Spatial Association of Social Determinants of Health and Health Care Access Markers to Acute Coronary Syndromes Mortality in Brazil

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute
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<u>ABSTRACT</u>

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Abstract

Introduction: Acute coronary syndromes (ACS) result in significant morbidity and mortality in low-and-middle-income countries (LMICs). Fifty percent of deaths in this region are from a cardiac etiology. Not much is known about the epidemiology of ACS in Brazil. Our aim was to describe the correlation between social determinants of health and access-to-care markers as related to ACS mortality and its geographic distribution in the country. Methods: Using the Brazilian National Health Database (DATASUS) and other nationally aggregated data sources, socioeconomic (SE) parameters, cardiovascular risk (CV) factors and an accessibility index for high complexity cardiac care centers (with hemodynamic monitoring and cardiac interventions) were obtained. To account for spatial dependency, geographic weighted regression (GWR) analysis was performed for all the predictor variables with respect to the outcome of deaths. Results: There were 776,449 ACS-related deaths from 2012 to 2018. The highest ACS mortality rate was in the South region of Brazil (104.7 per 100,000 population). The GWR analysis showed regional variability of socioeconomic factors as correlated with ACS mortality. A low accessibility-index in the North and Northeast regions of Brazil was strongly associated with ACS deaths. Conclusions: Spatial analysis allows for estimation of the local heterogeneity in the relationship between SE components, CV risk factors and access-to-

care markers as related to ACS mortality. Such analyses allow for improved understanding of the burden of ACS in Brazil.

Dedication

I dedicate this work to Jouri, my wife, who has spent her entire married life tolerating my idiosyncrasies and tangential academic aspirations, with grace and an abundance of love. Also, I would not be where I am today without my parents, who taught me compassion and empathy at an early age. They gave me my first education in science and rational thinking, then tempered it all with lessons in humility, so that I never think that “I know it all”.

Contents

List of Tables

List of Figures

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I owe a debt of gratitude to my supervisor, Dr João Ricardo Vissoci, for his infinite patience and his innate ability to pass on extremely complex concepts in simpler terms so that I could compose my thesis. This project could not have been finalized without his guidance every step of the way. I would also like to thank Dr. Catherine A. Staton and the group at the GEMINI Research Lab for allowing me to be a part of their team. A special thanks to Thiago Augusto Hernandes Rocha for the hours he spent on geospatial analysis of the data, and to Lincoln Luís for his work with the socioeconomic indicators used in this thesis. I also owe a huge thanks to Dr. Joseph Egger, at the DGHI's Research Design & Analysis Core, for helping me understand, statistics and epidemiology in general, but also to appreciate the ways these are applied to solving major global health issues.

I am particularly grateful to Dr. Gerald Bloomfield, who gave me critical insights related to the management of non-communicable diseases and cardiovascular illness on the global scale. This provided a clear context within which to anchor the findings of my thesis work. Finally, I want to thank Dr. Nathan Thielman, for his guidance and mentorship during my stay at DGHI. His encouraging words and his tolerance of my shortcomings gave me the courage to take on the challenges of this master's program. I cannot imagine having a career in global health were it not for his help.

1. Introduction

Mortality and morbidity from acute coronary syndromes (ACS) affect low and middle income countries (LMICs) disproportionately[1]. Greater than 50% of deaths and more than two-thirds of disability-adjusted life years (DALYs) from ischemic heart disease (IHD) occur in LMICs. In these countries, the overlap in epidemiological transitions from infectious causes of death and mortality from chronic diseases, such as IHD, have compounded the social and economic toll of these conditions[2]. Not only do individuals die at a younger age from IHD in LMICs, but in absolute terms, more people are being diagnosed with this chronic disease due to a rise in overall risk factors for ACS[3,4].

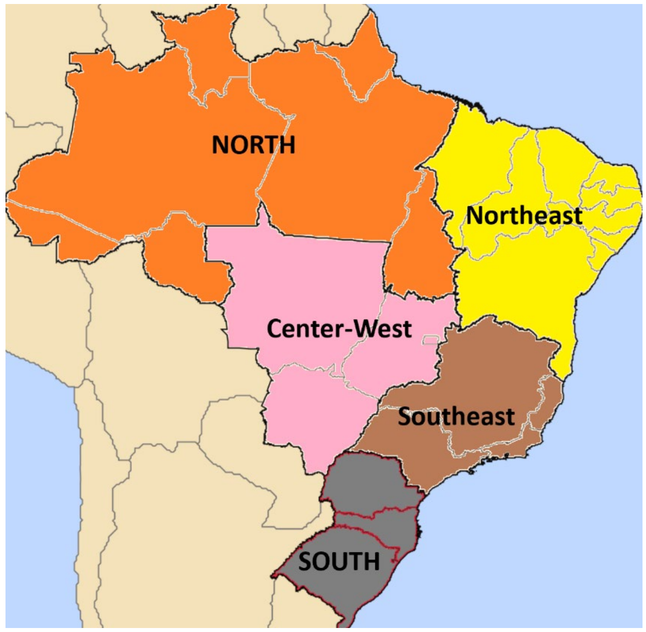
1.1 Brazil and the country's health system

Brazil is a middle-income country[5]. It is 47% of the landmass of South America with a population that is a mix of multiple nationalities. The Brazilian Institute of Geography and Statistics (IBGE) places the current population at 212,793, 373 with 48.9% being men[6].

The country has seen rapid economic development. It is the largest economy in Latin America and ranks as the eighth largest in the World by purchasing power parity in 2020. There is however significant income inequality in the country and the North and Northwest regions of Brazil are characterized by substantially negative economic indices. Taken nationally though affluence has resulted in risk behaviors such as a sedentary lifestyle and consumption of high-caloric unhealthy diets is on the rise[7]. Brazil has recorded a tripling of the prevalence of being overweight and of obesity in children from 4.1% to 13.9% between 1975 and 1997[8]. Similar trends continue to be reported in older age groups[9]. On a positive note, with the implementation of effective primary care and family health programs, with the creation of the National Health System in 1988, cardiovascular disease rates are falling in general[10].

The benefits of improved health have not been observed nationally, and this is likely representative of the socioeconomic disparities of the macro-regions of Brazil (see Figure 1) with resultant differences in accessibility and delivery of local health care[11]. A geographic analysis of the distribution of emergency health facilities in Brazil documents a greater density of high complexity care centers in urbanized areas of the country with scarcity in the rural parts and the Amazon region. An unequal spatial distribution of hospitals directly results in a lack of access to quality care[12].

