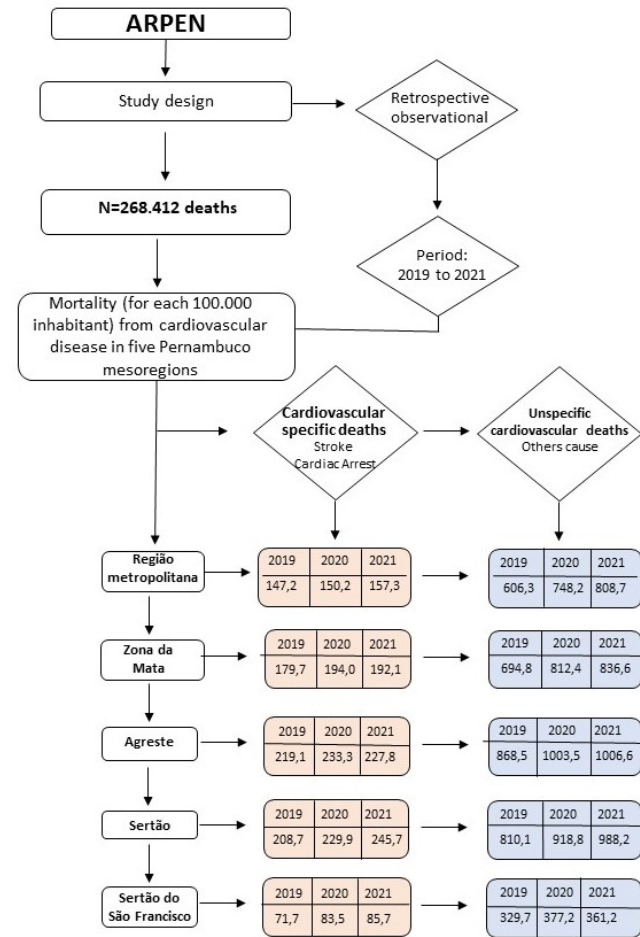


Figure 1. Deaths rate found in Pernambuco and the states' five mesoregions, separated in specific and unspecific cardiovascular deaths

with reductions in Pernambuco and other mesoregions. This reduction in deaths caused by stroke and infarction is explained by the significant increase in the mortality rate from cardiovascular disease from unspecific causes, drawing attention to the increase that occurred in the metropolitana region with a variation of more than 100% in the mortality rate when compared to the year 2019, as shown in Figure 3.

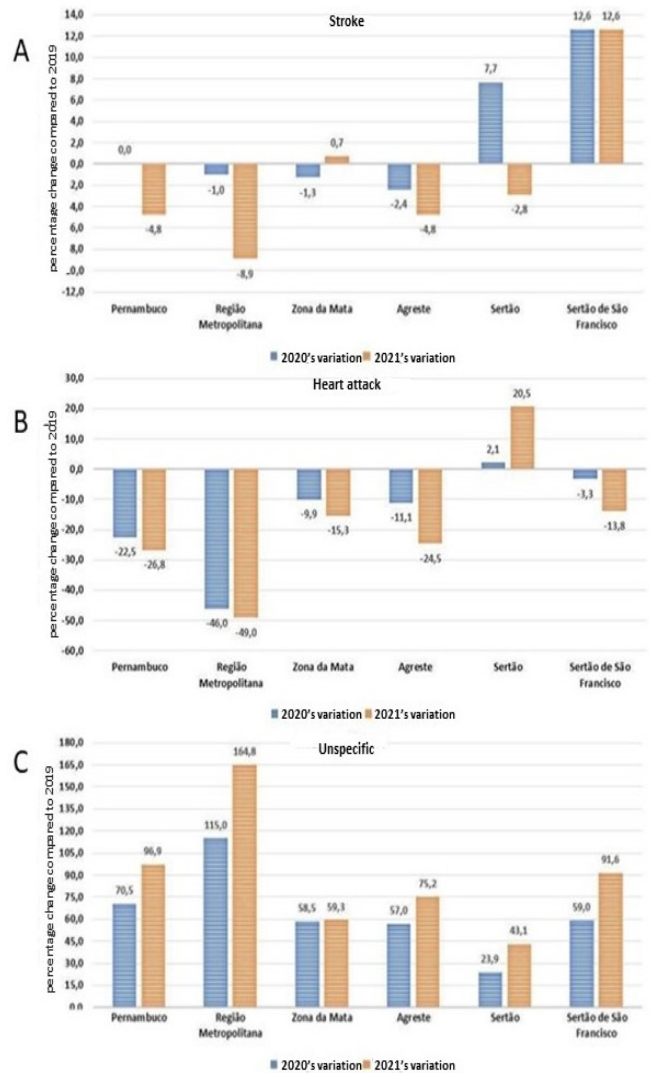


Figure 3. Percentage variation in the mortality rate due to cardiovascular disease according to the cause, in the years 2020 and 2021 compared to the year 2019, in Pernambuco and mesoregions