Figure 1: Macro-regions of Brazil.



The north and northeast of the country document the worst socioeconomic indicators. The southern region boasts the best standard of living in the country with a life expectancy of 70.8, higher average monthly income and the lowest unemployment rate[13]. Therefore Brazil offers a unique case study in health outcomes in low, middle, and high income population categories, depending on the region analyzed.

Brazil has a universal public health system (Sistema Único de Saúde [SUS])[14], that is administered at the municipality level but is funded by the federal government, states and municipalities. By 2015, 64% of the country's population (124 million inhabitants) and 98% of municipalities were covered by this program. It is centered on the primary healthcare model and strives to provide universal health coverage. The SUS gives access to specialized procedures, but it is also plagued by infrastructure deficiencies in the tertiary care setups and hospitals. The healthcare system relies on a robust health information system that records nationwide statistics on care measures and outcomes. This allows for performance of large ecological studies utilizing these datasets[15].

1.2 ACS in Brazil

Epidemiology of ACS in Brazil has been studied in clinical registries but the geographic disparities in ACS and regional characteristics related to access to care have not been well described. Cardiovascular disease has stayed the main cause of death in Brazil, since the 1960s. The factors driving this increase in mortality is increased urbanization, excessive caloric intake, and a rapidly aging population as a consequence of greater life expectancy[16]. The overall prevalence of diabetes in Brazil is 7.6%[17]. Tobacco use has declined rapidly in the past three decades[18]. From a population-based household survey, the prevalence estimate for hypertension is 28.7% consistent with an overall downward trend nationally[19]. However, there are negative signs with regards to increasing obesity and elevated cholesterol levels in Brazilian adults. Obesity is rising in men, especially in those living in rural settings, and for those with lower incomes[20]. In a convenience sample survey of 81,262 healthy individuals from 13 cities, conducted in 2002, 40% had a total cholesterol >200mg/dL[21]. Unlike smoking, hypertension or diabetes, hypercholesterolemia as a risk factor, occurred more often in the upper socioeconomic groups.

Brazil has contributed to many international multi-center trials and registries on ACS[22]. However, as in the case of the multinational observational ACCESS (ACute Coronary Events – a multinational Survey of current management Strategies) registry, there are limitations with respect to the findings due to an inherent selection bias with regards to the design of the study. The Acute Myocardial Infarction Risk factor Assessment in Brazil (AFIRMAR) case-control, hospital-based study, involving 104 hospitals in 51 cities in Brazil, found an association between smoking, diabetes, and obesity with myocardial infarction[23]. The INTERHEART study for Latin America, in the Brazilian cohort (313 cases and 364 controls), the highest population-attributable risks for myocardial infraction were for abnormal lipids, waist-to-hip ratio, permanent stress, hypertension, and smoking[24].

Our group, in an earlier paper, described substantial cardiac testing and treatment heterogeneity based on geography in Brazil with consequent "hot spots" for increased ACS morbidity and mortality in many municipalities[25].

1.3 Socioeconomic status, access to care and ACS

Socioeconomic disadvantage has an impact on the occurrence of ACS, the quality of care received for this condition, and the clinical outcomes[26]. Studies in the United States and Europe, have shown that social determinants of health are correlated with

ACS morbidity and mortality. Inequalities in health, driven by differences in education, occupation and income, are seen to be associated with higher death rates from cardiovascular disease[27,28]. At the same time however, social determinants are interrelated and it can be often difficult to prove the causal pathways causing increased predisposition to heart disease. Prediction models such as the Framingham Risk score for cardiovascular disease underestimate the risk in low socioeconomic status individuals[29,30]. This is because no single parameter encapsulates all aspects of the socioeconomic reality. Also, these factors vary by race, ethnicity, region and other variables that are unmeasured.

There are many postulated mechanisms by which socioeconomic factors could influence cardiac-related mortality. Challenges to access to care, differences in quality of clinical management and problems with long-term adherence to medications due to cost concerns likely play a role in perpetuating these trends. In a systematic review and meta-analysis, published in 2017, it was reported that there were treatment gaps for ACS related to lower adherence to guideline recommended therapies when comparing the lowest socioeconomic status groups to the highest[31].

In the US, compromised access to care is linked to increased mortality due to ACS. In a prospective cohort study, examining survivors of ACS-hospitalizations, issues with lack of routine health care and transportation challenges resulted in an increase in all-cause mortality after a 2-years follow-up period[32]. Similarly, using data from the TRACE-CORE longitudinal study of hospital survivors of an ACS, the authors reported that barriers to healthcare access affected health-related quality of life. This was due to poor adoption and adherence to secondary prevention measures for coronary heart disease[33]. The physical distance to a facility capable of providing high complexity cardiac care after an ACS-related event, such as an out-of-hospital arrest, had an unclear impact on survival, per the Danish Cardiac Arrest Registry[34]. Clearly, not all factors related to barriers to access to care, are adequately understood or defined.

It is still a valid goal however to demonstrate the magnitude of association of social determinants of health on adverse events from cardiac disease to help formulate treatment strategies focused on mitigation of these elements. Education and counselling programs, as well cardiac rehabilitation, geared towards vulnerable groups can potentially improve ACS-related outcomes[35].

1.4 Geospatial factors related to ACS

Spatial data analysis is now being utilized for different public health issues, such as assessing the role of social factors on life expectancy, mapping obesity in select populations, and studying the distribution of primary care facilities[36–40].

With respect to ACS there are certainly spatial factors that drive mortality from an ecological perspective. Due to how societies organize, social determinants are driven, diseases also tend to accumulate geographically.

In North America, spatial analytic techniques have been used to determine geographically which emergency departments see a higher number of patients presenting with acute cardiac conditions[41]. Interestingly, a lack of specialists in these regions, resulted in over-utilization of emergency services. In this study, conducted in the province of Alberta, in Canada, the state provided the geocoded data for analysis. This included the latitude and longitude for population-based centroids for the 70 smaller subregional health authorities.

A recent investigation of spatial patterns of myocardial infarction and stroke mortality, in the East Tennessee Appalachian Region, identified areas with the highest burden of these diseases[42]. The neighborhoods with the highest mortality were the ones with the lowest education attainment.

1.5 Rationale and Study Aims

The objectives of this study were to analyze the association between socioeconomic-demographic domains and markers of access to care with respect to ACS mortality, from 2012 to 2018, from a population health and health systems perspective. The first aim was to describe the geographical distribution of ACS mortality and the regional disparities, using the data from the Brazilian National Health System (DATASUS) to track deaths captured in the hospitalization database using ICD-10 codes (I.20, I.21, I.22, I.23, I.24 and I.25). The second goal was to characterize the health system infra-structure for ACS care, and to determine the access to care markers using the CNES (National Healthcare Establishments) registry to identify hospitals that provided high complexity ACS care with hemodynamic monitoring and surgical capacity. An accessibility index would be measured for each site. The third aim was to perform a geographic weighted regression (GWR) analysis to see the association between ACS mortality and all predictor variables.

2. Methods

2.1 Study design

This study is an ecological, cross-sectional analysis of secondary data from the Brazilian National Health System (Sistema Único de Saúde or SUS) database[15]. The information from the database was used to perform a spatial analysis of ACS mortality in the country and its geographic association with markers of access to care in the different municipalities of Brazil.

2.1.1 Ethics statement

This study received ethical approval from the Duke University Institutional Review Board; as the data analyzed here are de-identified and publicly available, the protocol was exempted from full board review.

2.2 Setting

According to current estimates, Brazil has a total population of around 212 million people. There are 5565 municipalities in the country. All analyses in this study were conducted at the municipality-level. The country’s gross domestic product in 2018 was 1,885.48 billion US dollars[43]. Not all segments of the Brazilian population have benefited uniformly from the rapid development, resulting in substantial income inequality within and between regions of the country.

Brazil is divided into five macro-regions, based on geopolitics, as defined by the Instituto Brasileiro de Geografia e Estatística[6]. The five regions are the South, Southeast, Central-West, North and Northeast. The high-income areas are the South and Southeast regions of the country. The Central-West is considered middle-income and the North and Northeast is mostly low-income.

2.3 Data sources and variables

Table 1 presents the sources of all data used in this analysis.

2.3.1 Socioeconomic and sociodemographic data

Socioeconomic data at the municipality level including GDP per capita, age distribution, unemployment rate, literacy rate, proportion of residents living in state-defined urban areas, and other statistics, were taken from the Brazilian Institute of Geography and Statistics (IBGE) and the World Bank. For purposes of data analysis, the proportion of elderly was defined as the proportion of residents over 65 years of age in each municipality.

Table 1: Data sources for analysis

Source	Variables		Date Range	Data entries	Scope
DATASUS - Mortality information system (SIM)	▪ Cause of death coded by ICD groups: I.20, I.21, I.22, I.23, I.24 and I.25 ▪ Municipality of residence of patients with ACS deaths ▪ Mortality rate by municipality		2012 – 2018		
CNES - National Registration of Health Establishments	▪ Geolocation ▪ Identification of high complexity hospitals		2012 – 2018		All deaths between 2012 and 2018
PNUD Brasil – UNDP Brazil & IBGE – Brazilian Institute of Geography and Statistics	All data pertaining to the following indicators (see appendix A for details): 1) Life expectancy 2) Young cities 3) Poverty 4) Inequity 5) Illiteracy 6) School attendance 7) Sanitation 8) Electricity 9) Unemployment 10) Formal jobs		2008 - 2014	5565 municip-alities	
SIAB – Primary care information system	▪ Prevalence of hypertension ▪ Prevalence of diabetes		2012 – 2014		

2.3.2 Access to care data

Primary care coverage information was accessed from the PMAQ database. Primary care coverage was defined as the ratio of primary care physicians to total municipality population.

Geolocation for all Brazilian public hospitals were obtained from Cadastro Nacional de Estabelecimentos de Saúde (CNES) / National Register of Health Facilities. High complexity hospitals were defined as those with capacity for continuous hemodynamic monitoring (ICU setting), cardiac catheterization, and cardiovascular surgery.

2.3.3 Cardiovascular risk factors data

Data about the population prevalence of hypertension and diabetes by municipality was obtained from the national primary care database (SIAB). The prevalence of these risk factors was determined within each municipality.

2.3.4 ACS mortality data

ACS mortality data was collected from the DATASUS Mortality Information System (SIM). The data used in this study was taken from the year 2012 to 2018 (the last year for which data regarding ACS mortality is available).

Causes of death were coded by ICD groups: I.20, I.21, I.22, I.23, I.24 and I.25. Municipality of residence of patients with ACS death was also recorded.

The mortality rate for each municipality was adjusted by only considering the population > age 20 years, as per American Heart Association guidelines[44].

2.4 Derivation of indicators and 2SFCA technique

2.4.1 Socio-economic status: Principal component analysis

The Brazilian Census has 232 sociodemographic variables. In order to derive the indicators of social determinant of health (SDOH) for each municipality, we performed a principal component analysis (PCA). This dimensionality reduction technique provides weights for each variable in order to be aggregated into a composite score, based on their shared variance. This means that variables with similar response patterns are grouped into larger indicator categories (components), pooled together and weighted by their level of association. Five sets of variables were analyzed using PCA and the resulting indicators of SDOH were: health, education, economy, occupation, and sanitation. Basically, the PCA reduced the number of variables in each indicator into 2 new variables (principal components). Therefore, each indicator's two principal components represented all of the variables of their respective indicator (see Appendix A).