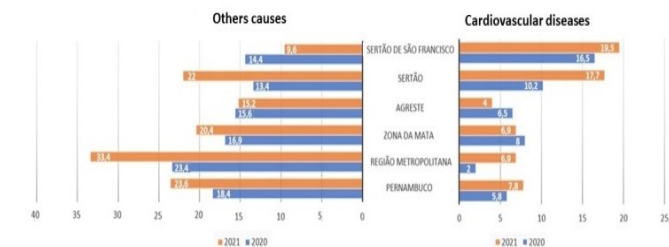


Figure 2. Percentage variation in the mortality rate from cardiovascular disease and other causes in the years 2020 and 2021 compared to the year 2019, in Pernambuco and mesoregions

Stratifying mortality rates by causes of death from cardiovascular disease, an interesting phenomenon was observed with an increase in stroke mortality in 2020 only in the regions of Sertão (7.7%) and Sertão do São Francisco (12.6%) with a reduction in the mortality rate in 2021, when compared to 2019, in all mesoregions and in Pernambuco. With heart attack as the cause of death, only Sertão de São Francisco had an increase in the mortality rate in 2020 and 2021,

Correlating the variation in the mortality rate from cardiovascular diseases in the municipalities of Pernambuco in relation to the HDI, the proportions of the number of doctors, nurses and hospital beds, it is observed that the correlation with the HDI and with the number of doctors per inhabitant proved to be significant between the municipalities in the Zona da Mata regarding the variation of the rate from 2019 and 2021, with a coefficient equal to -0.325 and -0.354, that is, an inversely proportional relationship between the variables, indicating that with the increase in the HDI of the municipality, it is expected an increase in the mortality rate from cardiovascular disease, as well as a higher proportion of physicians per inhabitant in this region, proved to be favorable to a lower mortality rate (Table3). The number of hospital beds showed a statistically significant correlation when evaluating the municipalities of Pernambuco, both for the variation in mortality from 2019 to 2020, and for the variation from 2019 to 2021. The correlation was positive, with values equal to 0.194 and 0.246, that is, municipalities with a higher ratio of the number of beds are related to a greater increase in the mortality rate from cardiovascular diseases.

Table 2. Number of cases and death and mortality rate per 100,000 inhabitants according to causes of cardiovascular disease in Pernambuco and in the five mesoregions of the state of Pernambuco

Cardiovascular disease	Pernambuco	RM	Zona da Mata	Agreste	Sertão	Sertão de São Francisco
Specific death						
Stroke						
2019						
Deaths	6.254	2.380	962	1.922	836	154
Mortality <sup>a</sup>	67,3	59,5	71,1	84,2	80,9	24,6
2020						
Deaths	6.255	2.357	949	1.876	900	173
Mortality <sup>a</sup>	67,3	58,9	70,2	82,2	87,1	27,7
2021						
Deaths	5.952	2.168	968	1.831	812	173
Mortality <sup>a</sup>	64,1	54,2	71,6	80,2	78,6	27,7
Heart attack						
2019						
Deaths	6.325	2.415	953	2.027	740	190
Mortality <sup>a</sup>	68	60,4	70,5	88,8	71,6	30,4
2020						
Deaths	4.899	1.302	858	1.800	784	755
Mortality <sup>a</sup>	52,7	32,6	63,5	78,9	73,1	29,4
2021						
Deaths	4.624	1.232	808	1.529	891	164
Mortality <sup>a</sup>	49,8	30,8	59,7	67	86,3	26,2
Unspecific death						
2019						
Deaths	3.335	1.090	515	1.051	575	104
Mortality <sup>a</sup>	35,9	27,3	38,1	46	55,7	16,6
2020						
Deaths	5.689	2.346	817	1.648	713	165
Mortality <sup>a</sup>	61,2	58,7	60,4	72,2	69	26,4
2021						
Deaths	6.572	2.890	821	1.839	823	199
Mortality <sup>a</sup>	70,7	72,3	60,7	80,6	79,7	31,8