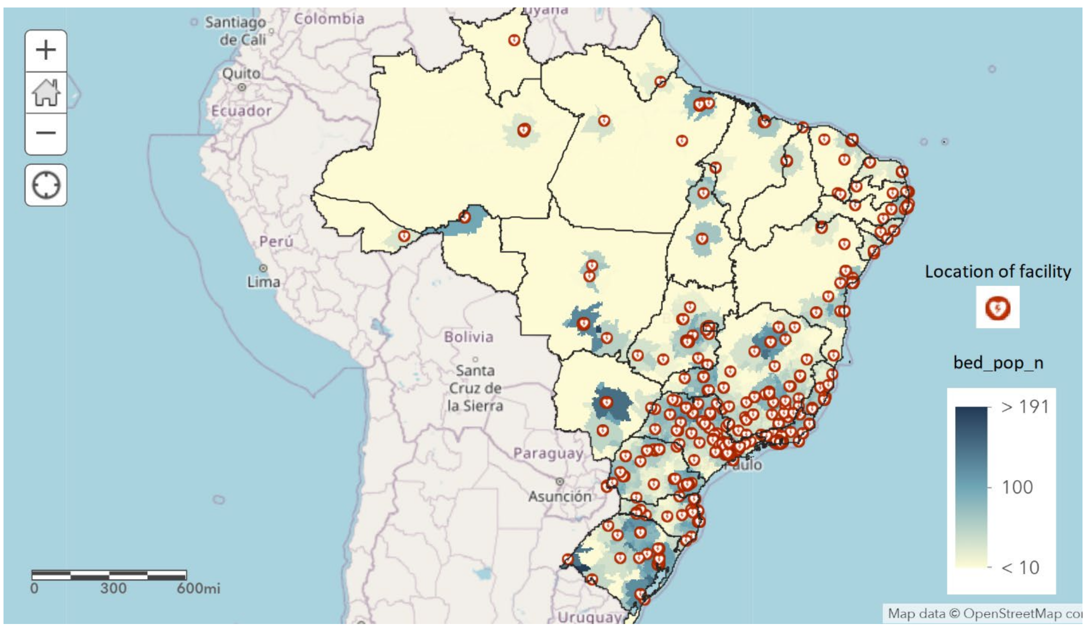
For example: The "health" indicator was composed of "life expectancy" and "young cities" principal components, which in turn had the following variables: "Life expectancy at birth", "Fertility rate", "Child mortality", "Mortality up to 5 years of age", "Dependency ratio", "Probability of survival up to 40 and 60 years", "Aging rate", and "% of women aged 10 to 17 who had children".

We used the SDOH indicators to adjust the geographically weighted regression.

2.4.2 Access to care: Two-step floating catchment area technique

Access to high complexity hospitals was defined by an accessibility index generated by the 2-step floating catchment area (2SFCA) technique (see Figure 2)[45]. The 2SFCA technique creates an index for availability and proximity of care weighted by population in two steps. First, a capability index for each high complexity hospital was calculated by dividing the total annual volume of admissions at each center by the number of persons living within 120 km from the facility. This distance was used as a proxy for a two-hour travel distance, the maximum distance recommended by the American Heart Association and European Society of Cardiology for travel to an advanced cardiac center. Secondly, the capability indices of all high complexity hospitals within 120 km from each municipality's centroid were summed to produce an accessibility index of high complexity care for each municipality. In a separate paper, the details of the methods used to generate the accessibility index for cardiac procedures has been described previously[25]. In our study, the accessibility index is essentially the number of high-complexity care beds available per 100,000 population.

Figure 2: Locations of high-complexity care hospitals and the distribution of hospital beds to population density, as determined by the accessibility index, in Brazil.



See: https://arcg.is/5vSL8

2.5 Analysis

Descriptive statistics were used to summarize variables of interest and a significance threshold of 0.05 was used in all analyses. A regression analysis was performed with the Ordinary Least Squares (OLS) model, which did not account for spatial dependency. Spatial dependency occurs when a variable in one location depends at least partially on the behavior of that variable in neighboring locations. For example, if a single municipality is likely to have a higher ACS mortality rate when neighboring municipalities also have high mortality rates (after adjusting for covariates), then spatial association is observed.

As the OLS model demonstrated high spatial autocorrelation of residuals, a second analysis was conducted using a geographically weighted regression (GWR) model. This method accounts for spatial dependency by performing multiple separate post hoc regressions for each geographic cluster in the study area of interest. GWR aggregates municipalities that exhibit similar behavior of the outcome variable (in this case, ACS-related mortality), and then generates a separate regression model for each cluster. Ultimately, GWR produces an estimation for the association between ACS-related mortality and its predictor variables for each municipality.

The regression models were evaluated with the Jarque-Bera method to assess the normality of the residuals, the Breush-Pagan and Koenker-Basset tests for heteroscedasticity, Moran's I and the Lagrange multiplier test for spatial dependency, and R2 and Aikake's information criterion (AIC) for overall model fit. ArcGIS Pro 2.7.1 software (Esri Inc, Redlands, California) was used to generate the OLS model, to perform the geographic weighted regression, and to generate the choropleth maps[46].

3. Results

A total of 776,449 ACS-related deaths occurred in Brazil, during the study period from 2012 to 2018, across 5565 municipalities. The average ACS mortality in the country was 90.32 per 100,000 persons annually. The highest mortality rate from ACS occurred in the South (104.7 per 100,000 persons annually), a region that also coincidentally had the largest proportion of elderly (14.9%). The next-highest ACS mortality rates were in the Northeast and Center-West regions. As a percentage of the population the North had the lowest number of elderly (8.0%). The lowest primary care coverage was in the North (70.23%) and the Southeast (75.82%). There were a total of 569 high-complexity care hospitals (HCH), with provisions for hemodynamic monitoring, cardiac catheterization, or cardiovascular surgery, identified in Brazil. The South and Southeast accounted for 361 (63%) of these facilities. 63.7% of municipalities in the North did not have even a single hospital that could be categorized as delivering high-complexity care. The country-wide accessibility index for high-complexity care was 42.3 (beds per 100,000 population). The highest accessibility indices were in the South and Southeast, and the lowest were in the North (see Table 2).

Table 2: Regional distribution of proportion of elderly, access-to-care markers and ACS mortality in Brazil.

		Brazilian regions					Brazil
		North	Northeast	Center-west	South	Southeast	
Municipalities	Number	449	1794	466	1188	1668	5565
ACS mortality	Total number of deaths	36,310	200,167	49,658	119,554	370,760	776,449
	Mortality rate per 100 K	58.22	95.51	85.11	104.70	84.59	90.32
Coverage of primary care services	Percent	70.23%	88.56%	82.40%	79.43%	75.82%	80.80%
Proportion of elderly	Percent	8.0%	11.6%	11.1%	14.9%	13.6%	12.6%
High complexity care hospitals (HCH)	Total number of HCH	34	118	56	99	262	569
	Municipalities without access to HCH (percent of total municipalities)	286 (63.7)	515 (28.7%)	203 (43.6%)	19 (1.6%)	42 (2.5%)	1065 (19.1%)
Accessibility index	beds per 100,000 population	18.16	22.62	29.11	65.68	57.00	42.30