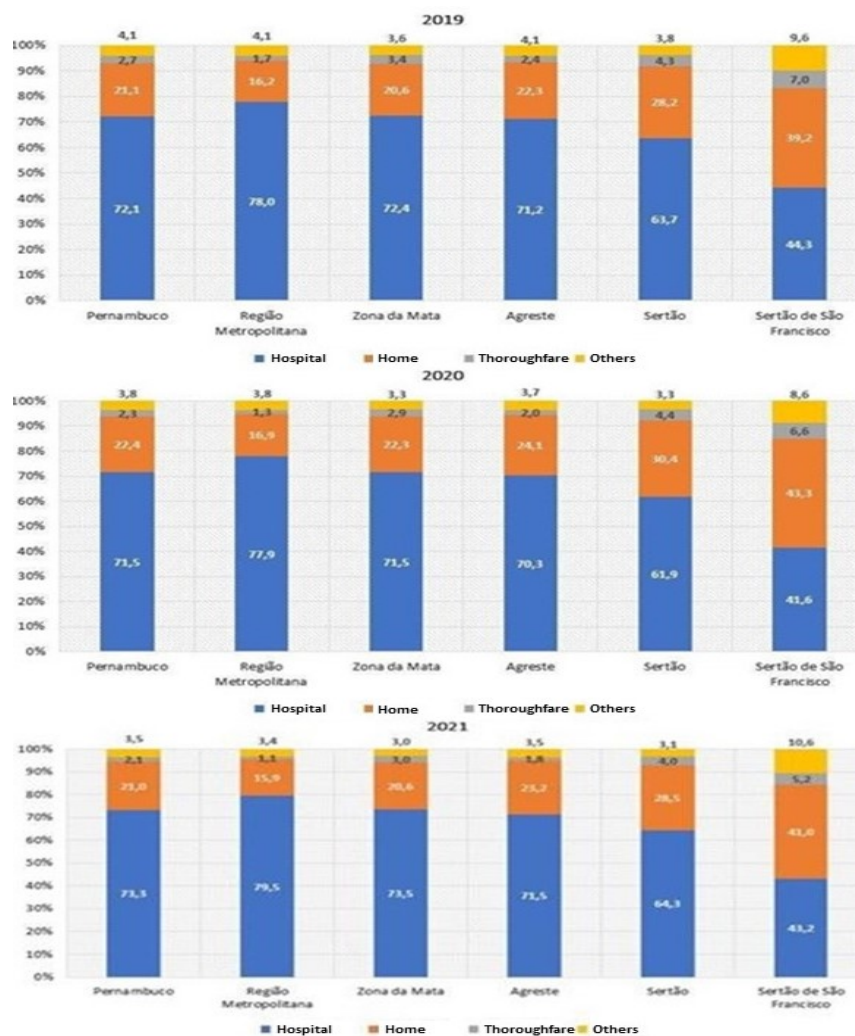


Figure 3. Percentage variation in the mortality rate due to cardiovascular disease according to the cause, in the years 2020 and 2021 compared to the year 2019, in Pernambuco and mesoregions

**Table 3. Correlation of the variation in the mortality rate due to cardiovascular diseases in the municipalities of Pernambuco in the years 2020 and 2021, having 2019 as a reference, and HDI, the proportions of the number of doctors, nurses and number of hospitals beds**

Mesoregion	HDI	Number of doctors (per 100 thousands inhabitants)	Number of nurses (per 100 thousands inhabitants)	Number of beds (per 100 thousands inhabitants)	Population
Variation from 2019 to 2020					
Pernambuco	-0,067 (p = 0,385)	0,017 (p = 0,827)	0,079 (p = 0,306)	0,194 (p = 0,012)	-0,031 (p = 0,689)
RM	0,142 (p = 0,643)	0,182 (p = 0,542)	0,112 (p = 0,716)	0,099 (p = 0,748)	-0,036 (p = 0,906)
Zona da Mata	-0,216 (p = 0,174)	-0,128 (p = 0,424)	-0,001 (p = 0,997)	0,187 (p = 0,241)	-0,041 (p = 0,799)
Agreste	-0,057 (p = 0,644)	-0,045 (p = 0,720)	0,018 (p = 0,884)	0,112 (p = 0,366)	0,077 (p = 0,538)
Sertão	-0,094 (p = 0,591)	0,083 (p = 0,636)	0,172 (p = 0,324)	0,253 (p = 0,142)	-0,151 (p = 0,385)
Sertão de São Francisco	0,039 (p = 0,905)	0,358 (p = 0,252)	-0,118 (p = 0,971)	-0,08 (p = 0,804)	0,094 (p = 0,772)
Variation from 2019 to 2021					
Pernambuco	-0,015 (p = 0,851)	-0,021 (p = 0,789)	0,089 (p = 0,249)	0,246 (p = 0,001)	-0,038 (p = 0,625)
RM	-0,019 (p = 0,952)	0,059 (p = 0,849)	0,051 (p = 0,867)	0,114 (p = 0,710)	-0,091 (p = 0,767)
Zona da Mata	-0,325 (p = 0,038)	-0,354 (p = 0,023)	-0,067 (p = 0,677)	0,125 (p = 0,437)	-0,131 (p = 0,413)
Agreste	0,001 (p = 0,946)	-0,112 (p = 0,365)	-0,036 (p = 0,776)	0,145 (p = 0,242)	0,015 (p = 0,901)
Sertão	-0,038 (p = 0,828)	0,093 (p = 0,596)	0,166 (p = 0,341)	0,353 (p = 0,037)	-0,191 (p = 0,273)
Sertão de São Francisco	0,411 (p = 0,184)	0,162 (p = 0,615)	0,377 (p = 0,226)	0,066 (p = 0,837)	0,173 (p = 0,589)

There is a greater need for assistance in large urban centers and, consequently, a greater impact of the pandemic on their health systems. In the municipalities of Sertão, a positive correlation was also observed between the number of beds and an increase in the mortality rate when considering the relationship between the mortality rate for the years 2019 to 2021 (Table 3). Figure 4 shows the distribution of deaths from cardiovascular disease in Pernambuco and in the mesoregions, according to the place of death, in the years 2019, 2020 and 2021. It is observed that hospital deaths had a higher percentage (about 70%) considering Pernambuco and the Metropolitana mesoregions, Zona da mata and Agreste, however, the distribution of deaths in the Sertão do São Francisco region, in which about 40% of deaths from cardiovascular disease occurred at home, and 44.3% in the hospital.

## DISCUSSION

Our data – the first comprehensive analysis of the Brazilian civil registry looking for specific patterns of excess mortality during the COVID-19 pandemic – show total excess mortality in the five mesoregions of the state of Pernambuco. Excess cardiovascular mortality occurred in most municipalities, due to the increase in CUD causes, and CSD, defined as ACS plus stroke, also increased significantly. There was a reduction in deaths from specified cardiovascular deaths, in parallel with the increase in the number of CUD, strongly correlated with the increase in household deaths (Painel, 2020; Datasus, 2020; Freire, 2020). The Brazilian civil registry database has the advantage of being the only readily available source of mortality data, with relatively short delays, important features during a pandemic. On the other hand, the registries serve demographic – not epidemiological – purposes and are not the official source of mortality data for Brazil. Thus, there is no investigation, coding or redistribution of causes of death. Therefore, the official data of the SIM may differ in the future, in relation to the Civil Registry. However, the direct analysis of the DC can partially overcome the risks of using official data, especially in countries with a lack of transparency in death notifications (Painel, 2022; Datasus, 2020; Freire, 2020; Freire, 2019). To minimize delays in notifications, it was decided to include only the mesoregions of Pernambuco in the present analysis.

In addition, there are several issues in the distribution of health resources in Brazil, which are concentrated in the most developed locations.<sup>15</sup> From the municipalities included in this analysis, it is possible to infer a clear gradient between the HDI – a measure of socioeconomic development – and the excess of mortality, especially in municipalities with lower socioeconomic limits. This is possibly associated with the basic preparation of local health systems, with regard to hospital infrastructure and the availability of high-level personnel, as well as access to health systems and emergency transport. The medical workforce is unevenly distributed in the macro-regions of Pernambuco, and the lowest numbers of nurses, doctors and specialists per inhabitant are in the Zona da Mata and Sertão regions.<sup>16,17</sup> Interestingly, the number of ICU beds per 100,000 inhabitants was not a proxy for health status in this analysis, although the collapse of intensive care resources was reported. Our finding can be explained by the fact that health resources in the less developed municipalities of Pernambuco are concentrated in the municipalities that suffered the greatest impacts of the pandemic throughout the state. The transportation structure of the municipalities certainly enhanced the negative impacts of COVID-19.