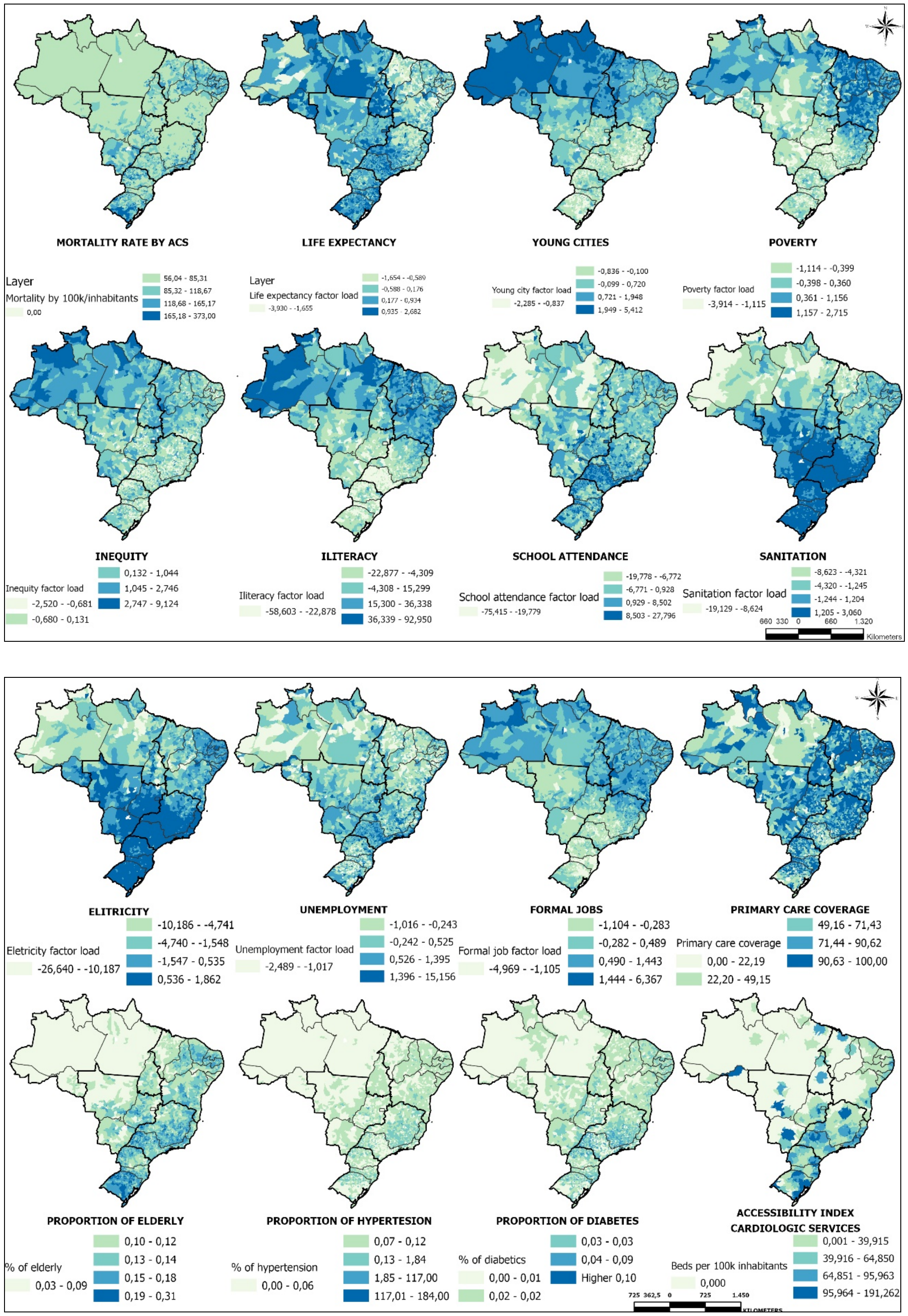
3.1 Distribution of socioeconomic and demographic factors

The choropleth maps (see Figure 3) revealed that the North and Northeast regions had similarities with respect to younger demographics, high poverty, high illiteracy, lower school attendance, and high inequity. However, in contrast to the North, the Northeast had lower life expectancy and a greater proportion of its population being elderly. The South, Southeast, and Center-West had higher life expectancy, more elderly, better infrastructure for electricity/sanitation, lower poverty, and higher school attendance.

3.2 Distribution of cardiovascular risk factors and healthcare access

On reviewing the distribution maps of predictor variables (see Figure 3), there were a greater percentage of elderly and individuals with hypertension and diabetes in the South, Southeast, and Northeast. A higher number of healthcare facilities providing complex cardiac care were concentrated in the South and Southeast in general. This meant that the highest accessibility indices were therefore also seen in these more economically advantaged regions. For the North, Center-West, and Northeast regions the high accessibility indices and complex care hospitals were aggregated in Metropolitan areas. Those living outside large cities were left with poor access to complex cardiac care.

Figure 3: Geographic variation in ACS mortality and predictor variables across Brazil.



3.3 Association of predictor variables to ACS mortality

In the unadjusted OLS model, there was high spatial dependency for the association of ACS mortality to the predictor variables. Attesting to this was a lower adjusted R-squared, a higher AIC and a high Moran's autocorrelation of the residuals. In this model, higher ACS-related mortality was associated with lower life expectancy, younger demographic cities, high poverty, high inequity, high unemployment, lesser formal jobs, greater proportion of elderly, and a higher accessibility index for cardiac services.

The post hoc analysis of the GWR model showed a high adjusted R-squared value, confirming a better fit. When adjusting for spatial dependency, the GWR model had higher ACS mortality rates with lower life expectancy, young cities, higher poverty, higher inequity, and higher unemployment. The strength of correlation between ACS mortality rates and proportion with hypertension was stronger when spatial attributes were taken into account. Diabetes mellitus was not significantly correlated either in the OLS or GWR models.

Some of the standard deviations of the estimated coefficients were large and therefore indicative of a varied relationship in different clusters based on the locally derived association. These predictors included the percentage of elderly, and the proportion with hypertension and diabetes (see Table 3).

Table 3: Regression coefficients of predictor variables correlated with ACS mortality in unadjusted ordinary least square model and geographic weighted regression model.

	Ordinary Least Squares (OLS)		Geographic Weighted Regression (GWR)	
Variables	**Est. coefficient**	**P-value**	**Est. Mean**	**Est.SD**
Life expectancy	-3,668993	0,000002	-4,63982379	1,957070145
Young cities	5,020415	0,000003	2,86215871	2,857957496
Poverty	9,269687	0,000000	4,566387146	4,21991534
Inequity	4,016253	0,000000	3,070851237	1,955819212
Illiteracy	0,079955	0,113986	0,103407228	0,139855474
School Attendance	0,074845	0,370189	-0,202139759	0,237238382
Sanitation	0,529839	0,157594	1,503531009	2,067561989
Electricity	2,634740	0,000000	2,422954442	2,518185718
Unemployment	5,479126	0,000000	4,583853653	2,20963372
Formal jobs	-5,779779	0,000000	-1,159218605	2,425454138
Primary care coverage	0,003128	0,878116	0,019400166	0,050993102
Proportion of elderly population	608,826327	0,000000	575,0703968	62,569831
Proportion of hypertension	-0,243660	0,132585	52,75534702	24,54401957
Proportion of diabetes	-38,099769	0,167761	-124,7706827	145,6502447
Access to high complexity cardiac care	-0,066149	0,000076	-0,054960543	0,043366307
AIC	55808,577074		54944,5010	
Adj. R2	0,206812		0,3301	

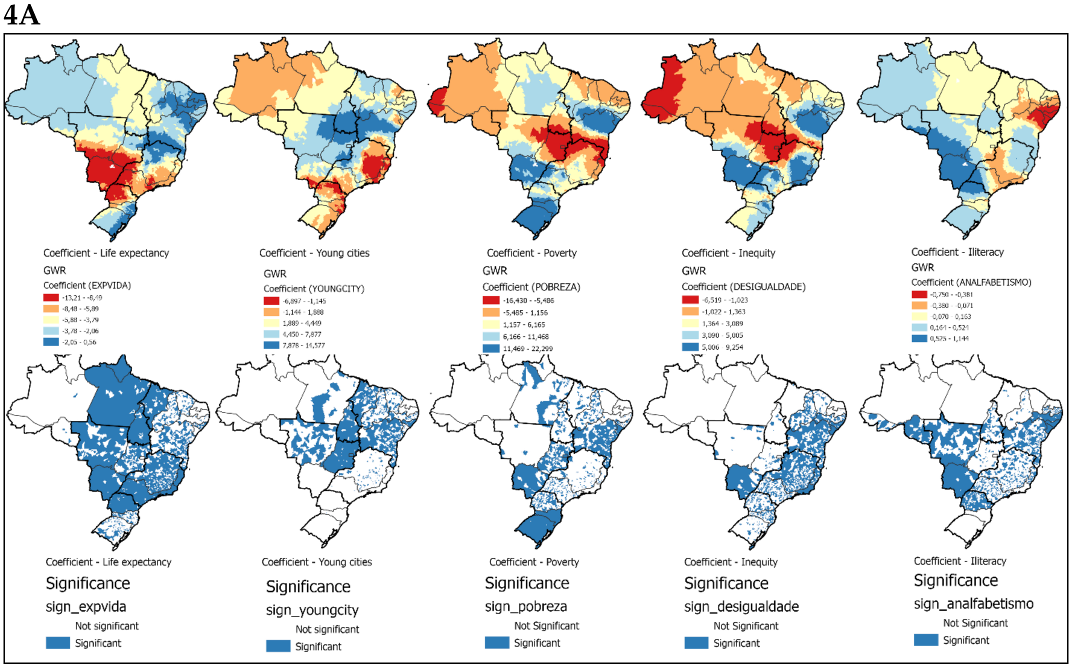
3.4 GWR maps of coefficients and the significance levels

3.4.1 Socioeconomic and sociodemographic components

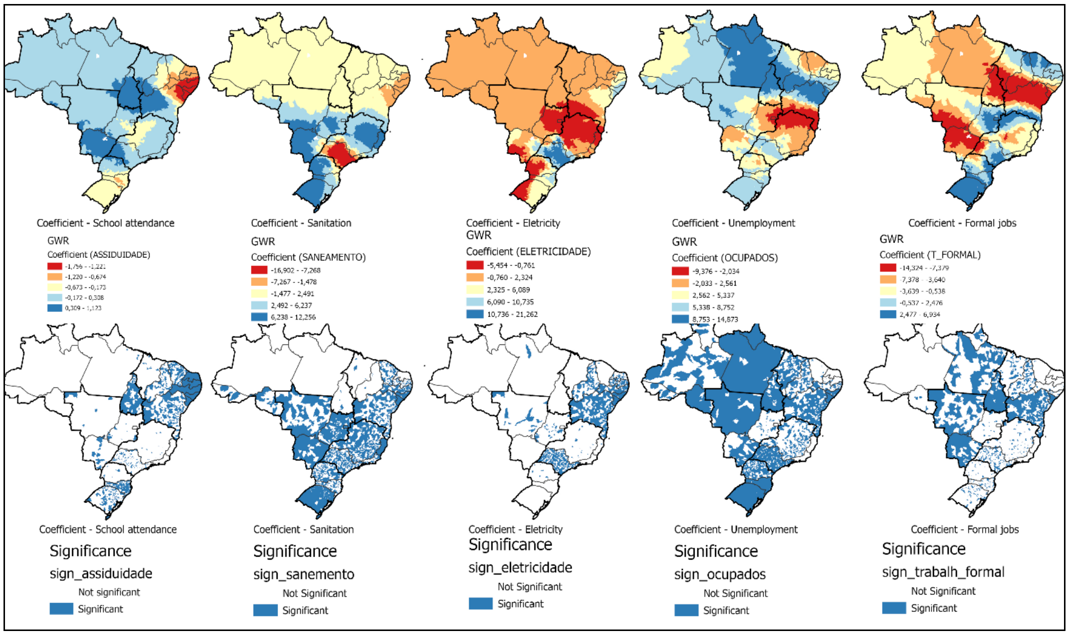
The magnitude of association between the predictor variable and the ACS morality is indicated by the blue/red color scale, by municipality, on the GWR map. The significance map complements this information by indicating areas where this relationship is statistically consistent (see Figure 4).

Figure 4: Coefficients for geographic weighted regression of socioeconomic domains as predictors of ACS mortality in Brazil, 2012-2018.