This suggests that the relationship between socioeconomic conditions and excess mortality goes beyond the health resource disparity. In addition to local infrastructure, the availability of tests for COVID-19 differed widely across Brazilian regions – even within the same region – and this may have contributed to the heterogeneity of death notifications. Presumably, there was underreporting across the country, considering the estimated number of tests per million inhabitants. Government decrees for social distancing policies were adopted from March 17 in some municipalities – there was a considerable delay in others<sup>1</sup>. Thus, our analysis reflects different stages of the pandemic, and the numbers may have dynamic behavior over time. Our results, with a significant reduction in CSD, may seem counterintuitive considering the reported cardiovascular effects of COVID-19 that can occur through: direct myocardial invasion by the virus, increased metabolic demand and systemic inflammatory response contributing to a pro- induced thrombosis. Additionally, an increase in risk factors for cardiovascular disease – such as tobacco use and reduced physical activity – has also been reported during the pandemic. From our data, thrombotic causes of death (CSD: ACS plus stroke) increased only in counties that experienced health

collapse. However, the reduction observed in the other cities followed the increase in the occurrence of deaths at home and with CUD. This can be explained by four factors: limited access to hospitals in places where there was overload, avoidance of medical care due to social distancing or concerns of contracting COVID-19 in hospital and isolation that impairs detection of cardiovascular symptoms by others, and even misuse of medications such as hydroxychloroquine, which can precipitate cardiac arrhythmias. The strong positive correlation between the increase in CUD and households corroborates these explanations, as it may suggest that at least some of the lost ACS and stroke deaths occurred at home, making a correct diagnosis impossible. On the other hand, CSDs may have declined in some locations due to competing risks and reduced exposure to secondary triggers of acute cardiovascular events, such as air pollution. In fact, ambient air pollution and climate change may be implicated in the incidence of cardiovascular events and COVID-19. In addition to patient-based factors, reorganization of acute care systems, such as: deactivation of services to meet urgent emergency or intensive care needs, delimitation of specific hospitals for COVID-19 and implementation of alternative therapeutic pathways, which aim to mitigate the effects of the pandemic, which may further impede the patient's attending medical care. Thus, public awareness campaigns about the importance of cardiovascular care are needed, even during this challenging time.

It is noteworthy that the deleterious effects on cardiovascular events may last longer than the pandemic itself, as primary and secondary preventions are being delayed in this context.<sup>20</sup> Different approaches to regulatory measures: while government decrees for social distancing policies were adopted as of March 17 in some capitals – especially in the South and Southeast – there was a considerable delay in others, notably in the North.<sup>21</sup> Thus, our analysis reflects different stages of the pandemic, and the numbers can have a dynamic behavior over time. Our study has several limitations. At first, raw data extracted from the Civil Registry were used, without epidemiological adjustments. Thus, there was no investigation, coding or reclassification of declared deaths, nor specific methodology for redistributing garbage codes. Second, the data mining algorithm considered all causes reported in the DC, without hierarchical classification or identification of the underlying cause of death. This is a technical limitation of the ARPEN database and can lead to errors in the identification of causes. In addition, delays in reporting can be differential between the various mesoregions of Pernambuco. When the ARPEN portal was only available for 2019, 2020 and 2021, limiting the comparison with the historical series. Finally, the availability of tests for COVID-19 is heterogeneous among municipalities in Pernambuco, which can further impact the notification of cases. However, despite these limitations, this is the most readily available data source in Brazil on excess mortality in the COVID-19 pandemic, allowing important epidemiological insights. The dissemination of SIM data, in the near future, will certainly provide more accurate data, considering its differentiated methodology for reporting deaths, including active investigation and standardized classification of causes of death.

## CONCLUSION

In the mesoregions of Pernambuco, there was an excess of mortality, with greater magnitude in the cities most lacking in terms of socioeconomic development and health resources. Overall, cardiovascular deaths increased primarily as a result of unspecified cardiovascular causes, which correlated with increases in household deaths, presumably as a result of impaired access to health care leading to misdiagnosis of specific cardiovascular causes such as ACS and accident. cerebrovascular. However, there was an excess of specified cardiovascular deaths, in addition to unspecified cardiovascular causes, which differs from reports of ICH and is possibly associated with worse health infrastructure. As the pandemic progresses to LMICs, investments in health resources are expected to improve.

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