4A



4B



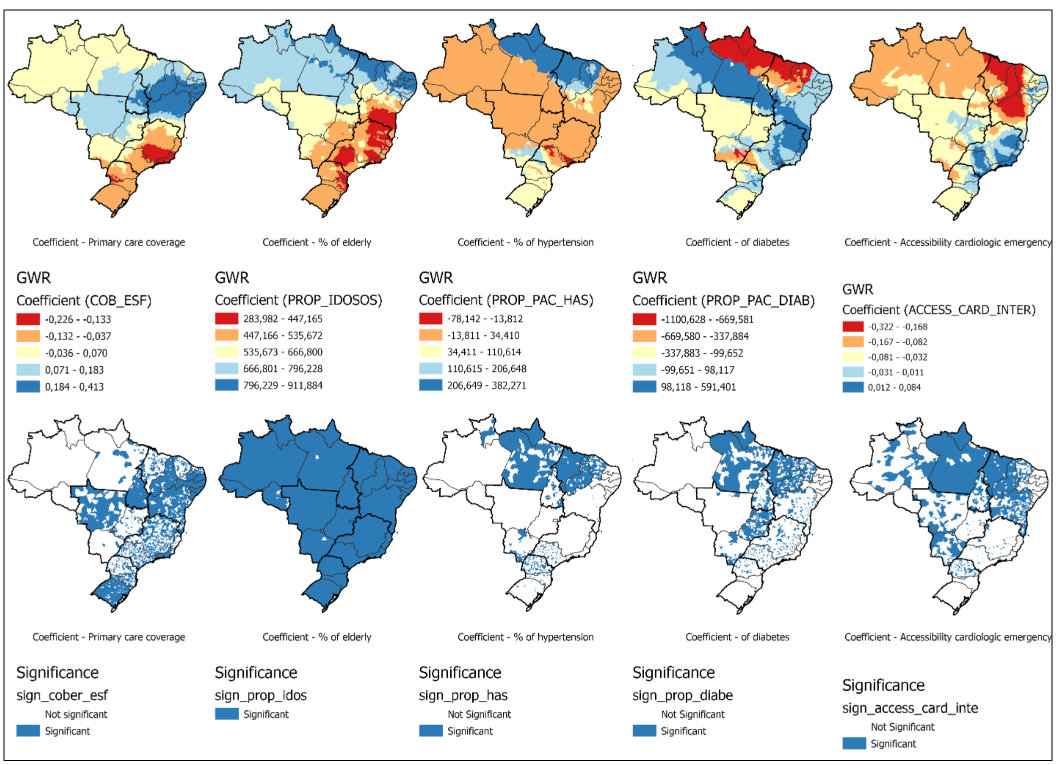
For the indicator variable, life expectancy, this was positively correlated in the coastal areas of the South with increased ACS related mortality in this region. The relationship was inverse in the Center-West, such that low life expectancy was associated with higher ACS deaths.

Increased ACS related deaths were correlated with; high poverty in the South, Center-West and Northeast; with high inequity in the Southeast, Center-West, and North; with young cities in the Center-West and Northeast; with high illiteracy in the Center-West and Northeast; with low illiteracy in the North; with decreased school attendance in the Northeast; with lack of formal jobs in the Center-West and Northeast, and finally with high unemployment in the North, Northeast, and South. Sanitation and Electricity indicators had high heterogeneity both between regions and intra-region.

3.4.2 Cardiovascular risk factors and markers of access-to-care

The map of coefficients for the GWR showed a positive relationship between high primary care coverage in the Northeast and Center-West with respect to ACS mortality. The strongest correlation between risk factors such as proportion of elderly, hypertensives, and diabetics and ACS deaths was in the Northeast and North of the country. Interestingly, the North and Northeast regions also had an inverse relationship for the Accessibility index to ACS mortality outcomes. Lower access to high-complexity care hospitals was associated with more cardiac deaths in these regions (see Figure 5).

Figure 5: Coefficients for geographic weighted regression of cardiovascular risk factors and markers of healthcare access as predictors of ACS mortality in Brazil, 2012-2018.



4. Discussion

This study examined ACS mortality in Brazil and the geographic heterogeneity around the country by analyzing how the different predictors varied in their correlation with cardiac mortality by taking spatial characteristics into account. Instead of using raw variables, and to avoid the issue of multicollinearity in the regression model, we used principal component analysis to derive 5 indicators for social determinants of health with 10 components. Our findings revealed that the social determinants of health rooted in the components identified were correlated with ACS morality in the spatial analysis. An association was seen with life expectancy, young cities, poverty, inequity, illiteracy, school attendance, and lack of formal jobs. Infrastructure markers, such as sanitation and electricity, were not statistically significant by the GWR model. Essentially SDOH were predictors for ACS mortality in regions of Brazil characterized by high-income.

The more affluent regions of Brazil, the South and Southeast, had a higher life expectancy and higher ACS mortality. As these were also the areas with a high accessibility index for complex care, a potential explanation is that the mere presence of these facilities meant more of the population availed themselves of these services. Hence, there was a greater documentation of ACS related morbidity and mortality. The finding of low life expectancy and high ACS mortality, in the Center-West and North (middle and lower-income regions respectively), that also had a scarcity of complex care hospitals (and hence a low accessibility index), there might be many undiagnosed cases of ACS where people die at home or elsewhere. It could also be that a confluence of many other variables not accounted for in our model drive mortality in the Center-West and North.

In the lower income parts of the country, the North and Northeast, the CV risk factors (higher percentage of elderly, hypertensives and diabetics) and a lower accessibility index for high-complexity care was associated with increased death from ACS.

A higher accessibility index for care in the South and Southeast, that were wealthier regions, did not show lower cardiac mortality. This can be due to many reasons. The first is that, there could be a minimum threshold of the number of high-complexity care hospitals needed, to prevent adverse mortality outcomes. At the same time, there might be a maximum threshold, above which the number of facilities with advanced care no longer improve outcomes. This hypothetical, constrained range of positive benefits, depending on the density of hospitals in an area, is unknown. Our study design was not capable of looking at this nuance.

Secondly, the availability of a particular cardiovascular service needs to be complemented by adherence to high performance measures (with respect to treatments) that allow for full utilization of that resource. The BRACE (Brazilian Registry in Acute Coronary SyndromEs) registry, was a cross-sectional, observational, and epidemiological accounting of ACS patients in Brazil[47]. This revealed that performance scores (derived from performance measures assessing adherence to evidence-based therapies) were correlated with in-hospital mortality. Teaching institutions performed better than non-teaching facilities with regards to performance scores. Age, renal disease, and prior history of coronary angioplasty also were associated with increased hospital deaths.

In a separate paper from our group, an examination of the geographic distribution of cardiac stress testing in Brazil showed that increased access to advanced diagnostics did not necessarily translate into a reduction in cardiovascular mortality[25].

Our analysis, in terms of the location of high-complexity care hospitals, showed that they were clustered mostly in economically well-off regions of the country (such as the South and Southeast) or aggregated around metropolitan areas (a trend observed across the entire country). This confirms what has been seen in the literature previously. In a paper, by Lawal et al (2019), healthcare facilities in Nigeria, were seen to be located more often near major urban centers or close to transit routes leading to these places[48].

Geographic attributes such as distance on a map to a particular healthcare facility is probably not the only dimension affecting the geospatial association between access to care and ACS mortality. The zoning characteristics of the neighborhood, ease of transport to a given coordinate, and the amenities and infrastructure adjoining a hospital, also play a role in how tertiary care is accessed. In addition to an accessibility index, there is maybe a role for a 'desirability index' of a location providing advanced high-quality care. A critical part of the equation is also the medical expertise and provision of evidence-based therapies at a hospital, and this was not accounted for in our study design.

Access to care, conceptually, has five elements underlying its construct; accessibility, availability, acceptability, affordability, and appropriateness (or quality)[49]. One can argue that only accessibility and availability have spatial attributes that can be studied with geo-analysis[50]. This is certainly a constraint we found in our study when looking at the results.

4.1 Implications for policy and practice

The demonstration of correlation between socioeconomic domains and CV risk factors, to ACS related deaths across geographically disparate units, helps solidify the evidence-base behind addressing social determinants of health and chronic conditions such as hypertension and diabetes to improve clinical outcomes. In addition, the role of increasing access to care in low resourced areas, as a goal to improve mortality rates, needs to be a policy initiative of great urgency in Brazil.

4.2 Implications for further research

Our work demonstrates the acute need to include geospatial attributes of predictor variables in modeling outcomes of interest. Geographic heterogeneity in our results speaks to the fact that many correlates between variables are influenced by the context of where they are located. More research will clarify the strength of these association when geographic characteristics are a part of the analytical approach.

4.3 Study strengths and limitations

To our knowledge, this is the first examination of ACS related mortality in Brazil with respect to its association with social determinants of health, CV risk factors, and access-to-care markers in the context of the geographic distribution. This is a particular strength of our study.

The national datasets of Brazil are meant to be accurate and detailed repositories of information. However, the quality of data is contingent upon reliable diagnoses of cases and ascribing the of cause of death may not be uniform across the various regions. Furthermore, aggregated data without personal identifiers makes claims of causality between factors and outcomes difficult.

The 2SFCA-based approach in the analysis assumes a steady distance-decay scenario. Variations in the catchment area sizes and non-uniform decay can change the model estimates. However, even with this limitation, the strength of the 2SFCA method is that it can be applied to both rural as well as urban settings.

5. Conclusion

Brazil provides a unique case study in the interplay between social determinants of health as related to cardiac deaths. This is due to the fact that the country has diverse tiers of income-levels based on the geographic regions. We set out to describe the association of socioeconomic factors, CV risk factors and access to care constraints, with respect to ACS mortality, depending on the geographic distribution, by performing a GWR analysis. Our study found that socioeconomic indicators and CV risk factors correlated with mortality, at varying degrees and polarity, with geographic heterogeneity in the spatial analysis. The access to care measure, the accessibility index for high complexity care, clustered in the higher-income parts of the country (the South and Southeast) or around big urban centers. A lower accessibility index was associated with higher ACS mortality in the lower income regions of Brazil.

Our results show that the weighting of a predictor variable for ACS mortality, in a certain geographic location, not only depends on the other coexisting determinants at that spot, but also with the relationship of these factors in neighboring areas. This understanding of socioeconomic indicators and other risk factors means that likely mitigation efforts and solutions, to improve cardiac mortality, will have to be regionally constructed for highest return on investment. Instead of a 'one size fit all' approach, in an economically diverse country such as Brazil, public health approaches will need to be tailored to the regions in question.

Appendix A

Table 4: Principal component analysis of socioeconomic and sociodemographic factors

Indicator	Principal component	Variables
Health	Life expectancy	Life expectancy at birth
		Fertility rate
		Child mortality
		Mortality up to 5 years of age
	Young cities	Dependency ratio
		Probability of survival up to 40 and 60 years
		Aging rate
		% of women aged 10 to 17 who had children
Education	Illiteracy	Expectation of years of study
		Illiteracy rate - 11 to 25 years and over
		% of 6 to 17 years old in basic with delay
		Gross to basic attendance rate
		Crude to fundamental frequency rate
		Gross to high school frequency rate
		Gross pre-school attendance rate
		Crude to superior frequency rate
		% of 0 to 17 years at school
		% aged 15 to 24 years in elementary school
	Schooling attendance	% of 4 to 5 years in elementary school
		% aged 18 to 24 years in high school
		% of 11 to 14 years old in the final years of elementary school or with complete elementary school
		% of children in households where no one has completed elementary school
		% of children aged 4 to 14 out of school
		% of people in households where no one has completed elementary school
		% of people in households vulnerable to poverty and in which no one has complete basic education.
		% of persons aged 18 or over with no complete elementary education and informally employed
		% of people aged 15 to 24 who do not study or work and are vulnerable to poverty.
Occupation	Unemployment	Economically active population 10 years of age and over
		Percentage of employed persons aged 18 or over who are self-employed.
		Percentage of employed persons aged 18 or over who are employers
		Percentage of employed persons in the agricultural sector
		Percentage of employed persons in the trade sector
		Percentage of employed persons in the construction sector
		Percentage of employed persons in the mineral extraction sector
		Percentage of employed persons in the services sector
	Formal work	Percentage of employed persons in the industrial utility sectors
		Percentage of employed persons in the manufacturing industry
		Percentage of employed persons aged 18 or over who are employed with a formal contract
		Percentage of employed persons aged 18 or over who are public sector workers.
		Percentage of employed persons aged 18 or over who are employed without a formal contract
		Theil-L index of earnings from work
		Unemployment rate of the population aged 10 to 29 years old
Economic	Poverty	Gini Index

		Proportion of extremely poor
		Proportion of extremely poor children
		Proportion of poor
		Proportion of vulnerable to poverty
		Percentage of total income appropriated by the 10% of the population with the highest per capita household income
	Inequality	Percentage of income from income from work
		Ratio 10% richer / 40% poorer
		Average per capita income
		Theil Index - L
		Average income of employed persons
Sanitation	Sanitation	% of the population in households with piped water
		% of the population in households with piped bathroom and water
		% of the population in households with garbage collection
		% of the population in households with electricity
	Electricity	% of people in households with inadequate water supply and sanitation
		% of people in households with inadequate walls
		% of people in households without electricity

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